60th ERA Congress, 15-18 June 2023

Congress Abstracts
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B2 - Glomerulonephritis & systemic diseases (AAV, SLE, etc.)

B3 - Epidemiology & outcome

B4 - Prevention, treatment & clinical trials

C1 - Basic sciences & experimental

C2 - Pathophysiology, risk factors & progression

C3 - Epidemiology & outcome

C4 - Co-morbidities (anaemia, cardiovascular, CKD-MBD, etc.)

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D3 - Epidemiology & outcome

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The ten best-ranked Abstracts were invited to prepare a Graphical Abstract.
All Abstracts have been published in their original format.
Background and Aims: Autosomal recessive polycystic kidney disease is caused by mutations in PKHD1 encoding FPC, and is characterized by severe renal cystogenesis in neonates, yet mouse models do not fully recapitulate the human phenotype. Indeed, even the Pkh1d null allele does not cause renal cystogenesis in the mouse. Several cleavage products of FPC are reported yet their function remains unknown. The aim of this study was to determine the function of the FPC cleavage products and their effects on cyst development in ARPKD.

Method: Three Pkh1d mutant mouse lines and the cystic Pkd1V mouse were crossed to produce digenic mice with which to study renal cystogenesis. Biochemical analysis was used to investigate FPC cleavage patterns using a panel of new antibodies. Cell models and electron microscopy revealed underlying mitochondrial defects in Pkh1d Knokout mice.

Results: Pkh1d mutation modifies a Pkd1 uncleavable mutant (Pkd1V), enhancing the cystic phenotype in both the kidney and pancreas. The hypomorphic Pkh1d mutant and Pkh1d KO both enhance the Pkd1V kidney phenotype, making distal tubule cysts more severe and initiating cystgenesis in the proximal tubules. FPC displays differential cleavage to produce fragments of unknown function. New antibodies were generated to interrogate FPC cleavage products. Three small C terminal cleavage fragments were identified which contain a mitochondrial targeting sequence and are recruited to mitochondria. Mitochondrial ultrastructural changes were evident after deletion of Pkh1d including mitochondrial fragmentation and dilated cristae, suggesting disrupted mitochondrial function. Deletion of just the C-terminal fragment of FPC (ΔC'T), the portion that directly corresponds to the portion that cleaves and localises to the mitochondria, is sufficient to enhance the renal cystic phenotype of the PCl cleavage mutant. Unlike the other Pkh1d mutants however, FPC (ΔC'T) does not result in the pancreatic cystogenesis when combined with Pkd1V, suggesting that the FPC C terminus is not required to prevent pancreatic cyst development.

Conclusion: Our results suggest that the C-terminus of FPC plays an important role in preventing renal cystogenesis via a newly discovered mitochondrial specific function. Our work reveal some aspects of FPC's function, in particular a previously unrecognised mitochondria function that is mediated through FPC cleavage products and is essential in the kidney to prevent the enhancement of cystogenesis in the digenic model.
Figure 1: *Pkhd1* mutation effect on *Pkd1* cystic kidney and pancreas. Haematoxylin and eosin (H&E) staining of representative kidney and pancreas sections. (A-F). H&E P0 kidneys, scale bar 500 μm. A) Wt, (B) *Pkhdi*−/−, (C) *Pkhdi*ΔCT/ΔCT, (D) *Pkd1*V/V, (E) *Pkhdi*−/−; *Pkd1*V/V, (F) *Pkhdi*ΔCT/ΔCT; *Pkd1*V/V. (G-L) H&E staining of representative pancreas sections from E17.5 mouse embryos, scale bar 500μm. (G) Wt, (H) *Pkhdi*−/−, (I) *Pkhdi*ΔCT/ΔCT, (J) *Pkd1*V/V, (K) *Pkhdi*−/−; *Pkd1*V/V cystic pancreas, (L) *Pkhdi*ΔCT/ΔCT; *Pkd1*V/V non-cystic pancreas.
EXPRESSION OF THE COLLAGEN IV α345 MOLECULE ALONG THE RENAL TUBULE IN HEALTH AND DISEASE

Lisa Loderbauer¹, Karen Schneider¹, Karl Knap¹, Florian Wopperer¹, Mario Schiffer¹, Kerstin Amann², Katharina Broeker¹, Maike Buettner-Herold² and Michael Wiesener¹

¹University Hospital Erlangen, Department of Nephrology and Hypertension, Erlangen, Germany, ²University Hospital Erlangen, Department of Nephropathology, Germany and ³University of Regensburg, Institute of Physiology, Germany

Background and Aims: Patients suffering from Alport Syndrome (AS) have a high life time risk of kidney failure and hearing loss. The underlying molecular cause is a germline mutation in one of the COL4A3/4/5 genes, whose gene products collectively form an important component of the glomerular basement membrane and the inner ear. Recent genetic studies have shown that the AS is much more prevalent than clinically recognized, suggesting that atypical clinical cases are frequent. Thus, patients with AS may phenocopy other kidney diseases. To date, pathomechanistic studies of the AS have focused on the glomerular membrane, yet equally strong expression of other kidney diseases. Therefore, we postulate that the pathogenesis of AS may in part stem from the (distal) tubular apparatus, which is already known from other diseases such as ADPKD and nephrophthisis.

#3460 DEVELOPMENT OF A NEW CELLULAR MODEL TO EVALUATE THE CLINICAL IMPACT OF PKD1 VARIANTS EXPLOITING CRISPR/CAS9 SYSTEM

Martina Migliorero¹, Donatella Marsalla¹, Claudia Saglia¹,², Valeria Bracciali¹,², Francesca Arruga¹, Antonio Amoroso¹, Tiziana Vaisitti¹ and Silvia Deaglio¹,²

¹University of Turin, Department of Medical Sciences, Torino, Italy and ²Città della Salute e della Scienza University Hospital, Immunogenetics and Transplant Biology Service, Italy

Background and Aims: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common single-gene disorder and the most frequent progressive kidney disease, which ultimately leads to kidney failure and renal replacement therapy. Almost 80% of cases of ADPKD are attributed to germline mutations in PKD1, even though at least one second somatic event such as the inactivation of the remaining wild-type PKD1 allele is required for the disease's manifestation. A significant portion of all variants identified in PKD1 is classified as “variant of unknown significance” (VUS) and understanding their functional impact may be of diagnostic importance for patients and their families. So, a proper experimental model to study the functional impact of different genetic lesions is needed to readily confirm their pathogenicity.

Method: The HEK293T cell line was modified to express an inducible Cas9 and afterwards transfected with a sgRNA targeting exon 15 of PKD1 to generate clones carrying homozygous or heterozygous nonsense variants, validated by Sanger sequencing. Transcript level and protein expression were evaluated, and then functional read-outs were set-up to validate the model. Heterozygous clones were used to introduce a second PKD1 variant, c.11614G>A (p.Glu3872Lys) in exon 42, using a modified CRISPR system called base editors, able to operate single-base substitutions (Figure 1A).

Results: Heterozygous (+/−) and homozygous (−/−) exon 15 PKD1 clones were generated. These cells showed a slight decrement in PKD1 mRNA levels, and PC1 protein loss was confirmed in full knock-out clones. Functionally, immunofluorescence staining highlighted a different cytoskeletal rearrangement in cells lacking PC1, which did not present actin protrusions characterized by increased viability, resistance to cell death and a disrupted autophagic pathway, as demonstrated by LC3BI-I-I conversion, which in PKD1−/− cells is diminished. Validation of the model is also supported by RNA sequencing data indicating that double knock-out cell lines display an upregulation of genes involved in proliferative pathways and epithelial-mesenchymal transition, as well as a down-regulation of genes involved in cytoskeletal organization.

We then used the heterozygous exon 15 clones to introduce a specific variant in exon 42, classified as C4 according to ACGM criteria. To do so, PKD1+/− and PKD1−/− cell lines were transfected with a sgRNA guide that correctly positioned the Cas9 NHEJ. Using this approach we could generate a double knock-out cell line on exon 42 and a “double hit” cell line carrying a heterozygous variant on exon 15 and an homozygous one on exon 42, which represents a more likely real-life situation. Functional assessment of the variant's pathogenicity and comparison with exon 42 double knock-outs is currently ongoing.

Conclusion: In conclusion, we generated a new PKD cellular model that can be easily exploited to reproduce some of the VUS variants identified, by clinical exome sequencing, in our cohort of ADPKD patients. Results obtained provide a proof-of-principle of the feasibility of this approach and allowed to identify selective read-outs (Figure 1B) to be used for a rapid screening to assess the phenotypic impact of specific PKD1 variants.
Background and Aims: Primary Distal Renal Tubular Acidosis (dRTA) is a rare genetic condition characterized by impaired capacity of A-type intercalated cells to excrete excess of H⁺ ions. The disease is caused primarily by pathogenic variants in the SLC4A1 gene encoding for the basolateral anion exchanger 1 (AE1) or the ATP6V1B1 and ATP6V0A4 genes encoding for two subunits of the apical proton ATPase. The latter also cause variable degrees of sensorineural hearing loss (SNHL). Additional genes include WDR72 that is associated with amelogenesis imperfecta and FOXI1 that also causes SNHL. To understand better the impact of alkali treatment on the natural history of dRTA, a European prospective registry has been created in collaboration with the ERKNet European Reference Network.

Method: We present a first interim descriptive analysis of first 182 patients that have been collected from 2019 to 2022. Treatment data are under analysis and are not included.

Results: To date, mostly paediatric patients (79%) have been included in the registry. A genetic diagnosis was available in 111/182 (61%) of patients and showed the following distribution of underlying genes: ATP6V0A4: 45%, ATP6V1B1: 41%, SLC4A1: 14%. Variants in WDR72 and FOXI1 were reported in one patient each. Overall, we observed no major differences in blood pressure and in urinary/blood parameters, when comparing children vs adults or proton ATPase vs AE1 defects (partially shown in tables 1 and 2). Adult patients were on average diagnosed later, had more frequently nephrolithiasis and higher BMI. In part, differences may reflect selection biases that will be assessed with the collection of longitudinal data. As expected, patients with proton pump defects were diagnosed earlier and had more frequently SNHL. The degree of nephrocalcinosis and the estimated glomerular filtration rates were similar when comparing all groups. None of the patients had developed end stage kidney disease.

Conclusion: This first report demonstrates successful enrolment of a cohort of patients with dRTA. Enrolment is still ongoing. Longitudinal data will allow assessing the impact of alkali therapy on the long-term outcome.
Table 1: Selected parameters comparing children vs adults.

<table>
<thead>
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<th>Unit</th>
<th>Children</th>
<th>Adults</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>N 144(79%)</td>
<td>38(21%)</td>
<td></td>
</tr>
<tr>
<td>Age years</td>
<td>10.0 [5.1–13.9]</td>
<td>24.9 [21.2–33.9]</td>
<td>N/A</td>
</tr>
<tr>
<td>Age at first symptoms</td>
<td>0.2 [0.1–0.4]</td>
<td>2.1 [0.9–4.8]</td>
<td>0.015</td>
</tr>
<tr>
<td>BMI Kg/m²</td>
<td>18.3 ± 4.1</td>
<td>24.7 ± 4.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>eGFR ml/min per 1.73 m²</td>
<td>103 ± 29</td>
<td>96 ± 32</td>
<td>0.29</td>
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<tr>
<td>Chronic kidney disease</td>
<td>Stage CKD 2-4</td>
<td>15/38 (40%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Serum bicarbonate mmol/l</td>
<td>22.0 ± 3.5</td>
<td>22.4 ± 4.4</td>
<td>0.68</td>
</tr>
<tr>
<td>Serum potassium mEq/l</td>
<td>3.9 ± 0.6</td>
<td>3.7 ± 0.6</td>
<td>0.23</td>
</tr>
<tr>
<td>Urine pH pH</td>
<td>7.5 ± 0.8</td>
<td>6.9 ± 0.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>Grade 0-3</td>
<td>19/144 (13%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nephrocalcinosis</td>
<td>Present</td>
<td>2.3 ± 2.0</td>
<td>2.0 ± 2.0</td>
</tr>
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Table 2: Selected parameters comparing gene defects.

<table>
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<tr>
<th>Unit</th>
<th>ATP6V1B1/ or ATP6V0A4</th>
<th>SLC4A1</th>
<th>p</th>
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<tr>
<td>Total number</td>
<td>N 96</td>
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<tr>
<td>Age years</td>
<td>10.9 [5.8–16.1]</td>
<td>12.5 [8.8–15.0]</td>
<td>0.28</td>
</tr>
<tr>
<td>Age at first symptoms</td>
<td>0.2 [0.1–0.3]</td>
<td>1.1 [0.1–2.6]</td>
<td>&lt; 0.001</td>
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<tr>
<td>BMI Kg/m²</td>
<td>20.0 ± 5.3</td>
<td>18.3 ± 3.2</td>
<td>0.22</td>
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<tr>
<td>eGFR ml/min per 1.73 m²</td>
<td>109 ± 13.9</td>
<td>101 ± 39</td>
<td>0.36</td>
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<td>Chronic kidney disease</td>
<td>Stage CKD 2-4</td>
<td>7/15 (47%)</td>
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<td>0.47</td>
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<td>Serum potassium mEq/l</td>
<td>3.8 ± 0.5</td>
<td>4.0 ± 0.4</td>
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<tr>
<td>Urine pH pH</td>
<td>7.7 ± 0.7</td>
<td>7.7 ± 0.8</td>
<td>0.93</td>
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<tr>
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<td>Grade 0-3</td>
<td>2.3 ± 1.9</td>
<td>2.0 ± 2.2</td>
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<tr>
<td>Nephrolithiasis</td>
<td>Present</td>
<td>5/96 (5%)</td>
<td>0/15 (0%)</td>
</tr>
<tr>
<td>SNHL</td>
<td>N 54/96(56%)</td>
<td>2/15 (13%)</td>
<td>&lt;0.001</td>
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#2684

DIAGNOSTIC YIELD OF A TARGETED GENE PANEL FOR MONOGENIC KIDNEY DISEASES: A EUROPEAN STUDY

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Background and Aims: Despite advances in understanding the underlying causes of CKD, 20% of cases remain unexplained (1). A genomic approach has the potential to identify the cause of CKD in a significant portion of pediatric and adult patients, with estimated diagnostic rates of 5-30% (2). However, there is a lack of consensus in the scientific community on the best diagnostic algorithm. The DECIDE project (Diagnostic Efficacy Kidney Disease European) is a European collaboration that aims to address this issue by evaluating the diagnostic rate of a targeted gene panel in a large cohort of patients.

Method: DECIDE involved three Italian and two Spanish centers, encompassing both pediatric and adult patients. The study used the Nephropathies Solution Panel (NES, SOPHIA Genetics), which covers 44 kidney-related genes, to test patients with a high suspicion of genetic kidney disease. The clinical presentation was classified into cystic disease, glomerulopathy, CAKUT, tubulopathy, nephrocalcinosis, other, and negative phenotype. The diagnostic yield of the NES panel was calculated. To assess the genotype-phenotype relationship, Kaplan-Meier analyses were performed. Additionally, the diagnostic results obtained from alternative technologies, such as larger panels, WES and hybridization arrays, in cases of NES panel negative results, were also collected.

Results: As far as now the DECIDE project collected 632 genetic data. To evaluate the diagnostic accuracy of the panel, the number of (likely) pathogenic variants correlated to phenotype was analyzed. The diagnostic yield is shown in Figure 1, with 46% for cystic disease, 41% for glomerulopathy, 33% for tubulopathies, 28% for CAKUT, 14% for nephrocalcinosis, 2% for Nephronophthisis.

Conclusion: New approaches are necessary to uncover the hidden genetic components of rare renal conditions.

REFERENCES


Table 1: Pathogenic and likely pathogenic variants in our cohort.

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</table>

Figure 1: Diagnostic yield of NES panel for each clinical presentation.

#2640
SINGLE TUBULE RNASEQ FROM GITLEMAN SYNDROME MICE REVEALING MAGNESIUM HANDLING IN DISTAL RENAL TUBULES
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1Division of Nephrology, Department of Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O. C. and 2Department of Pediatrics, National Defense Medical Center, Taipei, Taiwan

Background and Aims: Gitelman syndrome (GS) is characterized by salt-losing hypotension, hypokalemic metabolic alkalosis, hypomagnesemia, and hypocalciuria caused by a specific mutation in the thiazide-sensitive sodium chloride co-transporter (NCC) gene SLC12A3. However, magnesium (Mg2+) associated gene in the distal renal tubules remains unclear.

Method: We performed small samples RNA-seq from manual microdissection of distal convoluted tubules (DCT1s) in nonsense Ncc Ser707X (S707X) homozygous knockin mice (NccS707X/S707X mice) (n = 4) and wild-type (WT, n = 4). Cortical thick ascending limbs of Henle (cTALs), connecting tubule (CNT), cortical collecting duct (CCD) were also microdissected.

Results: Among DCT makers, Slc12a3 (NCC) and Psalb- (Parabumin) were significantly downregulated (Log2TPMWT/WT: −4.45, P = 0.0003; −6.888258295, P = 0.0003, respectively). Mg2+ transporters of Trpm6 gene expression were significantly downregulated. In addition, Egf and Cnnm2 have
been reported to increase TRPM6 trafficking or activity, were also decreased in DCT segment. Rack1 was also decreased in DCT1. Claudins including Cldn10, Cldn16, and Cldn19, involving paracellularly reabsorption of Ca\(^{2+}\) and Mg\(^{2+}\), were not changed in cTALs. All findings indicate chronic hypokalemia may mediate DCT1 remodeling and affect development. 

Conclusion: Our small samples RNA-Seq from dissected DCT highlight the possible molecular pathway of hypomagnesemia in GS. Chronic hypokalemia caused by inactivation of Slc12A3 gene may affect the DCT development causing loss of Mg\(^{2+}\) associated transporters.

### #3067

**Alport Syndrome Natural History from the Radar Registry: Associations with Gene, Variant Type and Sex**

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**Background and Aims:** Alport Syndrome (AS) is caused by pathogenic variants in COL4A3, COL4A4 & COL4A5 genes. The clinical course of AS can be highly variable, depending on gene affected, mutation type and Male (M) or Female (F) sex. Proteinuria is associated with worse prognosis. Previous genotype-phenotype correlation studies have shown protein length altering variants are associated with a more severe phenotype in males with COL4A5 variants, however studies in females have shown contradicting results. This study aims to describe demographics and investigate renal outcomes associated with pathogenic variant type in M vs F AS patients, using longitudinal data from the National Registry of Rare Kidney Diseases (RaDaR) which recruits patients at 108 UK renal clinics.

**Method:** RaDaR is linked to Regional Genetics hubs for clinical genetic reports, renal IT systems for routine test results and the UK Renal Registry for Renal Replacement Therapy (RRT) initiation data. eGFR was calculated using CKD-EPI Cr equation (2021) or Schwartz equation for those \(\leq 16\) yrs. eGFR slope was calculated over the last 3 years (or 3 years prior to End Stage Kidney Disease (ESKD)/death for patients who reached those outcomes), with patients required to have a minimum of 4 values over 2 years. For genotype data, variants classified in clinically issued reports as “Pathogenic” or “Likely Pathogenic” were included and classed as: 1. Protein Length Altering and 2. Missense variants. Where both protein length altering and missense variants in the same gene were identified in an individual, the missense variant was used. Data are presented as percentages for categorical variables and mean ± SD for continuous variables. Kaplan Meier analysis and the log rank statistic were used to compare age at RRT start, stratified by gender and variant types. Lower quartile (LQ) (25%) estimates are presented where too few events have occurred to calculate a median (50%) estimate.

**Results:** Between Jan 2013–Jul 2022, 920 AS patients were recruited; 53% M vs. 47% F. Genetic test reports were available for 343/920 (37%) patients. 294/343 (86%) reported a pathogenic or likely pathogenic variant, 140 protein length altering and 154 missense. Individuals with 2x COL4A3/COL4A4 variants were youngest at RRT start, whilst females with COL4A5 variants were oldest (LQ 20.1 vs 60.9 yrs, log-rank p < 0.0001) (Figure 1a). COL4A5 variants were younger at RRT start vs. those with missense variants (median age 30.2 vs 52.1 yrs, \(p = 0.01\)). Conversely 0/36 females with protein length altering COL4A5 variants had started RRT, compared with 6/37 with missense variants (\(p = 0.01\)) (Figure 1b-i). COLA3 or COLA4A4 variants Whilst females with homozygous protein length altering COL4A3/4 variants were younger at RRT start vs. those with missense variants (LQ 47.1 vs 64.9 yrs, \(p = 0.05\)), age at RRT start did not differ by mutation type for males with COLA3/4 heterozygous variants (Figure 1b ii-iv). However, males with homozygous or 2x protein length altering COLA3/4 variants were younger at RRT start than those with missense variants (median age 20.1 vs 24.3 yrs, \(p = 0.05\)), whilst no difference was observed by variant type for females with 2x COLA3/4 variants (Figure 1b v-vi). Proteinuria and eGFR slope were generally correlated with age at ESKD.

**Conclusion:** The observed effect of pathogenic variant type on renal outcomes varied by gene affected, number of mutations and sex. The relatively reduced severity among females harbouring a protein length altering COLA3/4 variant may represent an effect of skewed X-inactivation or a missense gain-of-function mechanism. RaDaR recruits patients with a clinical diagnosis of Alport syndrome or Thin Basement Membrane Nephropathy; ascertainment of individuals with a single COLA3 or COLA4A4 variant is therefore likely to favour those with more severe kidney disease. Linkage of the RaDaR AS cohort with genetic report data is ongoing; further correlations may be observed with larger numbers.
Figure 1: Kaplan Meier Survival Analyses of Age at ESKD stratified by (a) gene (b) variant type.
RAPIDLY PROGRESSIVE AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: RISK FACTORS FOR DISEASE SEVERITY DURING CHILDHOOD AND EARLY ADULTHOOD

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Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic kidney disease and is characterized by genetic complexity and phenotypic variability. The age of reaching kidney failure (KF) is variable and covers the complete age-spectrum. There is an unmet need for early biomarkers to differentiate between rapid and slow progressors. The PROPKD score identified hypertension before the age of 35 years as a risk factor for rapid kidney function decline. We aim to identify earlier risk factors for rapid disease progression by studying a population of ADPKD patients who reached kidney failure (KF) before the age of 40y.

Method: This multicentric retrospective study focuses on a unique population (n = 200) of ADPKD patients who reached KF before 40y. Kidney failure (KF) was defined as CKD5 or start of Kidney Replacement Therapy (KRT), whichever came first. Longitudinal data on childhood history, comorbidities and kidney function were collected. Life table and Proportional Hazards analysis were used to assess associations between clinical parameters and time to KF.

Results: Median age of ADPKD diagnosis was 22.3 (16.5 – 28.6) and median age of KF onset was 36.2 years (32.9-38.7 years). Forty-seven patients were genotyped (23.5%) of which 38 patients (81.0%) were PKD1T and 8 (17.0%) were PKD1NT and only 1 patient (2.1%) was PKD2. Median age at first urological event was 27.0 (20.7 – 32.0) years. 71 patients (35.5%) had history of UTI’s, 67 patients (33.0%) had hemorrhagic cysts on abdominal imaging, 66 patients (33.0%) presented with gross hematuria and 40 patients (25.0%) presented with kidney stones. There was a high prevalence of hypertension (N = 128, 64.0%). Four patients (N = 4/128, 3.1%) had a very early diagnosis of hypertension before the age of 10 years. Hypertension-onset before the age of 18 years correlated with a significantly faster progression (UV HR: 2.07 (1.32 – 3.25)).

Conclusion: This study describes a unique cohort of ADPKD patients with rapid disease progression. Hypertension at young age (<18) correlated with rapid disease progression, suggesting that ambulatory blood pressure in children might be useful to identify patients at risk for rapidly progressive ADPKD.

Figure 1: Survival analysis with endpoint defined as age of KF between patients with ADPKD and hypertension onset before or after 18 years old.
LONG-READ SEQUENCING IDENTIFIES NOVEL PATHOGENIC INTRONIC VARIANTS IN GITELMAN SYNDROME

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1Radboudumc, Physiology, Nijmegen, Netherlands. 2APHP, Paris, France and 3University of Münster, Pediatric Nephrology, Münster, Germany

Background and Aims: Gitelman syndrome is a salt-losing tubulopathy characterized by hypokalemic alkalosis and hypomagnesemia. It is caused by homozygous recessive or compound heterozygous pathogenic variants in SLC12A3, which encodes the Na+−Cl− cotransporter (NCC). In up to 10% of patients with Gitelman syndrome, current genetic techniques detect only one specific pathogenic variant. This study aimed to identify a second pathogenic variant in introns, splice sites, or promoters to increase the diagnostic yield.

Method: Long-read sequencing of SLC12A3 was performed in 67 DNA samples from individuals with suspected Gitelman syndrome in whom a single likely pathogenic or pathogenic variant was previously detected. In addition, we sequenced DNA samples from 28 individuals with one variant of uncertain significance or no candidate variant. Midigene splice assays assessed the pathogenicity of novel intronic variants.

Results: A second likely pathogenic/pathogenic variant was identified in 45 (67%) patients. Those with two likely pathogenic/pathogenic variants had a more severe electrolyte phenotype than other patients. Of the 45 patients, 16 had intronic variants outside of canonical splice sites (nine variants, mostly deep intronic, six novel), whereas 29 patients had an exonic variant or canonical splice site variant. Midigene splice assays of the previously known variant in introns, splice sites, or promoter explained aberrant splicing patterns.

Conclusion: Intronic pathogenic variants explain an important part of the missing heritability in Gitelman syndrome. Long-read sequencing should be considered in diagnostic workflows for Gitelman syndrome, especially in patients with one pathogenic variant.

SYSTEMIC OXALOSIS: AN OVERVIEW OF THE FINDINGS AND PREVALENCE IN PRIMARY HYPEROXALURIA

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Emma children’s hospital, Amsterdam UMC, Department of pediatric nephrology, Amsterdam, Netherlands

Background and Aims: Systemic oxalosis is a severe co-morbidity that may arise in patients with primary hyperoxaluria type 1 (PH1). It is caused by precipitation of calcium oxalate crystals in organs besides the kidneys, as a result of high endogenous oxalate production. In this study, we aimed to provide an overview of the prevalence, features, screening modalities and factors that play a role in developing systemic oxalosis as cohort studies are currently lacking.

Method: A retrospective registry study was conducted using data from the OxalEurope registry, one of the largest registries of patients with PH1. All patients with primary hyperoxaluria and data on systemic oxalosis were identified. Data was analyzed using descriptive statistics, Chi-square tests, Mann-Whitney U tests and Kaplan Meier analyses.

Results: A total of 159 out of 291 (55%) screened PH1 patients were diagnosed with systemic oxalosis. In addition, 110 patients were recorded having no signs of systemic oxalosis at follow-up, however screening was not performed. Sixty-two patients had already developed systemic oxalosis at diagnosis and systemic oxalosis was most often found in patients with ESKD (95%). The eyes, bones and heart are most frequently affected, nevertheless deposits occurred in many organs, as shown by obduction. Fundus photography (n = 16), X-ray (n = 43), and echocardiography (n = 59) are the modalities used most often to screen respectively the eyes, bones and heart. Patients who developed systemic oxalosis had significantly higher upper plasma oxalate levels (median 22 versus 175 umol/L, p<0.001). Furthermore, patients with systemic oxalosis had a significant higher mortality rate compared to patients without systemic oxalosis (48 out of 142 versus 10 out of 212, p<0.001), which difference persisted after correcting for ESKD (p<0.001). Kaplan Meier analysis (Figure 1) showed that pediatric patients with ESKD tended to developed systemic oxalosis more frequently than adults (p<0.001).

Conclusion: This is the first research to systematically study and report systemic oxalosis in patients with primary hyperoxaluria type 1. Systemic oxalosis is prevalent among PH1 patients, especially when ESKD is present, and may lead to significant morbidity and mortality. Patients with systemic oxalosis have a higher mortality rate and pediatric patients may develop systemic oxalosis more frequently than adults. Given the high incidence and possible implications, we would like to make an appeal on screening all patients with systemic oxalosis. Future research should focus on reliable screening modalities for early signs of systemic oxalosis.

Figure 1: Kaplan Meier analysis of systemic-oxalosis free survival in patients with primary hyperoxaluria, stratified by age at onset of end-stage kidney disease (ESKD). Log-rank analysis showed patients with ESKD before the age of one year had a significant lower systemic-oxalosis free survival (p<0.001), meaning these patients developed systemic oxalosis more frequently and earlier in the disease course.
Background and Aims: Cystinosis is a rare multisystem lysosomal storage disease due to variants in the CTNS gene, coding for the carrier protein cystinosin, a lysosomal membrane transporter causing cystine accumulation with a reported incidence of 1/180,000 live births. Specific treatment by cysteamine decreases renal and extrarenal complications frequency and increases life expectancy. Recently, new treatments for cystinosis entered into the European market with an extended-release formulation of cysteamine and a new formulation of eye drops. The aim of this project is to describe the natural history of the disease and long-term clinical manifestations.

Method: We set up a European, multi-centre, longitudinal, non-interventional cohort, ECYSCO, that uses observational study methods to collect uniform data. 243 patients with a confirmed diagnosis of cystinosis and followed in 25 French and 5 European centers (Belgium, Italy, Spain and Germany) were included. Data are collected on the secure RaDiCo platform, via an e-CRF (REDCap).

Results: Data from 180 patients (50.0% male) were analyzed. Median age at diagnosis was 1.3 years [IQ 0.8; 1.9], with earlier diagnosis since the 1980s, but no further improvement in the 2000s. Genetic analysis was available for 174 patients: 57 (32.8%) presented with homozygous 57kb deletion in the CTNS gene, 71 (40.8%) with heterozygous 57kb deletion associated with another variant and 46 (26.4%) with other variants. The type of variant had no impact on the age at diagnosis. Median age at cysteamine start was 1.6 years [IQ 1.0–3.0]. An improvement on age at treatment start was observed after the 1990s. All but 6 patients were treated with cysteamine. 71 patients received immediate release formulation (Cystagon®) and 103 received extended release formulation (Procybi®). Median white blood cell cystine level was correct at 1.2 nmol ½ cystine/mg protein [IQ 0.59; 2.20]. The median duration of treatment was 21.5 years [IQ 11.7; 31.1]. 167 (95.9%) patients also received cysteamine ocular gel, Cystadrops®. Median age at inclusion was 19.08 years [IQ 10.43; 31.41]. At that time, 104 patients (57.8%) had reached end-stage renal disease (ESRD). At the time of ESRD, 71 patients received immediate release formulation (Cystagon®) and 103 received extended release formulation (Procybi®). Median white blood cell cystine level was correct at 1.2 nmol ½ cystine/mg protein [IQ 0.59; 2.20].

Conclusion: Cystinosis is a good example of a pediatric disease with multiorgan involvement extending into adult care. More than half of patients are adults and have reached ESRD even if age at renal replacement therapy start has increased. The high frequency of extra-renal manifestations demonstrates the importance of a multidisciplinary follow up of these patients.
and serve as autoantigens against ANCA in a vicious cycle. Although the role of NETs in AAV has been revealed, its treatment for targeting NETs remains established. Since nuclear factor-erythroid 2-related factor 2 (Nrf2) regulates antioxidant proteins against oxidative stress and functions as a defense system, we investigated the role of Nrf2 in the development of AAV.

**Method:** In vitro, human neutrophils treated with the Nrf2 activator bardoxolone methyl (Bard) were stimulated with ANCA, and the effects on NETs formation and signaling pathways including intracellular ROS were evaluated by cell imaging and biochemical approaches. The effects of Nrf2 activators on NETs-induced cytotoxicity were examined using human renal glomerular endothelial cells (HRGECs). Nrf2 knockout or WT mouse-derived neutrophils were stimulated with anti-MPO antibody to induce NETs. In vivo studies, Bard was administered to ANCA-transfer AAV model or spontaneous AAV developing mice models (SCG/Kj). Renal function was assessed by biochemical analysis, and the expression of ROS and antioxidant protein NAD(P)H Quinone Dehydrogenase 1 (NQO1) in tissues was evaluated by fluorescent immunostaining and immunoblotting. The formation of NETs in the glomeruli was evaluated by immunostaining and glomerular vascular endothelial damage was assessed by the expression of CD31 and TUNEL positivity. To assess the role of Nrf2 in immunological abnormalities during AAV, murine splenocytes were collected and flow cytometry were conducted using CD4, CD8, B220, MCHCII, CD11c, F4/80, Ly6G, Ly6b, and CD11b antibodies. Moreover, to assess the genetic role of Nrf2 in AAV, we established SCG/Kj mice carrying a germ-line deletion of the Nrf2 genes. A spontaneous mouse model of vasculitis genetically deficient in Nrf2 was analyzed by the same parameters to evaluate the effect of Nrf2. N1 offspring mice were generated by crossing Nrf2/-/- mice with SCG/Kj mice. These backcrossed mice were obtained by crossing Nrf2/-/- mice to background SCG/Kj mice for three generations. The experimental group was mated to N4 heterozygous mice, and female mice in the experimental group were analyzed at 18 weeks.

**Results:** In vitro, pharmacological activation of Nrf2 suppressed ANCA-induced NETs via the upregulation of NQO1 and inhibition of ROS. While Nrf2-deficient neutrophils showed the massive NETs in response to ANCA, compared to WT neutrophils. Furthermore, Nrf2 activation directly protected endothelium from cellular injury caused by the exposure of ANCA-mediated NETs. In vivo, the pharmacological activation of Nrf2 ameliorated glomerulonephritis in two kinds of AAV models through the upregulation of antioxidant and inhibition of ROS-mediated NETs. In contrast, Nrf2 genetic deficiency exacerbated vasculitis in spontaneous AAV model. The activation of Nrf2 regulated the expansion of splenocytes in AAV mice. In particular, pan-T cells in spleen and the infiltration of Th17 cells in kidney were suppressed by Nrf2 activation. **Conclusion:** During ANCA-stimulation in neutrophils, the activation of Nrf2 initiates antioxidant system and inhibits intracellular ROS, leading to the suppression of NETs formation. Nrf2 may be a novel therapeutic target for AAV.

**B2 - GLOMERULONEPHRITIS & SYSTEMIC DISEASES (AAV, SLE, ETC.)

#3280

**B-CELL RECOVERY IN A RANDOMIZED CONTROLLED TRIAL OF B-CELL DEPLETION WITH OBITUNZUMAB FOR THE TREATMENT OF PROLIFERATIVE LUPUS NEPHRITIS (NOBILITY)**


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**Background and Aims:** B cells are central to the pathogenesis of systemic lupus erythematosus and lupus nephritis (LN). Obinutuzumab, a humanized type II anti-CD20 monoclonal antibody, induces more potent B-cell depletion than rituximab. Patients with LN who received obinutuzumab with standard-of-care (mycophenolate mofetil [MMF]) immunosuppression (Phase II NOBILITY trial; NCT02550652) showed improved clinical responses through Week 104 compared with those who received MMF alone. Further analysis could provide insights into the possible association between B-cell depletion duration and duration of renal response.

**Method:** A total of 125 patients with active Class III/IV LN receiving MMF and corticosteroids were randomized and received either obinutuzumab 1000 mg (n = 63) or placebo (n = 62) on Day 1 and Weeks 2, 24, and 26, and followed through Week 104 or to B-cell recovery, whichever was longer. B cells were measured using both a T and B natural killer cell (TBNK) assay with a lower limit of quantification (LLoQ) of 0 CD19+ cells/μL and a high-sensitivity minimal residual cell-1.1 (MRB1.1) assay with an LLoQ of 0.4 cells/μL. Peripheral B-cell depletion was defined as ≥ 0.4 cells/μL. Peripheral B-cell recovery was defined as ≥ 20 cells/μL or the patient's predose baseline, whichever was lower. Time to peripheral B-cell recovery after the last dose of obinutuzumab (Week 26 in 57 of 63 patients), the relationship of time to recovery to efficacy at Week 104 and safety throughout the main study and follow-up period were evaluated (severe adverse event [SAE] and infectious SAE rates, adjusted for patient-years [PY] at risk).

**Results:** Of 63 patients who received obinutuzumab, 4 did not achieve full B-cell depletion during the study. By Week 24, 59 patients (93.7%) achieved B-cell depletion (before obinutuzumab redosing) of those, 4 discontinued prior to B-cell recovery, and 4 completed the study at or after Week 104 but before achieving B-cell recovery. The remaining 51 patients constitute the population for this analysis. Based on the distribution of time to B-cell recovery, 93 weeks passed after their last dose of obinutuzumab infusion was used to group patients (Figure 1). Of the 51 patients, 3 (5.9%) recovered B cells before redosing at Week 26; 1 of the 3 achieved CRR at Week 104. A total of 37 patients (72.5%) attained B-cell recovery within 93 weeks of their last dose of obinutuzumab (median time to B-cell recovery, 78.1 weeks), 18 of 37 (48.6%) and 23 of 37 (62.2%) achieved CRR and overall renal response (ORR) at Week 104, respectively. In these 37 patients, SAE and infectious SAE rates per 100 PY were 13 and 8, respectively. In 11 patients (21.6%), > 93 weeks passed after their last dose to achieve B-cell recovery. Nine of 11 patients achieved B-cell recovery with a median time of 102 weeks, and 2 of 11 had not yet achieved B-cell recovery at the time of writing. Five of 11 patients (45.5%) achieved CRR, and 8/11 (72.7%) achieved ORR at Week 104. In these 11 patients, SAE and infectious SAE rates per 100 PY were 10 and 0, respectively.

**Conclusion:** Most patients in NOBILITY recovered peripheral B cells within 80 weeks after the last obinutuzumab dose. In 5.9% of patients, recovery occurred very rapidly, even before redosing at 26 weeks, whereas in ~20%, recovery occurred ≥ 2 years (102 weeks) after the last dose. B-cell depletion was similar among patients who recovered B cells within 2 years of their final obinutuzumab infusion, those who recovered later and those who are still depleted, suggesting a greater mechanistic effect of early sustained depletion vs duration of depletion. Within the limitation of small sample size, the SAE and infectious SAE rates appear to be similar regardless of duration of B-cell depletion.
REFERENCES


#5127

COMBINED ACTIVITY AND CHRONICITY SCORE FOR PROGNOSTIC ASSESSMENT IN ANCA-ASSOCIATED VASCULITIS WITH GLOMERULONEPHRITIS

Marta Casal Moura¹, Fernando Custodio Fervenza², Kenneth Warrington³, Ulrich Specks¹ and Sanjeev Sethi¹
Background and Aims: Previous studies have shown that chronic changes on kidney biopsy are useful for stratifying the risk of kidney failure in patients with AAV-GN. We aimed to evaluate the impact of inflammatory activity for the prediction of renal outcomes.

Method: A retrospective cohort study of MPO- or PR3-ANCA positive patients with AAV and active renal disease. Inflammatory activity was assessed by the Activity Index (AI): a ratio between the number of crescents and/or necrosis and the total number of glomeruli (in percent). We calculated the AI score: 0-5 = 0; 6-10 = 1; 11-15 = 2; 16-20 = 3; 21-25 = 4; 26-37.5 = 5; 37.6-50 = 6; 51-65 = 7; 66-80 = 8; 80-90 = 9; 90-100 = 10. Chronicity was evaluated with the Mayo Clinic Chronicity Score (MCCS). The combined score, we summed the MCCS and the AI.

Results: We analyzed 326 patients with kidney biopsies available to score. The biopsies had in median (IQR), 13 glomeruli (9-20), 4 crescents (2-6) and an AI of 28.6% (15.3-47.6). The population was classified according with the risk of progression to kidney failure (KF) in 3 classes as (i) low (0-6) – 114 (35.0%), (ii) intermediate (7-11) – 152 (46.6%), and (iii) high (≥12) – 60 (18.4%). Median eGFR at baseline correlated with the overall risk categories: 42.2 vs. 22.1 vs. 13.4 mL/min/1.73 m², p <0.0001. The proportion of patients with eGFR < 30 mL/min/1.73 m² was increased in patients classified as high: 88.3% vs. 66.4% vs. 36.0%, p <0.0001. Renal recovery was more frequent in patients at low risk of progression: 87.7% vs. 64.6% vs. 36.6%, p <0.0001, whereas kidney failure at 12 months and dialysis were more frequent in patients at higher risk (36.7% vs. 12.4% vs. 3.8%, p <0.0001; 35.6% vs. 13.0% vs. 2.9%, p <0.0001, respectively). The combination of AI with MCCS independently predicted the risk of KF at 12 months (HR 1.916, 95%CI 1.210 - 3.033, p = 0.006), particularly increased in patients classified as high risk (HR 3.124, 95%CI 1.224 – 7.970, p = 0.017) and in patients with PR3-ANCA (HR 1.896, 95%CI 1.012-3.551, p = 0.046) independently of eGFR at AAV-GN diagnosis and adjusted for severity of renal involvement and age.

Conclusion: The combined assessment of acute inflammatory activity and chronic changes on kidney histology independently predicted renal outcomes in patients with AAV-GN. The impact of the inflammatory activity is cumulative to the chronic changes.

Figure 1: Kaplan Meier plots of kidney failure (KF) over 12 months according with the risk group defined by the AAV kidney score.
LONG-TERM PROGNOSIS OF LATE-ONSET LUPUS NEPHRITIS

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Background and Aims: Systemic lupus erythematosus (SLE) occurs mainly in young women of child-bearing age and is not commonly found in the elderly population. Several studies have described that an early onset of lupus nephritis (LN) has a worse prognosis than a late-onset, presenting with greater complications and higher mortality, whereas other studies have shown that late-onset SLE present higher rate of organ damage and mortality. There are no series of late-onset LN that have been described in a European population to date. The KDIGO guidelines do not distinguish early from late-onset LN regarding their immunosuppression strategy recommendations. The objective of this study was to compare the presentation, course and outcomes of late-onset LN compared to early-onset LN in a Spanish population, and detect differences in outcomes according to treatment received.

Method: We performed an observational retrospective multicenter study that included adult patients who developed LN confirmed by a kidney biopsy after the age of 50 years, defined as late-onset LN. We compared them to a group of selected patients aged younger than 50 years at the diagnosis (early-onset LN), matched for disease duration. Baseline demographic, clinical, serological and histological characteristics were compared between both groups. We compared the course of the disease in both groups including renal flares, serious adverse effects, and a composite outcome defined as doubling serum creatinine, developing end-stage kidney disease and/or death. Cox regression analysis was used to examine the association between late-onset LN and its outcomes.

Results: The study included 229 patients; 67 with late-onset LN and 162 early-onset LN patients. Late-onset LN patients presented more frequently hypertension (p < 0.001) and diabetes (p = 0.008). There was a lower frequency of cutaneous manifestations (p < 0.001) and oral ulcers (p = 0.008), higher frequency of hematological manifestations (p = 0.015) and Sjogren syndrome (p = 0.05). Patents with late-onset LN showed a worse baseline kidney function (p < 0.001) and higher serum complement levels (p < 0.001). Late-onset LN patients showed higher chronicity indices in kidney biopsies, with more glomerulosclerosis (p = 0.003), interstitial fibrosis (p = 0.021) and tubular atrophy (p = 0.011). There were no differences in the distribution of LN histological classification between both groups. We did not find significant differences between early and late-onset LN as regards induction and maintenance immunosuppression therapies, showing only a lower rate of antimarial drug use in late-onset LN as maintenance therapy (p = 0.001). After a median follow-up of 7.4 (2.8-13) years, patients with late-onset LN showed a lower number of flares (p = 0.015), and a higher rate of serious adverse events related to immunosuppression, particularly infectious complications (34.3% vs 18.5%, p = 0.01). There were no differences in complete or partial remission or kidney function between both groups at the end of follow-up, however mortality was higher in late-onset LN patients, developing more frequently the composite outcome (19.4% vs 8%, p = 0.014). No significant difference was found in kidney survival (log-rank chi-square = 2.09, p = 0.148). Cox regression analysis showed that late-onset LN (hazard ratio = 3.26, 95% CI 1.18-8.98, p = 0.02), % sclerosed glomeruli (HR = 1.03, 95% CI 1.01-1.06, P = 0.019) and presence of severe side effects related to immunosuppression (HR = 10.09, 95% CI 3.2-31.7, p < 0.001) were independent risk factors for reaching the composite outcome.

Conclusion: Although patients with late-onset LN present with worse kidney function and more severe chronic lesions in kidney biopsy, they show comparable kidney outcomes to patients with early-onset LN, and despite receiving similar immunosuppressive regimens they develop less renal flares but more serious adverse events, leading to a worse overall outcome. Minimization of immunosuppression regimens in late-onset LN may be an adequate option to improve patient outcomes.

Table 1: Kidney function, histopathology, and outcomes of patients with Anti-Neutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis (AAV) glomerulonephritis (AAV-GN) based on the AAV combined score (combination of the chronicity score and activity index) (n = 326).

<table>
<thead>
<tr>
<th>AAV kidney score categories</th>
<th>Low n = 114 (35.0%)</th>
<th>Intermediate n = 152 (46.0%)</th>
<th>High n = 60 (18.4%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR at diagnosis, median (IQR), mL/min/1.73m²</td>
<td>42.2 (22.3 – 71.1)</td>
<td>22.1 (14.5 – 35.7)</td>
<td>13.4 (7.7 – 21.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>eGFR at diagnosis &lt; 30 mL/min/1.73m², n (%)</td>
<td>41 (36.0)</td>
<td>101 (66.4)</td>
<td>53 (88.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>eGFR at diagnosis &lt; 15 mL/min/1.73m², n (%)</td>
<td>19 (16.7)</td>
<td>46 (30.3)</td>
<td>36 (60.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Activity index (% crescents or necrosis / total number of glomeruli)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤10%</td>
<td>37 (32.5)</td>
<td>17 (11.2)</td>
<td>0 (0.0)</td>
<td></td>
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<tr>
<td>11 – 25%</td>
<td>47 (41.2)</td>
<td>44 (28.9)</td>
<td>8 (13.3)</td>
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</tr>
<tr>
<td>26 – 50%</td>
<td>29 (25.4)</td>
<td>59 (32.2)</td>
<td>24 (40.0)</td>
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<tr>
<td>&gt; 50%</td>
<td>1 (0.9)</td>
<td>42 (27.6)</td>
<td>28 (46.7)</td>
<td></td>
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<tr>
<td>Mayo Clinic Chronicity Score</td>
<td>77 (67.5)</td>
<td>24 (15.8)</td>
<td>0 (0.0)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Minimal</td>
<td>35 (30.7)</td>
<td>59 (38.8)</td>
<td>12 (20.0)</td>
<td></td>
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<tr>
<td>Mild</td>
<td>2 (1.8)</td>
<td>36 (23.4)</td>
<td>24 (40.0)</td>
<td></td>
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<tr>
<td>Moderate</td>
<td>0 (0.0)</td>
<td>13 (8.6)</td>
<td>21 (35.0)</td>
<td></td>
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<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Renal Outcomes, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Renal recovery</td>
<td>57 (87.7)</td>
<td>80 (64.6)</td>
<td>15 (13.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>6 (5.3)</td>
<td>20 (13.2)</td>
<td>22 (36.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>12 months</td>
<td>12 (10.5)</td>
<td>30 (19.7)</td>
<td>28 (46.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dialysis</td>
<td>7 (6.3)</td>
<td>22 (14.7)</td>
<td>22 (36.7)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
#3155

APOL1 GENOTYPE IS A MAJOR DETERMINANT OF LUPUS NEPHRITIS SEVERITY IN PATIENTS OF AFRICAN ANCESTRY

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Background and Aims: Two polymorphisms of APOL1 gene, G1 and G2, exclusively found among patients of African ancestry, have been associated with chronic kidney disease (CKD) and end-stage kidney disease (ESKD)1. These high-risk polymorphisms have also been associated with collapsing glomerulopathy in various diseases. We aimed to evaluate the impact of APOL1 G1 and G2 polymorphisms on the clinical and pathological course LN which is already known to be more severe among patients of African ancestry2.

Method: We included patients from 6 hospitals in Paris and Marseille in France, between January 2017 and March 2020, with biopsy-proven LN, African ancestry and age >18 years at the time of inclusion. We excluded those with HIV infection. The data were retrospectively collected at LN diagnosis, 1 year after diagnosis and at last follow-up. APOL1 genotyping was performed and we divided patients in 2 groups: the high-risk genotype (HRG) group with 2 risk alleles and the low risk genotype (LRG) group with 1 or 0 risk allele. All patients signed a consent form for the genetic analysis and protocol approval was obtained from the ethic committee CERAPHP (Comité d’Ethique de la Recherche AP-HCP Centre), registration number 00011928.

Results: Ninety-nine patients were included in the study, 13 in the HRG group and 86 in the LRG group. The median duration between LN diagnosis and inclusion in the study was 9.6 years [4.9-16.9]. At LN diagnosis, clinical and biological characteristics were similar except for kidney function that was lower in the HRG group compared to the LRG group with a median serum creatinine of 151 μmol/L [69-687] versus 66 μmol/L [52-133] (p = 0.0085). Patients in the HRG group were more likely to have a serum creatinine above 200 μmol/L compared to the LRG group (45.5% versus 10.5%, p = 0.0096, OR 7.1[1.8-28.6]), and required acute haemodialysis more frequently (30.8% versus 1.3% respectively, p = 0.0012, OR 34.7[3.5-345.1]). Collapsing glomerulopathy was more frequent in the HRG group (45.5% of patients, versus 4.5%, OR 17.5[3.3-91.9], p = 0.001). No significant difference was observed in the proportion of kidney response at 12 months, however, patients in the HRG group were more likely to develop CKD (33.3% versus 4.9%, OR 9.6[2.0-46.1]). Median follow-up from LN diagnosis to the end of study, ESKD or last follow-up was 7.9 years [3.4-13.3] and was similar between the 2 groups. At last follow-up, median eGFR was 22mL/min/1.73m² [10-98] vs 99mL/min/1.73m² [55-118] respectively, p = 0.0189. Survival without ESKD was poorer in the HRG group than in the LRG group with a hazard ratio (HR) of 5.0[1.6-15.8], p = 0.006, even after adjusting with the kidney response at 12 months (adjusted HR 6.24[1.8-21.6], p = 0.004) (Figure 1).

Conclusion: APOL1 genotype affects LN prognosis, resulting in a worse kidney function at diagnosis, development of collapsing glomerulopathy and higher risk of subsequent ESKD. Kidney survival remained significantly lower in the HRG group, after adjustment for kidney response at 12 months, suggesting that the progression of LN is heavily driven by APOL1 genotype regardless of the kidney response. APOL1 inhibitors are currently being developed, and could be used in the next future, for HRG patients with primary or secondary forms of collapsing glomerulopathy.

REFERENCES


Figure 1: Patient survival without End-Stage Kidney Disease. Data were censored at 15 years after LN diagnosis. Kaplan Meyer curve was analyzed with the log rank test. ESKD: End stage kidney disease; HRG: High risk genotype; LRG: Low risk genotype; HR: Hazard Ratio. Hazard ratio was calculated based on the Cox regression, and was adjusted with the kidney response at 12 months (overall response versus none).
COVID VACCINE RESPONSES DURING SIBEPRENLIMAB TREATMENT OF IGA NEPHROPATHY (IGAN): AN INTERIM ANALYSIS

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Background and Aims: ENVISION, an ongoing global P2 trial of sibeprenlimab, a mAb that neutralizes A Proliferation Inducing Ligand (APRIL) for the treatment of IgAN, previously reported an interim 43% placebo (pbo)-adjusted reduction from baseline in 24-hour uPCR at 9 months. The trial has been conducted through the ongoing COVID pandemic. To assess the effect of sibeprenlimab on COVID-risk, infection and vaccination (vac) data were recorded for all subjects. For consenting substudy subjects (SS) (n = 72), serologic responses to SARS-CoV2 proteins were measured monthly.

Method: Serum IgG antibodies specific for SARS-CoV-2 antigens were quantified using Meso Scale Discovery (MSD) V-PLEX SARS-CoV-2 Panel 24, a validated multiplexed assay. IgG levels were reported in WHO binding antibody units (BAU)/mL. Peak Receptor Binding Domain (RBD) IgG antibody titers were evaluated for SS following primary (2-dose) mRNA vaccination. Slopes of IgG RBD decline were utilized to generate preliminary estimates of time above protective threshold. A Welch two-sample t-test was applied to the log-transformed peak RBD titer values for significance testing.

Results: Among 155 IgAN patients enrolled and followed for 16 months (with 12 monthly sibeprenlimab or pbo infusions) between August 2020 and the present, COVID infection was reported in 55 overall. Two patients were hospitalized in accordance with standard local COVID protocols; none were admitted to ICU or mechanically ventilated and there were no fatalities. All other episodes of COVID infection were considered to be of mild or moderate severity (treatment status remains blinded for AE evaluation). COVID vaccination was administered to 46 SS; including 34 recipients of mRNA vaccines only (1, 2, 3 or 4 doses). There were no identified IgAN disease flares following vaccinations. Parameters characterizing IgG RBD titer were obtained from subjects receiving a 2-dose mRNA primary vaccination with sufficient data, excluding subjects with confounding COVID infection at the time of vaccination (n = 22). All subjects achieved a peak titer of >935 BAU/mL, with similar kinetics between arms. Geometric mean peak RBD IgG antibody level (Fig. 1) following vaccination was higher in pbo recipients (5600 BAU/mL) vs Sibeprenlimab (2410 BAU/mL) (p = 0.033). RBD IgG decline post mRNA vaccination (in any patient with at least one mRNA dose without confounding subsequent vac or infection) was evaluable in 28 SS. Rates of decline were similar between groups (Fig. 2), with comparable modeled time above an arbitrary protective threshold of 300 BAU/mL (~ 5-6 months, data not shown). In addition, there was no evidence that sibeprenlimab impeded robust humoral immune responses to actual infection.

Conclusion: Sibeprenlimab is a promising immunomodulatory therapy for treatment of IgAN. COVID-specific vaccine and infection-induced humoral immune responses were preserved during Sibeprenlimab therapy.

Figure 1: Peak IgG levels achieved following primary (2-dose) mRNA vaccination to SARS-CoV2 Receptor Binding Domain of envelope protein (IGG-RBD). Geometric Mean Cmax 5600 and 2410 BAU/mL for pbo and sibeprenlimab, respectively. Dotted line: 300 BAU/mL, a previously estimated Day-29 post-vac RBD BAU/mL level with ~90% vaccine efficacy (Gilbert et al, Science, 2022)

Figure 2: Observed data, decline of IGG-RBD antibody titers in pbo and sibeprenlimab recipients, with time of mRNA vaccination established as day 0.
INVESTIGATING THE ROLE OF CFH VARIANTS AND HAPLOTYPES AS A RISK FACTOR OF IGA NEPHROPATHY IN A FRENCH COHORT

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Background and Aims: Excessive complement activation is particularly important in the pathogenesis of IgAN nephropathy (IgAN). The relationship of complement CFH gene genetics and IgAN phenotype has not been clearly established in IgAN.

Method: We performed a genetic analysis of 234 French IgAN patients by next generation sequencing and Sanger. CFH polymorphisms were combined into haplotypes using the Michigan imputation Server1. CFH rare variants and haplotypes frequencies were compared to the 1k genome population of European ancestry. Recombinant full-length FH rare variants were produced and studied functionally in vitro.

Results: Genetic analysis revealed an enrichment in CFH non-synonymous rare variants in IgAN patients (n = 234) compared to the reference population (n = 503) (5.1 versus 1.8%, p = 0.010). Interestingly, the identified variants preferentially located in FH functional domains. In vitro functional studies based on new functional Luminex® assays showed a decrease in C3b-binding, C3bBB decay-accelerating activity and/or C1r/C1s cofactor activity for 4 variants, classifying a newly identified variant as a pathogenic variant. CFH haplotypes distribution differed between the IgAN group and controls (p = 0.001), with a higher prevalence of the H3 haplotype (rs80029 c.184G>A, rs1061170 c.1204T>C, rs542235 chr1:196854483 A>G, GTA) in IgAN patients (28.2 versus 21.1%, p = 0.0029), but this haplotype was not associated with renal survival.

Conclusion: In our series of French IgAN patients, CFH rare variants and haplotypes are associated with disease’s susceptibility. Our results support the hypothesis of a complement dysregulation underlying the IgAN pathogenesis.

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1. Available from https://imputationserver.sph.umich.edu

#3266

PROGNOSTIC FACTORS IN RENAL AND PATIENT SURVIVAL IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS

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Background and Aims: The most important determinant of renal and patient survival in anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is early initiation immunosuppressive (IS) therapy. Other factors associated with survival are age, sex, renal functional and renal involvement at diagnosis. The prognosis is poor in patients with AAV who do not receive IS treatment. The effect of plasma exchange (PE). in patients who underwent plasmapheresis with IS treatment has been questioned in recent studies. Renal histology is a predictor of long-term risk of renal failure in patients with crescentic glomerulonephritis, and prognostic histological scorings have been developed. In this study, we investigated clinical and pathological risk factors that may affect patient and renal survival in patients with AAV.

Method: Data of 225 AAV patients diagnosed by renal biopsy in the age range of 16-85 years in 30 centers were used which were obtained from the Turkish Society of Nephrology Glomerular Diseases (TSN-GOLD) Working Group database. Patients who did not have regular follow-up for at least
Table 1: Logistic Regression Analyses for survival of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Adjusted HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.035 (1.001-1.069)</td>
<td>0.041</td>
<td></td>
</tr>
<tr>
<td>female gender</td>
<td>1.511 (0.628-3.637)</td>
<td>0.357</td>
</tr>
<tr>
<td>IF &gt; %25</td>
<td>0.439 (0.150-1.285)</td>
<td>0.133</td>
</tr>
<tr>
<td>plasma albumin</td>
<td>0.488 (0.241-0.987)</td>
<td>0.046</td>
</tr>
<tr>
<td>Plasma exchange</td>
<td>2.958 (1.000-8.746)</td>
<td>0.050</td>
</tr>
</tbody>
</table>

Abbreviations: HR; hazard ratio, CI; confidence interval, IF; interstitial fibrosis

3 months, patients with immunocomplex glomerulonephritis, and patients with rapidly progressive glomerulonephritis who were positive for anti-GBM antibodies were excluded from the study. Patients with negative ANCA (n: 17) and unknown ANCA results (n: 28) were included in the study according to their renal biopsy findings.

Results: The mean age of the study population was 52.1±15.2 years and 126 (50%) were male. After renal biopsy, 154 patients (85.1%) received only cyclophosphamide and steroid treatment as initial IS treatment, 23 patients (12.6%) also received PE. When the clinical results of the patients were evaluated, end-stage renal disease (ESRD) was detected in 50 (22.2%) patients, while 36 (16%) patients died. When the factors affecting the development of ESRD were evaluated with the logistic regression analysis model, it was shown that the low albumin level of the patients at the time of diagnosis and the percentage of interstitial fibrosis (IF) >25% in renal pathology were more effective for the development of ESRD (p = 0.02, p = 0.01). When the factors affecting the survival of the patients were evaluated with the logistic regression analysis model, we demonstrated that there was no significant effect of PE and IF > 25% in renal pathology; age [HR = 1.035 (1.001-1.069)] and patients with lower albumin value [HR = 0.488 (0.241-0.987)] were found to be more risky in terms of death (p = 0.041, p = 0.004) (Table 1).

Conclusion: In this study, the serum albumin level of the patient at the time of biopsy was determinant in renal and patient survival in AAV. IF > 25% in renal pathology was effective in renal survival, but it was not found to be effective in patient survival. Plasma exchange did not provide additional benefit to standard treatment. Prospective and multicenter studies with a larger number of patients are needed to confirm our findings.

B3 - EPIDEMIOLOGY & OUTCOME

#3524 INCIDENCE AND OUTCOMES OF KIDNEY REPLACEMENT THERAPY FOR END-STAGE KIDNEY DISEASE DUE TO PRIMARY GLOMERULONEPHRITIS IN THE ERA REGISTRY

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Background and Aims: Primary glomerulonephritis (PGN) is among the leading causes of end-stage kidney disease (ESKD) in patients initiating kidney replacement therapy (KRT). To date, most studies have examined KRT outcomes from all PGN subgroups combined. Using data from the European Renal Association (ERA) Registry we examined trends and outcomes in individuals with PGN and its subgroups commencing KRT. Firstly, we described the incidence of KRT for ESKD due to PGN for all countries combined and by country; and secondly, we compared patient characteristics, survival outcomes, and causes of death.

Method: We used data from 31 national and regional renal registries providing individual patient data to the ERA Registry for at least three years between 2000-2019. PGN was categorized into six subgroups based on the ERA primary renal disease codes: Immunoglobulin A nephropathy [IgAN], membroproliferative glomerulonephritis [MPGN] (type I and type II), membranous nephropathy [MN], focal segmental glomerulosclerosis [FSGS], crescentic glomerulonephritis [crescentic GN], and other PGN (historically examined and histologically not examined). The age-and-sex-standardized incidences were estimated using the 2015 EU28 population as a reference. Jointpoint regression analysis was used to determine the annual percentage change (APC) in the incidence. Kaplan Meier and Cox regression analyses were used for the survival analyses. We adjusted for age, sex, KRT initiation era, and country.

Results: In total, 69,854 individuals started KRT due to PGN between 2000-2019, of whom 27.8% had IgAN, 15.8% FSGS, 8.5% MPGN, 5.8% crescentic GN, and 4.5% MN. The remaining 37.7% were categorized as other PGN (14.1% not biopsied). The standardized incidence of KRT due to PGN was 16.6 per million population (pmp), ranging from 8.8 pmp in Serbia to 20.0 pmp in France. The incidence was the highest for IgAN (4.6 pmp) and FSGS (2.0 pmp) particularly in age group 65-74 year. The incidence of KRT due to PGN [APC: -1.8% (-2.2; -1.4)] declined between 2000-2013, then it stabilized. Conversely, the incidence of KRT due to IgAN [APC: 5.1% (2.7;7.6)] between 2012-2019 and due to FSGS [APC: 3.1% (2.3-3.8)] between 2000-2019 increased. During a five-year follow-up 8,928 patients died. The five-year survival probabilities varied from 57.0% for crescentic GN to 83.6% for IgAN. The risk of death was highest in crescentic GN [The adjusted hazard ratio: 1.8 (95% confidence interval: 1.6-1.9)] compared to IgAN. Cardiovascular disease was the most common cause of death (33.9%) followed by infection (18.5%).

Conclusion: The incidence of KRT due to PGN was highest in IgAN and FSGS and varied largely across the European countries. The number of non-histologically examined PGN cases may reflect a lack of renal biopsy facilities which in turn hamper reporting of the true histological diagnosis. There was an initial decline in the incidence of KRT due to PGN, followed by stabilization. This could imply advances in the management protocols with better prognosis. Further studies are needed to explain the observed difference in the incidence over time and to identify factors leading to less initiation of KRT among patients with PGN.

#3649 EPIDEMIOLOGY OF IGA NEPHROPATHY AT A UK CENTRE OVER 2 DECADES – EFFECTS OF IMMUNOSUPPRESSION

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Background and Aims: IgA nephropathy (IgAN) is the most common glomerulonephritis worldwide. The clinical course is heterogeneous. As such, determining which patients to treat with immunosuppression (IS) is often the key decision in management. Here, we present a 20-year retrospective study from a single centre with the following aims: to describe the epidemiology of our cohort, to assess outcomes (such as progression to end-stage kidney disease [ESKD] requiring renal replacement therapy [RRT] and mortality), and to determine the effect of IS.

Method: We collected all cases of IgAN from our biopsy database between January 2000 and December 2019. After exclusion, the total number for analysis was 401 patients. We collected demographic data for each patient, along with creatinine and proteinuria values over time, MEST-C histological scores, progression to ESKD, mortality, use of renin-angiotensin system blockade (RAS) blockade and IS treatment. CKD progression in the overall cohort was computed using the rate of change of estimated glomerular filtration rate [eGFR] (delta eGFR) from baseline to study endpoint, with the linear regression slope generated using all available eGFR measurements. Similarly, the rate of change of urine protein creatinine ratio [uPCR] (delta uPCR) from baseline to study endpoint was calculated using linear regression from serial uPCR measurements.

Results: Median age of the cohort was 45.0 years, with 69.6% male and 87.5% were Caucasian. Baseline laboratory values (median) included: mean estimated Etonnium 142μmol/L, eGFR 46.7ml/min/1.73 m², uPCR 183mg/mmol/L. The median rate of decline of eGFR was -1.31ml/min/1.73 m²/yr and median change in uPCR was -4.46mg/mmol/yr. RAS blockade was used in 79.6% and IS in 20.4%. Progression to ESKD requiring RRT was seen in 29.7% and mortality in 19.7%. Median follow up duration was 51 months. Cox regression analysis revealed several factors associated with mortality, including increasing age, non-Caucasian ethnicity, diabetes, hypertension, cardiovascular disease, systolic blood pressure, creatinine, uPCR, ACEI/ARB use, and E and T score on biopsy. Several factors were associated with need for RRT including hypertension, various histological markers, creatinine, uPCR and ACEI/ARB use. IS was not found to be a factor associated with all-cause mortality or RRT. Those treated with IS (table 1) had a higher uPCR (301.5mg/mol vs 141mg/mol, p<0.001), were more likely to have a C score (37.7% vs
Table 1: Baseline characteristics, laboratory values and outcomes for those who received IS and those who did not.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Immunosuppression (n = 69)</th>
<th>No immunosuppression (n = 277)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>42.0 (31.0–59.5)</td>
<td>45.0 (29.0–60.0)</td>
<td>0.988</td>
</tr>
<tr>
<td>Male</td>
<td>45 (65.2)</td>
<td>196 (70.8)</td>
<td>0.370</td>
</tr>
<tr>
<td>Caucasian</td>
<td>60 (87.0)</td>
<td>244 (88.1)</td>
<td>0.835</td>
</tr>
<tr>
<td>C1 score</td>
<td>26 (37.7)</td>
<td>30 (10.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total MEST-C score</td>
<td>29 (42.0)</td>
<td>81 (29.2)</td>
<td>0.041</td>
</tr>
<tr>
<td>Creatinine at biopsy, μmol/L</td>
<td>166.5 (94.25–241.75)</td>
<td>137.0 (90.0–217.5)</td>
<td>0.096</td>
</tr>
<tr>
<td>uPCR at biopsy, g/mol</td>
<td>301.5 (193.25–523.5)</td>
<td>141.0 (59.3–286.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR, ml/min/1.73 m²</td>
<td>40.5 (23.7–73.4)</td>
<td>48.4 (27.2–83.4)</td>
<td>0.137</td>
</tr>
<tr>
<td>IgA, g/L</td>
<td>3.17 (2.49–4.19)</td>
<td>4.09 (3.06–5.24)</td>
<td>0.003</td>
</tr>
<tr>
<td>Delta uPCR, mg/mmol/year</td>
<td>−16.8 (−46.87–11.07)</td>
<td>−2.65 (−14.56–5.50)</td>
<td>0.003</td>
</tr>
<tr>
<td>Delta eGFR, ml/min/1.73 m²</td>
<td>−1.18 (−5.10–1.39)</td>
<td>−1.32 (−5.85–0.54)</td>
<td>0.703</td>
</tr>
<tr>
<td>ACEi/ARB</td>
<td>58 (84.1)</td>
<td>234 (84.8)</td>
<td>0.881</td>
</tr>
<tr>
<td>Mortality</td>
<td>9 (13.0)</td>
<td>48 (17.3)</td>
<td>0.391</td>
</tr>
<tr>
<td>Follow up duration, months</td>
<td>64.0 (26.0–97.5)</td>
<td>60.0 (29.0–105.5)</td>
<td>0.410</td>
</tr>
</tbody>
</table>

Conclusion:
This is one of the largest retrospective observational studies assessing clinical and histological characteristics, along with outcomes, for IgA nephropathy (IgAN). This provides important real-world data which will be useful for clinicians, particularly as the IgAN landscape changes with the introduction of novel therapies. Whilst IS was associated with a greater proteinuria reduction over time, this did not translate into an amelioration of eGFR decline.

The study received grant support from CSL Vifor.

B4 - PREVENTION, TREATMENT & CLINICAL TRIALS

#4503

ESTIMATING DELAY IN TIME TO KIDNEY FAILURE OR DEATH FOR TREATMENT EFFECTS ON PROTEINURIA IN IGA NEPHROPATHY
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GRAPHICAL ABSTRACT

Background and Aims: Reduction in proteinuria is associated with lower risk of kidney failure (KF) in IgA nephropathy (IgAN) (Thompson et al, 2019). In phase 3 randomized controlled trials in IgAN patients, a treatment effect on proteinuria reduction is typically evaluated as a mean percent change in proteinuria from baseline at 6-9 months. In this study, we aim to estimate the delay in time to KF or death associated with treatment effects of 40% and 50% reduction of proteinuria at this timepoint.

Method: In this study, we used individual patient level data from the UK National Registry of Rare Kidney Disease (RaDaR) IgAN cohort. Adult IgAN patients (n = 535) with a urine protein-creatinine ratio ≥ 100 mg/mmol (0.88 g/g) ≥ 6 months from diagnosis (time point defined as baseline) and eGFR ≥ 30 ml/min at baseline (study population mean = 61 ml/min/1.73 m² [SD 26]) were included. Predicted risk of KF (eGFR < 15 ml/min, initiation of dialysis, transplantation/doubling serum creatinine/death) associated with treatment effects reducing proteinuria by 40% and 50% at 9 months were calculated from IgAN trial level analysis data (Thompson et al, 2019). Accelerated failure time modelling was used to analyse time to KF/death during follow up in the RaDaR IgAN study population, and to estimate the effect that changes in hazard ratio had on median survival time and 5-year survival rates. Weibull, Log-Logistic and Log-Normal distributions were applied with the fitted survivor function reported from the model with the lowest AIC.

Results: Treatment effects reducing proteinuria by 40% and 50% in IgAN patients predict a 59% and 67% lower risk of KF/death, respectively. A 59% reduction in risk, is estimated to extend the median time to KF/death by 6.3 years, from 8.6 years (95% CI 7.8, 9.5) to 14.9 years (95% CI 13.6, 16.4), while the corresponding extension in median time to KF/death estimate for a 67% reduction in risk is 8.5 years (from 8.6 years [95% CI 7.8, 9.5] to 17.1 years [95% CI 15.6, 18.8]) (Figure 1). Five-year KF/death free survival rate increased from 75% to 89% and 91%, for 59% and 67% reduced risk in KF/death, respectively.

Conclusion: Therapeutic interventions that reduce proteinuria and the risk of KF can confer important and clinically meaningful extensions in the time patients are alive and free from KF.

ESTIMATING DELAY IN TIME TO KIDNEY FAILURE OR DEATH FOR TREATMENT EFFECTS ON PROTEINURIA IN IGA NEPHROPATHY
PHASE I STUDY OF THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF POVETACICEPT FOR AUTOIMMUNE GLOMERULONEPHRITIDES

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Background and Aims: B cell activating factor (BAFF) of the tumor necrosis factor (TNF) family and a proliferation-inducing ligand (APRIL), cytokines which bind and signal through BAFF-R, transmembrane activator and CAML interactor (TACI), and/or B cell maturation antigen (BCMA) on B cells, play overlapping and non-redundant roles in B cell development, proliferation, function, and survival. Therapeutic agents targeting BAFF and/or APRIL have demonstrated promising clinical potential in autoantibody-related glomerulonephritides (GN) such as lupus nephritis (LN), immunoglobulin (Ig) A nephropathy (IgAN), membranous nephropathy, and other B cell-related diseases such as systemic lupus erythematosus (SLE); however, there is still need for more safe and efficacious therapies. Povetacicept (ALPN-303) is an Fc fusion protein of an engineered TACI variant TNFRSF domain (vTD) with enhanced affinity for APRIL and BAFF which mediates more potent inhibitory activity than wild type (WT) TACI-Fc or BAFF- or APRIL-specific antibodies. In preclinical studies, povetacicept demonstrated enhanced pharmacokinetic (PK) and immunomodulatory properties vs. WT TACI-Fc, which may translate to lower and/or less frequent doses in humans. Povetacicept also suppressed autoantibodies, renal IgG deposition, and nephritis in mouse models. Povetacicept may therefore significantly improve clinical outcomes in autoantibody-mediated GNs and other B cell-related diseases.

Method: In this first-in-human study (NCT05034484), 66 healthy adult volunteers were randomized 4:2 into single ascending dose cohorts of intravenous (IV) or subcutaneous (SC) povetacicept or placebo. Participants were followed to assess safety and PK, circulating Ig, galactose-deficient IgA1 (Gd-IgA1), and circulating leukocyte populations.

Results: Povetacicept has been well tolerated in all cohorts evaluated as single IV or SC doses of up to 960 mg. Overall, it exhibits dose-related PK and expected pharmacodynamic (PD) effects, including dose-related reductions in serum IgA, IgM, IgG, and Gd-IgA1 (Figure 1), and in circulating antibody-secreting cells (ASC: plasmablasts and plasma cells) (Figure 2). In the same setting, these PD effects appear greater than those reported for WT TACI-Fc molecules and appear to be saturated at doses ≥80 mg. Coverage of free APRIL was maintained for 2-3 weeks with 80 mg and ≥4 weeks with 240 mg, respectively. The most frequent adverse event has been mild headache. To date, there have been no imbalances of infections between placebo and povetacicept groups, no treatment-related reactions other than mild injection site pain, and no adverse trends in safety laboratories.

Conclusion: To date, povetacicept has demonstrated acceptable safety and tolerability as single IV or SC doses, exhibiting dose-dependent PK and PD that appear to differentiate favorably vs WT TACI-Fc. Based on the magnitude and duration of the observed PD effects, dose regimens of 80-240 mg SC every 4 weeks are anticipated for use in future studies. Overall, the study findings support future clinical development of povetacicept in multiple autoantibody-related GN, as well as other B cell- and/or autoantibody-related diseases such as SLE and autoantibody-associated cytopenias.
Figure 1: Povetacicept Dose-Dependently Reduces Circulating Immunoglobulins and Gd-IgA1 Levels. Top six panels: Effects generally appear saturated ≥ 80 mg for ≥ 4 weeks. Bottom two panels: Serum galactose-deficient IgA1 (Gd-IgA1) levels were measured using an ELISA kit using the KM55 rat anti-human Gd-IgA1 antibody (Immuno-Biological Laboratories/IBL). The % change from baseline (predose) values are plotted.
Figure 2: Povetacicept Dose-Dependently Reduces Circulating Antibody-Secreting Cells. Human peripheral blood mononuclear cells (2 × 10⁷) collected from healthy volunteers treated with a single IV or SC dose of placebo (PBO) or povetacicept at the various dose levels indicated were evaluated by flow cytometry. After an initial gating step to remove CD45⁻⁺⁺⁺⁺, CD3⁺, CD14⁺, doublets, and debris, %antibody secreting cells (plasmablasts and plasma cells) were gated as CD19⁺ CD27⁺ IgD⁻ CD38⁺⁺ cells.

#3848
ORIGIN TRIAL: 24-WK PRIMARY ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PH2b STUDY OF ATACICEPT IN PATIENTS WITH IGAN
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Background and Aims: IgA nephropathy (IgAN) is the most common primary glomerulonephritis in the world. Galactose-deficient IgA1 (Gd-IgA1), anti-Gd-IgA1 autoantibodies (anti-Gd-IgA1), and IgA-IgG-containing immune complexes (ICs) are central in the pathogenesis of IgAN, contributing to kidney damage. The potential of targeting these disease-causing species was demonstrated in the Phase 2a JANUS trial (NCT02808429), evaluating the safety and efficacy of atacicept in patients with IgAN. Atacicept is a fusion protein that binds B-lymphocyte stimulator (BlyS) and a proliferation-inducing ligand (APRIL) inhibiting maturation and class-switching of B-cells and plasma cells. In JANUS, patients treated with atacicept 25 mg or 75 mg experienced stabilization of estimated glomerular filtration rate (eGFR) compared with placebo over 72 weeks. Patients in the atacicept arms also experienced dose-dependent reductions in Gd-IgA1, anti-Gd-IgA1 and ICs during the treatment period compared with placebo. The Phase 2b ORIGIN trial (NCT04716231) is a dose-ranging study evaluating atacicept versus placebo in an IgAN population with significant proteinuria.

Method: ORIGIN is a double-blind, placebo-controlled Phase 2b clinical trial including 116 patients with biopsy-proven IgAN, 24-hour urine protein > 0.75 g per day or urine protein-to-creatinine ratio (UPCR) > 0.75 g/g, and eGFR > 30 mL/min/1.73 m² despite optimized renin–angiotensin system blockade. Patients were randomized to atacicept 150 mg, 75 mg, or 25 mg, administered by subcutaneous injection once per week versus placebo (2:2:1:2) for up to 36 weeks followed by an open-label extension during which all patients may receive active atacicept 150 mg for an additional 60 weeks. The primary endpoint was the change in 24-hour UPCR at 24 weeks in the pooled atacicept 150 mg and 75 mg arms compared with placebo. Secondary objectives include UPCR at additional time points, the effect of atacicept on change in eGFR, safety and tolerability.

Results: Between May 2021 and June 2022, 232 patients were screened. Of these, 116 patients were randomized and included in the primary analysis (33, 33, and 16 receiving atacicept 150, 75, and 25 mg, respectively; and 34 receiving placebo) of the intent-to-treat (ITT) population. At 24 weeks, mean UPCR was reduced from baseline by 31% in the pooled atacicept 150 mg and 75 mg arms compared with a 7% reduction from baseline in the placebo (Δ = 25%, p = 0.037). The atacicept 150 mg arm achieved a 33% reduction from baseline at Week 24 and was the only individual treatment arm that showed a statistically significantly greater reduction than placebo (Δ = 28%, p = 0.047). Results of the ITT analysis are supported by a pre-specified per-protocol (PP) analysis (n = 27, 32, and 14 for atacicept 150, 75, and 25 mg, respectively; n = 29 placebo): the atacicept 150 mg arm showed a 41% reduction from baseline in UPCR at 24 weeks compared with a 10% reduction in the placebo arm (Δ = 34%, p = 0.025). The secondary endpoint, eGFR, showed stability at 24 weeks. Gd-IgA1 reduction of 60% was achieved at Week 24 with atacicept 150 mg. The safety results indicated that atacicept was generally well-tolerated with no increased rate of infections compared to placebo, a low rate (2%) of serious AEs overall with none in the atacicept 150 mg group, and no study drug discontinuation or interruptions due to hypogammaglobulinemia.

Conclusion: The ORIGIN Ph2b study met its primary endpoint demonstrating a favorable impact on disease biomarkers and a clinically meaningful reduction in proteinuria and demonstrated a favorable safety profile. These promising results at Week 24 support atacicept 150 mg for further evaluation as a potential disease modifying treatment of patients with IgA nephropathy.

#4057
SUPERIOR PROTEINURIA REDUCTION WITH SPARSENTAN IN IMMUNOGLOBULIN ANEPHROPATHY (IGAN): A PROTECT STUDY INTERIM ANALYSIS
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Background and Aims: IgAN is the most common glomerular disease worldwide. Despite optimized standard of care, most patients with IgAN progress to kidney failure within 10-15 years, consequently seriously affecting their quality of life and mortality. Treatments that reduce proteinuria and risk of kidney disease progression are urgently needed for IgAN. Sparsentan is a novel, oral, non-immunosuppressive, single molecule that is a dual endothelin and angiotensin receptor antagonist being investigated for IgAN and focal segmental glomerulosclerosis. The Phase 3 PROTECT study is examining the long-term antiproteinuric and nephroprotective potential and safety of sparsetan compared with an active control, angiotensin receptor blocker (ARB) irbesartan, in adults with IgAN. Reported here are the PROTECT pre-specified interim primary efficacy endpoint and safety outcomes.

Method: PROTECT is an ongoing, global, Phase 3, multicenter, randomized, double-blind, active controlled study designed to evaluate the efficacy and safety of sparsetan versus the active control irbesartan in adults with IgAN with overt proteinuria despite receiving maximized treatment with an angiotensin converting enzyme inhibitor (ACEI) and/or ARB. The study duration is 270 weeks; the double-blind period is 114 weeks (110 treatment and 4 follow-up) with an open-label extension period up to 156 weeks. Adult patients with biopsy-proven IgAN (excluding IgAN secondary to another condition or IgA vasculitis), urine protein excretion value ≥1.0 g/day, eGFR ≥30 mL/min/1.73m², systolic/diastolic blood pressure ≤150/100 mmHg,

Abstracts
and on a stable dose of ACEi and/or ARB therapy for at least 12 weeks prior to screening that is both the patient's maximum tolerated dose and at least one-half of the maximum labeled dose were eligible for inclusion. Patients took their last ACEi and/or ARB dose the day before randomization. Patients were randomized 1:1 to sparsentan or irbesartan (target dose 400 and 300 mg/day, respectively), stratified by screening eGFR and urine protein excretion values. The pre-specified interim primary efficacy endpoint of change from baseline in urine protein/creatinine ratio (UP/C, based on a 24-hour urine sample) at week 36 was analyzed using a mixed model repeated measures analysis. The safety evaluation included assessment of treatment emergent adverse events.

Results: A total of 671 patients were screened; 406 patients from clinical sites in 18 countries, including sites in North America, Europe, and Asia Pacific, met eligibility criteria and were enrolled and randomized into PROTECT. Two randomized patients withdrew from the study prior to initiating study treatment. The 404 randomized patients who received study drug were included in the primary analysis population. The mean reduction in UP/C from baseline at 36 weeks was significantly greater in the patients who received sparsentan (-49.8%) versus irbesartan (-15.1%, P < 0.0001). Proteinuria reduction changed across baseline demographic and clinical characteristics and rates of complete and partial remission are reported, as well as sustained proteinuria reduction over time. Safety outcomes related to edema and liver function tests are reported. Overall, sparsentan was generally well-tolerated and comparable to irbesartan.

Conclusion: The interim results of the PROTECT study show that in adult patients with IgAN and persistent proteinuria above 1 g/day despite being treated with ACEis and/or ARBs, once-daily treatment with sparsentan produced a robust and clinically meaningful reduction in proteinuria. The safety of sparsentan was consistent with previous studies in FSGS and comparable to irbesartan.

#3032
EFFICACY AND SAFETY OF VOCLOSPORIN IN PATIENTS WITH PROTEINURIA ≥2 MG/MG: AN INTEGRATED ANALYSIS OF THE AURA-LV AND AURORA 1 STUDIES
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Background and Aims: Proteinuria has been established as a mediator of progressive renal damage in many nephropathies. However, recent studies of several monoclonal antibodies demonstrated a lack of efficacy in patients with lupus nephritis and moderate to high levels of proteinuria (UPCR ≥2 to ≥3 mg/mg), potentially due to an increase in renal antibody clearance.1-4 Given that, we examined the efficacy and safety of voclosporin in patients with lupus nephritis and a UPCR of ≥2 mg/mg using the pooled dataset from the Phase 2 AURA-LV and Phase 3 AURORA 1 trials.

Method: Both studies enrolled patients with biopsy-proven LN (Class III, IV, or V ± III/IV), biopsied within 6 months in AURA-LV or up to 2 years in AURORA 1) and proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V). Patients were randomized to receive either voclosporin (23.7 mg BID) or placebo and treated for up to one year (48 weeks [AURA-LV], 52 weeks [AURORA 1]); all patients received MMF and low-dose steroids. For this post-hoc analysis, changes in UPCR and renal response rates were evaluated in patients with baseline UPCR ≥2 mg/mg. Complete renal response (CRR) was defined as UPCR ≤0.5 mg/mg with stable renal function, low-dose steroids, and no rescue medication; partial renal response (PRR) was defined as ≥50% reduction in UPCR from baseline. Safety outcomes were also assessed.

Results: The pooled analysis included 268 and 266 patients in the voclosporin and control arms, respectively. Of those, 217 and 215 patients had UPCR ≥2 mg/mg (baseline mean [SD], 5.2 [3.4] vs. 4.6 [2.9] mg/mg, respectively). A significantly greater percentage of voclosporin-treated patients achieved a CRR at one year compared to the control arm (41.0% vs. 21.9%; odds ratio [OR] 2.48, p < 0.0001). Similarly, significantly more patients in the voclosporin arm (69.6%) than control arm (50.0%) achieved a PRR at the same time point (OR 2.3, p < 0.0001); this endpoint was met significantly earlier in voclosporin-treated patients as well (29 vs. 57 days, hazard ratio [HR] 2.0, p < 0.0001). The median time to UPCR <0.5 mg/mg was also significantly earlier in the voclosporin arm (211 days); less than 50% of the control arm achieved this endpoint within the study period (OR 1.9, p < 0.0001, Figure 1B). Adverse event rates were comparable in both arms (Table 1), and mean eGFR levels were similar and stable over the study period, a trend that was maintained for AURORA 1 patients who continued randomized treatment for another two years in the AURORA 2 study.

Conclusion: Consistent with results from the overall pooled study population, patients with UPCR ≥2 mg/mg at baseline treated with voclosporin achieved significantly higher renal response rates and significantly earlier reductions in UPCR than patients treated with MMF and low-dose steroids alone. These findings are clinically important given the lack of effective therapies available for patients with high baseline proteinuria.

REFERENCES

Table 1: Summary of Adverse Events.

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Voclosporin n = 217</th>
<th>Control n = 215</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event (AE)</td>
<td>200 (92.2)</td>
<td>187 (87.0)</td>
</tr>
<tr>
<td>Serious AE (SAE)</td>
<td>49 (22.6)</td>
<td>42 (19.5)</td>
</tr>
<tr>
<td>Treatment-related SAE</td>
<td>8 (3.7)</td>
<td>7 (3.3)</td>
</tr>
<tr>
<td>AE Leading to Study Drug Discontinuation</td>
<td>30 (13.8)</td>
<td>29 (13.5)</td>
</tr>
<tr>
<td>Death</td>
<td>6 (2.8)</td>
<td>3 (1.4)</td>
</tr>
</tbody>
</table>

Includes adverse events starting on or after the first dose of study drug up to 30 days after the last dose and all events of death reported during study follow-up; all events of death have been previously reported. AEs were reported using Preferred Terms (PT) based on investigator clinical judgement and discretion. AEs were aggregated by System Organ Class (SOC) and coded using Medical Dictionary for Regulatory Activities (MedDRA) version 20.0.
MODELLING LONG-TERM OUTCOMES FOR PATIENTS WITH IMMUNOGLOBULIN ANEPHROPATHY (IgAN) FROM SHORT-TERM PROTEINURIA DATA

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Background and Aims: Immunoglobulin A nephropathy (IgAN) is rare kidney disease that leads to glomerular injury, progressive loss of kidney function and progression to kidney failure. Pre-specified interim proteinuria data from ongoing clinical trials is being used as the basis of regulatory approval of new therapies but little is known about the translation of these results to long-term patient outcomes; a topic of particular interest to health technology assessment (HTA) groups looking to inform decisions on reimbursement before final renal outcome data are available. The objective of this study was to model long-term outcomes for patients with IgAN based on short-term proteinuria data.

Method: We developed a de novo model including a short-term (36-week) decision tree and a long-term Markov model to capture expected lifetime outcomes associated with treatment for IgAN. We used achievement of proteinuria <1 g/day as a clinically relevant treatment target. The short-term model included data on proteinuria level and distribution of chronic kidney disease (CKD) health states (CKD 1/2, 3, 4, and 5). At the end of 36 weeks of treatment, patients were categorized into groups based on their proteinuria level (<1g/day and ≥1g/day) and CKD stage before transitioning to the long-term Markov model. In the long-term model, proteinuria level-based, CKD health state transition matrices derived from analysis of UK National Registry of Rare Kidney Disease (RaDaR) data, and transition matrices to dialysis and transplant derived from the US Renal Data System (USRDS) were used. Other included clinical inputs of complications and mortality were derived from extension of US Optum data analyses and literature. Health-related quality of life (HRQoL) was assessed as health state utilities and disutility associated with complications. Hypothetic scenarios of improvement in short-term proteinuria and impact on long term outcomes were tested. Model outputs included life years (LYs) and quality-adjusted life years (QALYs). Effectiveness was discounted at 3% annually. Deterministic sensitivity analysis was conducted.
Results: Over a lifetime, patients receiving treatment that increased the probability of achieving proteinuria $<1$ g/day by 10% in the short-term, were modelled to have gained an additional 0.388 LYs from reduced CKD/transplant/dialysis-related mortality and 0.633 QALYs from delaying CKD progression to kidney failure. As expected, results improved when the probability of achieving proteinuria $<1$ g/day increased; with a 30% increase in the probability of achieving proteinuria $<1$ g/day, LYs gained were 0.562 (Figure 1) and QALYs 0.968 (Figure 2). Results were most sensitive to time horizon and long-term extrapolation of CKD health state transition matrices. Conclusion: Despite challenges inherent in the translation of surrogate endpoints to long-term outcomes, combining short-term proteinuria from clinical trials and long-term CKD data from real-world registry and claims-based data provides a solution. Based on modelling, treatments that increase the probability of achieving $<1$ g/day in the short-term, are expected to provide benefits to patients with IgAN in the long-term including less time with advanced kidney disease, less time on dialysis and avoiding the need for kidney transplant resulting in improved survival, and better quality of life. Refinement and customization of country-specific model inputs will help ensure outputs are relevant for different jurisdictions and as representative of anticipated real-world outcomes as possible.
Background and Aims: Several retrospective observational studies have supported kidney protective effects of arteriovenous fistula (AVF) formation. However, these studies were limited by immortal time and selection biases. We investigated whether AVF formation delays the initiation of kidney replacement therapy (KRT) in patients with stage 5 CKD by applying target trial emulation methods, which do not suffer from these biases.

Method: We included adult patients who had an eGFR \(\leq 15 \text{mL/min/1.73m}^2\), attended the 'low clearance' nephrology clinic in the West of Scotland between January 1st 2010 and May 1st 2022, and had no prior AVF or AV graft formation. Available data were obtained from the Strathclyde Electronic Renal Patient Record. The target trial would randomize patients to either receive an AVF immediately or to not receive an AVF. To emulate this trial, we matched each patient who underwent AVF formation to patients who had not undergone AVF formation but remained eligible to participate in the trial, and were matched in sex, age (within 5 years) and eGFR (within 0.5 mL/min/1.73m\(^2\)). Inverse probability of treatment weighting was used to adjust for baseline confounders, including age, sex, comorbidities, medication use, serum and urine biochemical measurements (eGFR CKD-EPI, eGFR CKD-EPI slope for 6 months preceding trial, haemoglobin, C-reactive protein, albumin, phosphate, adjusted calcium, ferritin, urine protein:creatinine ratio), and blood pressure. The primary outcome was kidney replacement therapy. The eGFR slope closest to the time of AVF creation was estimated as a co-primary endpoint. We estimated hazard ratios using Cox regression and estimated restricted mean survival time (RMST) from the Kaplan-Meier curves. The eGFR slope co-primary endpoint was analysed with a mixed-effects model.

Results: Among 2,988 included patients (55% men; mean [SD] age 64 [15] years), AVF formation was associated with a higher risk of KRT (HR 1.45; CI 1.20–1.49, \(p < 0.001\), Figure 1) and a lower risk of death (HR 0.68; (0.64–0.80, \(p = 0.001\)). The AVF group had a lower KRT-free survival with an estimated RMST difference of 265 days (95% CI \(-331 \text{ to } -199, p < 0.001\) and higher overall survival (RMST difference of 191 days; 95% CI 57 to 326, \(p = 0.005\)). Finally, we used a mixed-effects model to analyse the association between eGFR CKD-EPI, time, and AVF formation. AVF formation and time were both associated with a negative slope in the model (estimates \(-1.28; 95\% \text{CI } -1.36 \text{ to } -1.19, p < 0.001\) and \(-0.01; 95\% \text{CI } -0.01 \text{ to } -0.01, p < 0.001\), respectively, Figure 2). Their interaction was also associated with a negative slope (estimate \(-0.001; 95\% \text{CI } -0.0022 \text{ to } -0.0004, p < 0.001\), suggesting those undergoing AVF formation had a more rapid eGFR decline compared to the control group.

Conclusion: Unlike what was observed in previously published work, we did not identify a kidney protective effect of AVF formation. The estimated time of dialysis initiation remains the main determinant for timing of access surgery. These findings illustrate the usefulness of target trial emulation in approaching research questions where randomised controlled trials would be impractical.
Background and Aims: The transition to kidney failure is the period of the highest risk for adverse outcomes in chronic kidney disease (CKD). A smooth and timely transition of care, assuring informed and patient-centric decision-making, is paramount to fostering better kidney care. We described the two-year incidence of clinical outcomes and nephrology practices among advanced CKD patients in CKDopps.

Method: CKDopps is a prospective cohort study designed to describe and evaluate variations in CKD practices and outcomes in nephrologist-led CKD clinics. For this analysis, we included CKDopps participants who reached a three-month average estimated glomerular filtration rate (eGFR) of less than 20 mL/min/1.73 m² in the US, France, and Brazil. Time at risk for outcomes started at the end of the first three-month window in which the average eGFR was lower than 20 mL/min/1.73 m² during study follow-up. Education was defined as participation in at least one educational session about KRT modalities. They were considered to have been referred to vascular access (VA) creation if reported in medical records. Education or VA referral happening before the start of follow-up were classified as occurring at baseline. Patients were considered waitlisted if they had been registered on a pre-emptive kidney transplant waiting list. Cumulative incidence functions adjusting for the competing risk of mortality or KRT were used to estimate the 2-year probability of clinical outcomes and planning events.

Results: 2,645 patients were included – 51% from France, 36% from the US, and 14% from Brazil. Overall, 56% of patients were male, the mean age was 66 ± 14 years, approximately 50% had diabetes, 27% had coronary artery disease, and 16% had heart failure. Patients in Brazil tended to be younger (63 years) than those in France (67) and the US (67); patients in the US had the greatest burden of cardiovascular comorbidities. The mean eGFR at the study baseline was 16.6 mL/min/1.73m² (15.4 in Brazil, 15.9 in the US, and 17.3 in France). Over a median follow-up of 15.7 [7.2–24] months, 1140 patients (43.1%) started KRT, whereas 377 (14.3%) died before KRT. The 2-year cumulative incidence of KRT was 32% in Brazil, 33% in France, and 44% in the US (Figure 1). The median eGFR at KRT initiation was 11.7 in Brazil, 9.0 in France, and 10.3 in the US. Pre-KRT death risk in two years was 7.3% in Brazil, 10.9% in France, and 16.4% in the US. In two years, approximately one-third of patients had a VA created across countries (Table 1). The probability of transplant waitlisting was higher in France and the US, while patient-reported KRT education was more common in Brazil (Table 1).

Conclusion: In this international analysis of advanced CKD patients, we found important variations in nephrology practice and outcomes across countries. Patients in the US have a higher risk of both pre-KRT death and KRT. Patient-reported education was far more common in Brazil than in the US and France. Although patients in Brazil are referred for VA creation earlier in the course of advanced CKD, 2-year cumulative incidences for such are similar across countries. The 2-year probability of pre-emptive kidney transplant listing was higher in France and the US. Further international studies evaluating risk factors for adverse outcomes and barriers to KRT planning among advanced CKD patients are warranted.
Figure 1: Cumulative incidence functions for end-stage kidney disease (ESKD) and pre-ESKD death across countries.

Table 1: Cumulative incidence of kidney replacement therapy education, vascular access creation, and listing to pre-emptive kidney transplant across countries.

<table>
<thead>
<tr>
<th>Country</th>
<th>Brazil (n = 336)</th>
<th>France (n = 1391)</th>
<th>United States (n = 917)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KRT Education</td>
<td>Vascular Access</td>
<td>Tx Waitlisting</td>
</tr>
<tr>
<td>Baseline *, %</td>
<td>57.7</td>
<td>18.8</td>
<td>4.2</td>
</tr>
<tr>
<td>1 year, %</td>
<td>73.0</td>
<td>26.6</td>
<td>10.1</td>
</tr>
<tr>
<td>2 years, %</td>
<td>75.7</td>
<td>30.4</td>
<td>16.4</td>
</tr>
</tbody>
</table>

* Baseline events occur at or before the start of follow-up in the study (left-censoring).

#6569

PREDICTION OF ALL-CAUSE MORTALITY FOR CHRONIC KIDNEY DISEASE PATIENTS USING FOUR MODELS OF MACHINE LEARNING

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Background and Aims: Prediction tools developed from general population data to predict all-cause mortality are not adapted to patients with chronic kidney disease (CKD), as this population has a higher risk of mortality. This study aimed to create a clinical prediction tool with good predictive performance to predict 2-year all-cause mortality in patients with stage 4 or 5 CKD using an innovative approach with machine learning models and a synthetic population.

Method: The national, observational, descriptive and prospective PhotoGraphe 3 study was used to create the learning database. Four models (i) logistic regression; (ii) deep learning; (iii) random forest and (iv) Bayesian network were used to create four prediction tools. The performance of each model, including the area under the receiver operating characteristic curve (AUC-ROC) value, accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), was evaluated and compared using 10-fold cross-validation. The prediction tool with the best performance was selected and optimized using a synthetic population and the explanatory variables most related to mortality. The synthetic population was created by the Bayesian imputation method. The variables most associated with 2-year all-cause mortality were determined by compromising the number of variables selected and the AUC-ROC value when successively adding the variable according to its percentage variance value. The performance of the optimized prediction tool in predicting 2-year mortality was then evaluated by 10-fold cross validation.

Results: All prediction tools except the one developed with the random forest model showed satisfactory discrimination (AUC-ROC ≥ 0.70). Overall, the prediction tools developed using the Bayesian network and logistic regression tended to have better performance. Although not significantly different from logistic regression, the prediction tool developed using the Bayesian network was chosen for further development because of its advantages.

From the 534 patients in the study population, a synthetic population of 2000 patients (survivor:death ratio = 1:1) was created. The seven most informative variables ranked in descending order were: age, ESA, CV history, smoking status, 25-OH vitamin D level, PTH level, and ferritin level (Figure 1). The optimized clinical prediction tool had satisfactory internal performance. The mean accuracy was 73.8% (SD = 3.6), the mean AUC-ROC was 0.81 (SD = 0.03), the mean sensitivity was 71.0% (SD = 5.4), the mean specificity was 76.5% (SD = 3.0), the mean PPV was 75.1% (SD = 3.2), and the mean NPV was 72.6% (SD = 4.1).

Conclusion: Bayesian network model was used to create a seven-variable prediction tool to predict the 2-year all-cause mortality in patients with stage 4–5 CKD. This prediction tool has a satisfactory performance. Prior to external validation, the proposed prediction tool can be used at: https://bit.ly/3JPhrkh for research purpose. This is the first time that a synthetic population has been applied to create predictive models. In this study, the synthetic population showed its advantage in dealing with sample size issues in developing predictive models and in improving the performance of the prediction tool in terms of sensitivity and PPV.
#2647
MENOPAUSAL HORMONE THERAPY AND RISK OF DEMENTIA IN WOMEN WITH PRE-DIALYSIS CKD: A NATIONWIDE OBSERVATIONAL COHORT STUDY
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Background and Aims: The risk of dementia is increased in postmenopausal women. The incidences of premature menopause and dementia are increased in patients with chronic kidney disease (CKD). Therefore, the potential benefit of hormone replacement therapy (HRT) for cognitive function may be a more critical issue in CKD patients.

Method: Menopausal women over 40 years with or without HRT were identified through the National Health Screening questionnaire in 2009. Among the subjects, those newly diagnosed with CKD between 2009 and 2013 were enrolled. HRT was used as an exposure variable and was followed from the day when CKD was diagnosed to December 2019. The hazard ratio (HR) of dementia was evaluated using a Cox proportional hazards regression analysis.

Results: We included 755,426 postmenopausal women with CKD. The median follow-up period was 7.3 (IQR, 5.8-8.7) years. All-cause dementia occurred in 107,848 (14.3%), Alzheimer’s disease in 87,833 (11.6%), and vascular dementia in 10,245 (1.4%). HRT was significantly associated with a lower risk of dementia in the adjusted Cox regression model (all-cause dementia: hazard ratio [HR] 0.796, 95% confidence interval [95% CI] 0.776-0.816, P < 0.001; Alzheimer’s disease: HR 0.795, 95% CI 0.773-0.818, P < 0.001; vascular dementia: HR 0.803, 95% CI 0.743-0.868, P < 0.001).

Conclusion: HRT was significantly associated with a lower risk of CKD-related cognitive dysfunction in postmenopausal women. Prospective studies on whether HRT lowers the risk of dementia in menopausal women with CKD are needed.
Figure 1: Cumulative incidence of outcome according to hormone replacement therapy. The x-axis indicates the time (years), and the y-axis indicates the cumulative incidence (percentage) of dementia during the observation period. The survival curves are stratified by hormone replacement duration (black: No replacement; red: duration <2 years; green: 2-5 years; and blue: ≥ 5 years).

#6111
FIRST IDENTIFICATION AND CHARACTERIZATION OF MICROPLASTICS IN HUMAN KIDNEY AND URINE
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Background and Aims: Microplastics (MPs), plastic fragments less than 5mm in diameter, have been recognized as a global environmental issue. Various studies have shown their ubiquitous presence and their toxicity on marine and terrestrial fauna. Currently in humans, the presence of MP has been evidenced in lungs, placenta, blood, and liver. However, there is still very little knowledge about their presence in different organs and tissues and their prospectivetoxicity. The objective of this study was to investigate the presence of microplastics in human kidneys and urine.

Method: We obtained 10 urine samples from healthy individuals and 10 kidney healthy tissue samples from nephrectomies in renal cancer. The detection and characterization of microplastics was performed by a light microscope (Leica, total magnification of 800x) coupled to a Raman spectrometer (Renishaw System 2000). To this purpose, specimens were digested by a 10% KOH solution at 60°C and subsequently filtered on membrane filters with micropores of 0.2 μm to retain possible particles. This procedure was performed adopting a “plastic-free” protocol. Procedural blanks were performed as controls using the same protocol. To determine the nature of the detected particles, Raman spectra were compared to the ones present in the Renishaw spectrometer database (inorganic materials, polymers and forensic materials) [i], in the SLOPP Library of Microplastics [ii], and in the IRUG Spectral Database (pigments section) [iii]. A home-developed software was employed to compare spectra. Data analysis was performed by using the statistical software package Prism6 (Graphpad Software) Chi-square test, Student’s t-test were performed to compare data accordingly. The significance threshold was set at p < 0.05.

Results: 17 fragments (mean 1.7±2.11/sample) were identified and characterized on 7 out of 10 human kidney samples. The result was significant (p.value 0.041) compared with controls (mean 0.33±0.49/blank). 9 fragments were identified and characterized on 7 out of 10 human urine sample (mean 1.28±0.49/sample) highly significant (p.value 0.0002). Spectra analyzed by microRaman showed the presence polymers, polymers additives and pigments associated to polymers such as: hematite, Cu-phthalocyanine blue, Cerulean Blue, Polystyrene, Styrene-Isoprene and polyethylene.

Conclusion: We first demonstrated the presence of MPs in human kidneys, and we also confirm their presence in urine assuming the presence of a kidney clearance mechanism. Using Raman Microspectroscopy, it was also possible to determine the nature and quantity of MPs. The remarkable relevance of this identification, potentially concern much of the humans, deserve a widespread attention of the medical community for its potential implications. Further studies are urgently needed to investigate the possible nephrotoxicity of MPs, mechanisms of kidney clearance and tissue accumulation.

<table>
<thead>
<tr>
<th>Sample, Total n</th>
<th>Positive sample for particles; total particles</th>
<th>Cu-phthalocyanine blue</th>
<th>Hematite</th>
<th>Cerulean blue</th>
<th>Polyethylene</th>
<th>Polystyrene</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine, n 10</td>
<td>7;9</td>
<td>1</td>
<td>4</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Kidney, n 10</td>
<td>7;17</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1: Synoptic view of the microplastics particles detected by μ-Raman spectroscopy.
**ESTIMATED GLOMERULAR FILTRATION RATE BY FIVE DIFFERING MEASURES, RACE, GENETIC RISK AND PREDICTION OF CARDIOVASCULAR DISEASE AND MORTALITY**

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**Background and Aims:** Estimated glomerular filtration rate (eGFR), a significant measurement of chronic kidney disease (CKD), is associated with adverse health outcomes in the general population but whether its utility differs by race and genetic risk remains unclear. The current study aims to investigate the performance of CKD staging and risk prediction in cardiovascular disease and mortality based on five eGFR measures among people of different ethnic groups and genetic background.

**Method:** In this prospective cohort study, we included 431,126 participants from the UK Biobank, deriving hazard ratios and 95% confidence intervals from multivariable adjusted Cox proportional hazards models. C statistic and net reclassification improvement (NRI) were utilized for comparing the predictive benefit of eGFR measures when added to the traditional cardiovascular risk factors.

**Results:** Over a median of 13.4 (IQR 12.7-14.9) years of follow-up, 27,757 (6.4%) participants died from any cause, of which 3272 (0.8%) died primarily from CVD. 39,522 (9.2%) incident composite CVD hospitalization and 911 (0.2%) ESRD occurred. Two new eGFR equations refitted without race provided lower estimates in Black population but higher in other ethnic backgrounds than the corresponding old ones. The relative risk of adverse outcomes was generally greater in Blacks and participants with low genetic susceptibility to impaired kidney function. The superiority of cystatin C-based eGFR measures in risk prediction did not differ by race and genetic risk.

**Conclusion:** Eliminating the use of racial categories in eGFR calculation help enhance the access to specialist care and intervention at the early stage of CKD for Black population. Cystatin C-based eGFR measures can be extensively used in risk assessment in clinical practice.

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**INTEGRATED KIDNEY MARKERS AND CARDIOVASCULAR MORTALITY: A SURVIVAL ANALYSIS IN UK BIOBANK**

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**Background and Aims:** The estimated glomerular filtration rate (eGFR) and other kidney function markers are associated with cardiovascular disease (CVD) mortality [1]. It remains unclear whether integrating multiple kidney markers together can improve CVD mortality risk prediction and what would be an appropriate method of integration. In a small general population sample, we recently showed that confirmatory factor analysis (CFA) may predict CVD risk better than single markers, but it did not outperform cystatin C-based eGFR (eGFRcys) [2]. To assess whether our findings were context-dependent and to which extent they may extend to mortality risk assessment, we applied CFA and exploratory factor analysis (EFA), integrating five kidney function markers in the UK Biobank (UKBB) study, comparing risk discrimination for CVD mortality and renal failure mortality versus established eGFR formulas.

**Method:** We analyzed data from 366,758 UKBB participants (mean age 56.6 years; females 53.7%) without clinical history of kidney failure at baseline. Information on participants’ mortality was collected from the National Health System registry, using ICD-10 codes I00-I99 and N17-N19 to identify CVD mortality and renal failure mortality. We applied CFA and EFA to creatinine- and cystatin C-based estimated glomerular filtration rate (eGFRcre), eGFRcys, blood urea nitrogen (BUN), uric acid (UA), and serum albumin (Alb). EFA was fitted using maximum likelihood. Promax rotation was then applied. We fitted Cox regression models to examine the associations of mortality with kidney markers: CFA-based kidney index [CFA]; 1st EFA-based kidney index [EFA1]; 2nd EFA-based kidney index [EFA2]; eGFRcrecys; eGFRcys, and creatinine- and cystatin C-based eGFR (eGFRcyscrecs). Models were adjusted for sex, age, body mass index, education, self-reported ancestry, hypertension, diabetes, and tobacco smoking. The receiver operating characteristics (ROC) curve and the DeLong test were used to compare discriminatory ability of each index.
EVENTS: THE CKD-REIN COHORT STUDY

ASSOCIATED RISKS OF MAJOR ADVERSE CARDIOVASCULAR EVENTS: THE CKD-REIN COHORT STUDY

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Background and Aims: Anemia in chronic kidney disease (CKD) has been repeatedly associated with increased cardiovascular and all-cause morbidity and mortality. Most observational studies have focused on one single measurement of hemoglobin, but very few have investigated the trajectory of hemoglobin over time. Our aim was to identify, in moderate to severe CKD, typical profiles of hemoglobin trajectories, and to estimate their associated risk of major adverse cardiovascular event (MACE).

Method: We used data from the CKD-REIN cohort, which included 3033 patients with moderate to severe CKD from 40 nationally representative nephrology clinics in France between 2013 and 2016. A minimum of one hemoglobin measurement was necessary to be included. The primary endpoint was MACE defined as the first event among cardio-vascular death, myocardial infarction, stroke or hospitalization for acute heart failure. Secondary events included initiation of kidney replacement therapy (KRT) and death. A joint latent class mixed model was used to identify classes of hemoglobin trajectory and estimate the risk of each event. Once the model had identified classes and assigned participants in their class, we described the characteristics of patients in each class a posteriori. We also performed a posterior analysis to describe the course of estimated glomerular filtration rate (eGFR) in each class.

Results: A total of 3011 subjects were included in the analysis: 66% were men, median age at inclusion was 69 years. A total of 33874 hemoglobin measurements have been analyzed (median of 10 per patient). A total of 460 MACE, 522 KRT before MACE and 216 deaths before MACE or KRT, were recorded over a median follow-up of 4.3 years (Interquartile Range IQR 2.3-5.0). Five distinct classes were identified with a predominant one, Class-1 (‘constant’) including 63% (n = 1885) of the studied population with an overall stable trajectory surrounding a hemoglobin concentration of 13 g/dl. (See figure below). For this class, risks of events were very low throughout the follow-up. Patients in this class had fewer cardiovascular risk factors, lower eGFR, and less often increased proteinuria at baseline than in other classes.

Class-2 trajectory (late strong decline, n = 75, 2.5%) had an abrupt decline at 2 years of follow-up; concomitantly risks of KRT and death before MACE emerged but the risk of MACE remained low over the follow-up. Patients classified in this class had more often tubulo-interstitial or unknown nephropathy than in other classes. Classes 3 (late moderate decline, n = 438, 14.6%) and 4 (early moderate decline, n = 356, 11.8%) exhibited more
Figure 1: Trajectories of hemoglobin and associated risk of MACE, KRT before MACE or death before KRT or MACE, n = 3011, CKD-REIN study.

A moderate decline of hemoglobin level occurring on average at 3 and 1 year of follow-up, respectively. For these two classes, the risk of KRT before MACE increased from the start of these declines but their risks of MACE increased from the cohort entry. Class-5 (early strong decline, n = 257, 8.5%) had a collapsing trajectory right from the entry into the cohort, and had a risk of MACE increasing rapidly in the very first year. Patients from Class-3 and Class-5, who had the highest risk of MACE, also had a worse cardiovascular profile at baseline. The average eGFR trajectories estimated in each of the 5 identified classes of hemoglobin showed similar patterns as those for hemoglobin.

Conclusion: In patients with CKD under nephrology care, most of patients have normal and stable hemoglobin values over time. In about one third of patients, 4 profiles of hemoglobin decline were observed, likely matching those of eGFR decline. These 4 classes with declining profiles had different levels of MACE risk and a strong increased risk of KRT after hemoglobin decline. This study suggests that more attention should be paid to dynamic changes of hemoglobin in the management of CKD.

#4177
PREVALENCE OF UNRECOGNIZED CHRONIC KIDNEY DISEASE IN THE LOLLAND-FALSTER HEALTH STUDY: A POPULATION-BASED STUDY IN A RURAL-PROVINCIAL AREA OF DENMARK
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Background and Aims: In order to improve renal and cardiovascular outcome in patients with chronic kidney disease (CKD), it is important to identify patients with CKD in early stages of the disease. Given the asymptomatic nature of early-stage CKD, the majority of the CKD patients are living with an unrecognized condition. There is limited knowledge about the Danish prevalence of CKD stage 1-4. Moreover, previous studies have shown association between CKD and low socio-economic status. This study aims to increase the insights into prevalence and risk factors of CKD in a population living in a part of Denmark where income and life expectancy is below the national average.

Method: Data was derived from The Lolland-Falster Health Study (LOFUS) which is a population and household-based prospective cohort study at Lolland-Falster, a mixed rural-provincial area in Denmark. Data was obtained between 2016 and 2020 from questionnaires, clinical- and paraclinical evaluation. CKD was defined according to KDIGO classification (single test) as urinary albumin-to-creatinine ratio (UACR) >30 mg/g and/or estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m2. Univariate and multiple logistic regression models were used to evaluate potential risk factors for CKD.

Results: The study included 16,142 adult individuals. Characteristics of the population are reported in Table 1. The median age was 58.6 years (IQR 44.7-68.6) and 53% of the population were women. The overall CKD prevalence was 17.7% and was higher in women than in men (19.2% versus 16.0%, p-value < 0.001). Of the 2856 participants with CKD, 71.1% had CKD based on elevated UACR, 19.0% had CKD based on reduced eGFR and 9.9% had CKD based on reduced eGFR combined with elevated UACR. Among the participants with CKD, 31.8% had CKD stage 1, 39.2% had stage 2, 28.0% stage 3, and 1.1% had CKD stage 4-5. Less than 2% (n = 207) of the total population had a self-reported kidney-related diagnosis which correspond to only 4.5% of the individuals with CKD identified in the study. Among those with CKD stage 3-5, more than 27% did not report any kidney-related diagnosis. In univariate analyses, female sex (OR 1.25, 95% CI 1.15 – 1.35), age above 55 years (OR 3.55, 95% CI 3.01 – 4.20), BMI > 25 kg/m² (OR 1.02, 95% CI 1.02 – 1.03), diabetes (OR 3.38, 95% CI 2.89 – 3.95), hypertension (OR 3.34, 95% CI 3.06 – 3.65) and low income (OR 1.24, 95% CI 1.12 – 1.37) were associated with CKD.
Table 1: Characteristics of the population.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N = 16,142)</th>
<th>No CKD (N = 13,241)</th>
<th>CKD (N = 2,856)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex – n (%)</td>
<td>8,563 (53.0)</td>
<td>6,899 (52.1)</td>
<td>1,664 (57.5)</td>
</tr>
<tr>
<td>Age [years] – median (IQR)</td>
<td>58.6 (44.7-68.6)</td>
<td>56.6 (44.5-66.9)</td>
<td>67.8 (56.8-75.2)</td>
</tr>
<tr>
<td>BMI category – n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0-29.9 kg/m²</td>
<td>6,133 (38.2)</td>
<td>5,062 (38.4)</td>
<td>1,061 (37.5)</td>
</tr>
<tr>
<td>&gt; 30 kg/m²</td>
<td>4,105 (25.6)</td>
<td>3,237 (24.5)</td>
<td>853 (30.2)</td>
</tr>
<tr>
<td>Plasma creatinine [μmol/L] – mean (SD)</td>
<td>74.7 (17.4)</td>
<td>72.9 (12.9)</td>
<td>82.8 (29.1)</td>
</tr>
<tr>
<td>UACR category – n (%) &lt;30 mg/g</td>
<td>13,267 (85.4)</td>
<td>12,765 (100)</td>
<td>502 (17.8)</td>
</tr>
<tr>
<td>30 to &lt;300 mg/g</td>
<td>2122 (13.6)</td>
<td>0</td>
<td>2,122 (75.4)</td>
</tr>
<tr>
<td>≥300 mg/g</td>
<td>191 (1.2)</td>
<td>0</td>
<td>191 (6.8)</td>
</tr>
<tr>
<td>Self-reported CKD – n (%)</td>
<td>207 (1.4)</td>
<td>83 (0.7)</td>
<td>123 (4.3)</td>
</tr>
<tr>
<td>Self-reported cardiovascular disease – n (%)</td>
<td>447 (2.9)</td>
<td>302 (2.4)</td>
<td>145 (5.3)</td>
</tr>
<tr>
<td>Diabetes – n (%)</td>
<td>710 (4.4)</td>
<td>423 (3.2)</td>
<td>287 (10.1)</td>
</tr>
<tr>
<td>Hypertension – n (%)</td>
<td>7,164 (44.4)</td>
<td>5,192 (39.2)</td>
<td>1,957 (68.6)</td>
</tr>
<tr>
<td>Current or former smoking – n (%)</td>
<td>8,282 (54.3)</td>
<td>6,658 (53.2)</td>
<td>1,599 (59.2)</td>
</tr>
</tbody>
</table>

CKD denotes chronic kidney disease and UACR urine albumin-to-creatinine ratio. Missing observations: Plasma creatinine n = 174; UACR category n = 562

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#4140

**DAPRODUSTAT VERSUS RECOMBINANT HUMAN ERYTHROPOIETIN FOR TREATING ANAEMIA OF CHRONIC KIDNEY DISEASE: COST EFFECTIVENESS MODEL METHODOLOGY AND FINDINGS**

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¹GSK, Stevenage, Hertfordshire, United Kingdom, ²GSK, Brentford, London, United Kingdom, ³GSK, Mississauga, ON, Canada and ⁴FIECON, St Albans, United Kingdom

**Background and Aims:** Anaemia is a common manifestation in patients with chronic kidney disease (CKD). Daprodustat, a hypoxia-inducible factor prolyl hydroxyylase inhibitor, offers an alternative to conventional treatment with recombinant human erythropoietins (rhEPOs). This study reports the development of a cost-effectiveness analysis to support reimbursement discussions for daprodustat in Canada.

**Method:** A Markov model was developed to conduct a cost-utility analysis to compare expected costs and outcomes associated with daprodustat, vs two rhEPO treatment comparators (darbepoetin alfa [DA] or epoetin alfa [EA]), which represent standard of care. The model used a lifetime time horizon, and a publicly funded Canadian healthcare payer perspective for adults with anaemia of CKD (on/not on dialysis). Clinical inputs for the model were obtained from two Phase 3 clinical trials: ASCEND-D¹ (daprodustat vs DA or EA in 2964 dialysis patients) and ASCEND-ND² (daprodustat vs DA in 3872 non-dialysis patients). Efficacy and adverse event profiles of both rhEPOs were assumed equal. Patients entering the model (Figure) receive daprodustat, DA or EA. The model includes five health states informed by ASCEND-D and ASCEND-ND: non-dialysis, dialysis, kidney transplant, post-transplantation and terminal care. While in the dialysis or non-dialysis health state, costs and utilities are assigned based on three haemoglobin (Hb) levels: <10g/dL, 10–11.5g/dL or >11.5g/dL. A monthly cycle length is utilised and aligned with the ASCEND study visits and observations up to Week 52. Hb concentrations from ASCEND-D and ASCEND-ND are used to estimate proportions of patients in the target Hb range of 10–11.5g/dL, and non-target Hb levels. They were assumed to have different utility values. Patients could transition from non-dialysis to dialysis; in the latter state, patients could die or receive a kidney transplant, and transition to a post-transplantation state. Transition probabilities were derived from ASCEND-D and ASCEND-ND data and the literature. The median follow-up durations in ASCEND-D and ASCEND-ND were 2.5 and 1.9 years, respectively, necessitating extrapolation to the model time horizon; increases over time in the transition probabilities were applied. It is assumed that patients cannot transition back to non-dialysis from the dialysis state. Patients may transition to death from any health state, with mortality risks informed by the ASCEND trials and Canadian all-cause mortality data. Costs in the model included treatment acquisition and administration, cold-chain storage, dialysis, kidney transplant, transfusions of red blood cells and iron, and adverse events (AEs). All costs were sourced from fee schedules (2022 SCAd) or the literature. Utilities for health states and HB levels were obtained from the ASCEND trials; AE-associated utility decrements could not be estimated from ASCEND data due to low event rates – hence, disutilities were sourced from the literature.

**Results:** In the probabilistic reference case analysis, daprodustat was less costly (comparison with DA: -$8763; EA: -$13,864) and produced more quality-adjusted life years (DA: +0.012; EA: +0.018; Table). The incremental savings with daprodustat versus DA and EA were -$860 and -$1033, respectively, in the non-dialysis state, and -$7904 and -$12,831 in the dialysis state. Contributors to the cost savings with daprodustat include an absence of cold-chain storage costs and reduced administration costs.

**Conclusion:** This study indicates that daprodustat is less costly and originates more QALYs than DA and EA in the treatment of anaemia due to CKD. In this setting, daprodustat may provide cost savings from a Canadian public payer perspective. The model described here could be adapted to other perspectives, including European countries.

**REFERENCES**

#2560
HEMOGLOBIN VARIABILITY AND ADVERSE CLINICAL EVENTS IN PATIENTS WITH NON-DIALYSIS-DEPENDENT CHRONIC KIDNEY DISEASE AND ANEMIA IN CONTINUOUS CARE
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Background and Aims: Anemia management in non-dialysis dependent chronic kidney disease (NDD-CKD) patients has attracted attention with the introduction of new treatment options, such as prolyl hydroxylase domain enzyme inhibitors (HIF-PHI). However, studies reporting comprehensive information on anemia management in NDD-CKD patients are limited. While previous studies reported increased risks of adverse clinical events associated with hemoglobin (Hb) fluctuation in hemodialysis patients, limited information is available in NDD-CKD patients.

Method: A retrospective cohort study was performed using a Japanese nationwide electronic medical record-based hospital database. Patients with...
stage ≥3a NDD-CKD, aged ≥18 years, and at least one recorded Hb <11 g/dL between January 1st 2013 and April 30th 2021 were included. Patients already receiving any anemia treatment (erythropoiesis stimulating agent (ESA), iron, or HIF-PHI) were excluded. Hb levels were collected at the index date (the date of the first recorded Hb <11 g/dL) and during the follow-up period. Clinical events included all-cause death, cardiovascular (CV) events (myocardial infarction, unstable angina pectoris, stroke, or hospitalization for heart failure), dialysis introduction, and red-blood-cell transfusion. Time-dependent Cox proportional hazard models, adjusted by clinically relevant variables were applied to assess the risk of clinical events associated with transitioning Hb fluctuation patterns, categorized into six groups: within the target Hb range (11–13 g/dL); consistently below the target (low); consistently above the target (high); low-amplitude fluctuation around the upper limit of the target (LAH); low-amplitude fluctuation around the lower limit of the target (LAL); and, high amplitude fluctuation across the target (HA).

**Results:** Of 162,170 patients with CKD, 26,626 (16.4%) NDD-CKD patients with Hb <11 g/dL were identified (median follow-up length, 1.9 years). The mean age was 75.9 years, and 37.8% were female. In overall patients, the mean (±SD) Hb levels at index and at 3, 6, and 12 months of follow up were 9.9±1.2 g/dL, 10.6±1.5 g/dL, 10.8±1.6 g/dL, and 10.9±1.6 g/dL, respectively. The proportion of patients with Hb <10 g/dL at index and at 12 months were 34.3% and 23.9%, respectively. In the subgroup of patients treated with ESA or HIF-PHI (n = 8,876), the mean Hb (±SD) levels had increased from 9.3±1.3 g/dL to 10.3±1.5 g/dL at 3 months, 10.5±1.5 g/dL at 6 months, and 10.6±1.5 g/dL at 12 months after treatment initiation. In this subgroup, the proportion of patients with Hb <10 g/dL had decreased from 70.0% to 30.1% at 12 months. Fig. 1 shows the Hb levels and proportions of patients with Hb <10 g/dL by treatment type. During the follow-up period, 5,991 (22.5%) deaths, 3,545 (13.3%) CV events, 4,231 (15.9%) dialysis introductions, and 5,561 (20.9%) red-blood-cell transfusions were observed. The risks of clinical events were significantly higher in the low and LAL Hb groups than in the target Hb group (Fig. 2). The hazard ratios (95% CIs) for death, CV events, dialysis introduction, and red-blood-cell transfusion in the low Hb group, compared to the target Hb group were 1.35 (1.20–1.52), 1.90 (1.58–2.27), 1.75 (1.39–2.20), and 2.80 (2.28–3.43), respectively, and in the LAL Hb group were 1.28 (1.14–1.43), 1.71 (1.43–2.04), 1.85 (1.48–2.33), and 1.64 (1.33–2.02), respectively. In HA Hb group, significantly higher risks for dialysis introduction and red-blood-cell transfusion were observed.

**Conclusion:** This study reports comprehensive information on anemia management in NDD-CKD patients in clinical practice. Despite treatment for Hb correction, 20–30% of patients persistently remained at low Hb levels. The increased risk of adverse clinical events associated with Hb fluctuations suggest that stable Hb control within the target range is important to reduce the risk of mortality and morbidity in patients with NDD-CKD and anemia.
#3676

EVALUATION OF HAEMOGLOBIN RESPONSE IN PATIENTS WITH CKD-RELATED ANAEMIA NOT ON DIALYSIS RECEIVING DAPRODUSTAT OR CONTROL IN ASCEND-ND

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**Background and Aims:** Daprodustat (Dapro) is a novel hypoxia-inducible factor prolyl hydroxylase inhibitor being investigated in anaemia of chronic kidney disease (CKD). ASCEND-ND achieved non-inferiority (NI) for Dapro vs darbepoetin alfa (Darbe) in both coprimary endpoints, mean change in haemoglobin (Hb) levels from baseline to the evaluation period (EP; Week [Wk] 28–Wk 52) and first occurrence of a composite major adverse cardiovascular event, in patients (pts) with anaemia of CKD not on dialysis. Here, we present key Hb efficacy data and evaluate differences in Hb response within ASCEND-ND subgroups.

**Method:** Pts with Stages 3–5 CKD (not on erythropoiesis stimulating agents [ESAs]; Hb 8–10g/dL; on ESAs: Hb 8–11g/dL) were randomised 1:1 to Dapro or Darbe. Statistical analysis methods for the coprimary endpoint have been published.1 Secondary endpoints evaluated during the EP included: 1) the percentage of Hb responders (pts with mean evaluable Hb within the analysis range [10–11.5g/dL]); 2) the percentage of time Hb was within the analysis range; 3) analysis of Hb change from baseline to Wk 52. Secondary endpoints were analysed as follows: 1) Cochran-Mantel-Haenszel test adjusted for ESA use and region; 2) Rosendaal method (evaluable Hb values) and Hodges-Lehmann and stratified Mann-Whitney estimates of treatment effect, analysed with a van Elteren’s test stratified by ESA use and region; 3) mixed model repeated measures analysis (on-/off-treatment, observed Hb values from Wks 28–52) with factors for ESA use, region, baseline Hb (by time), treatment by time interactions. Secondary and subgroup analyses were not multiplicity adjusted.

**Results:** Of 3872 pts in ASCEND-ND (Dapro n = 1937; Darbe n = 1935), mean baseline Hb levels were similar for both treatment arms and mean change in the EP Hb level for Dapro and Darbe met the prespecified NI margin of –0.75 g/dL (difference = 0.08g/dL; 95% confidence interval [CI] = 0.03, 0.13).1 Subgroup analyses were consistent with coprimary analyses (Table), with little or no heterogeneity between most groups: 7/22 subgroups (ethnicity, high-level race, region, ESA use at randomisation, pre-ESA dose group, history of stroke, and hospitalisation 6 months prior to screening) had interaction p values <0.1; however, all subgroups met the NI criterion with between-group differences that were not clinically meaningful. Proportions of pts within the Hb analysis range were higher for Dapro than Darbe in the EP overall and regardless of baseline ESA use and similar for region (Table). The median (interquartile range) percentage of time Hb was in the analysis range during the EP was 70.5% (45.3%–93.2%) for Dapro vs 63.2% (33.7%–88.9%) for Darbe. Daproduction was associated with a nominally NI (margin of –15%) and significant increase in percentage time in analysis range during the EP (estimate of median difference [95% CI] = 4.57% [2.04%, 7.11%; one-sided p <0.0001]). The estimate (95% CI) for the probability that Dapro had a greater percentage of time Hb within the analysis range than Darbe was 0.55 (0.53, 0.57); the lower boundary of the 95% CI exceeded 0.50, representing equal probability between the two treatment arms. Results by region were similar for Dapro vs Darbe (treatment effect): Asia Pacific = 0.56; Eastern Europe/South Africa = 0.51; Western Europe/Canada/Australia/New Zealand/Israel, 0.58; Latin America, 0.58; USA, 0.55). In mixed-model repeated measures analysis, g/dL Hb change (standard error) at Wk 52 was 0.76 (0.029) with Dapro and 0.73 (0.029) with Darbe (difference [95% CI] = 0.03 [−0.05, 0.11]). Hb efficacy was similar regardless of ESA use (Figure).

**Conclusion:** Daprodustat was effective and NI to Darbe for maintaining Hb in non-dialysis pts with anaemia of CKD, and results of subgroup analyses were consistent with the coprimary analyses. Additionally, Daprodustat raised and maintained Hb within the analysis range regardless of baseline ESA use or region. These preliminary analyses indicated a nominal NI showcasing greater Hb time in range with Daprodustat vs Darbe; further analyses will be presented to fully characterise this interaction.
Note: Error bars indicate Confidence Interval. Baseline and visits on or before Day 1 include only pre-treatment values. Post-randomisation values include observed on and off treatment values. The horizontal reference lines in the figures represent the Hb analysis range (10-11.5 g/dL). The Hb target range for dose changes 10–11 g/dL. The dashed vertical lines represent the evaluation period (Week 28 to Week 52).

Dapro, daprodustat; Darbe, darbepoetin alfa; ESA, erythropoiesis stimulating agent; Hb, haemoglobin; SCR, screening.

Figure. Post-randomisation Hb data by visit and ESA use at baseline
REFERENCE


#2889
CAROTID PLAQUE THICKNESS PREDICTS CARDIOVASCULAR EVENTS AND DEATH IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background and Aims: Classical risk scoring systems highly underestimate the elevated risk of cardiovascular (CV) disease in chronic kidney disease (CKD) (1). Coronary artery calcification score (CACS) has improved prediction of CV events in patients with CKD (2). Recently, ultrasound examination of the carotid arteries with measurement of maximal carotid plaque thickness (cPTmax) has demonstrated similar predictive value as CACS in the general population (3). This is the first study to investigate whether cPTmax can predict CV events in patients with CKD. We also compared the predictive value of cPTmax and CACS.

Method: Two hundred patients with CKD stage 3 from the Copenhagen CKD Cohort underwent ultrasound scanning of the carotid arteries in 2016 to 2017. The assessment consisted of finding areas with plaque, if there were any, and measuring the thickest part of the plaque, cPTmax, defined as the radial distance from the media–adventitia interface to the intima–lumen interface towards the center of the arterial lumen. For the statistical analysis only the anatomical side with the highest cPTmax was used. The intra-observer coefficient of variation was 9%. Based on the distribution of cPTmax, the subjects were divided into 3 groups: No plaques, cPTmax 1.0-1.9 mm and cPTmax > 1.9 mm (the median cPTmax in the group was 1.9 mm). One hundred and seventy-five of the patients underwent a non-contrast CT scan of the coronary arteries, which was used to measure CACS. The patients were divided into the following categories: no calcification, CACS = 1-100, CACS = 101-400 and CACS > 400. The follow-up time was time elapsed from the ultrasound scan and until a predefined end-date or the time of first event, which was defined as a composite of major CV events or death of any cause (MACE). CV events included: myocardial infarction, percutaneous coronary intervention, coronary bypass surgery, ischemic stroke, carotid endarterectomy or stenting, non-traumatic lower limb amputation, lower limb artery bypass graft, percutaneous transluminal angioplasty of a lower limb.

Results: The average follow-up time was 5.4 years. Twenty patients (10%) experienced a CV event and 28 patients died (14%). In a crude absolute risk plot (Figure), patients with no plaque at baseline showed the lowest risk of MACE, whereas patients with cPTmax 1.0-1.9 mm showed an intermediate risk, and patients with cPTmax >1.9 mm the highest risk (log rank test, p<0.0001). When using the group of patients with no plaque as the reference in an unadjusted Cox-regression analysis, the hazard ratio (HR) of MACE was significantly increased in patients with cPTmax 1.0-1.9 mm (HR = 3.8 (CI: 1.5 - 9.9), p<0.01) and in patients with cPTmax >1.9 mm (HR = 8.4 (CI: 3.4 – 20.8), p<0.0001). After adjustment for age, sex, diabetes, smoking, hypertension, and hypercholesterolemia, only patients with cPTmax >1.9 mm showed a significantly increased HR of MACE (HR 3.2, CI 1.1-9.3), p<0.05. We applied C-statistics to assess which imaging technique had the best predictive value of MACE in this cohort. The differences in C-statistics were similar for the two imaging methods: cPTmax (0.21, p<0.0001) and CACS (0.21, p<0.0001).

Conclusion: Our results indicate that measurement of cPTmax may be a useful method for prediction of MACE in CKD.

In the present small study, cPTmax and CACS showed equal potential for predicting MACE. Ultrasound imaging is more convenient, more widely available, and without radiation exposure. To further assess the value of cPTmax in predicting CV risk in CKD, a larger study of patients with all CKD stages is needed.
REFERENCES


#3986
THE ROLE AND MECHANISM OF EZH2 IN VASCULAR CALCIFICATION ASSOCIATED WITH CHRONIC KIDNEY DISEASE
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Background and Aims: Vascular calcification (VC) is a prevalent complication in chronic kidney disease and contributes to increased cardiovascular morbidity and mortality. EZH2 (Enhancer of zeste 2 homolog-2) is reported as a key epigenetic regulator involved in various kidney diseases such as acute kidney injury, renal fibrosis, diabetic nephropathy, and lupus nephritis. In this study, we aimed to investigate the role of EZH2 in chronic kidney disease associated vascular calcification.

Method:
1. Patients and Radial Artery Analysis
Radial arteries with or without calcification from patients with end-stage renal disease that underwent arterial venous fistular operation were collected for Von Kossa staining and immunohistochemical (IHC) staining.

2. Animal model of Chronic renal failure-Vascular Calcification (CRF-VC) (in vivo)
An adenine and phosphate (1.2%) diet-induced CRF mouse model was designed following an 8-week program. The thoracoabdominal arteries of mice and rats were dissected to assay Ca deposition and histological analysis. Plasma levels of Alkaline phosphate (ALP), and phosphate (Pi) were measured. The transcription level of EZH2 and Runt-related transcription factor 2 (Runx2) were measured by real-time PCR and IHC staining.

3. Aortic ring calcification (ex vivo)
Thoracic aortas were dissected from SD rat. To induce calcification, Pi (NaH₂PO₄/Na₂HPO₄ [pH = 7.4]) was added to HG-DMEM at a final concentration of 2.6 mmol/l. After the indicated incubation periods (3, 5, 7 days), samples were taken for Calcium deposition assay, Western blotting and histological analysis.

4. Cell culture and treatment (in vitro)
Calcification of rat smooth muscle embryonic thoracic aorta cell line A7r5 (VSMC) was induced by incubation in calcifying media. 3-deazaneplanocin A (3-DZNeP), a carbocyclic analog of adenosine was added right after Pi to block EZH2 activation. After the indicated incubation periods, samples were collected for Calcium deposition assay and Western blotting analysis.

Results:
1. In vivo, EZH2 protein level was increased in calcified radial arteries from patients with end-stage renal disease that underwent arterial venous fistular operation. In CRF-VC mice model, the aortic calcium deposition markedly aggravated in the group induced by adenine diet. Severe vascular calcification was also induced as shown by increased intensity of von Kossa. Moreover, IHC and q-PCR results showed that the protein and transcriptional levels of EZH2 expression were upregulated in calcified aortas of CRF mice, in paralleled with the increased expression Runx2 in protein and transcriptional levels.

2. Ex vivo, histological analysis revealed significant medial vascular calcification in the aortic ring culture with this calcifying medium for 7 days. Similarly, WB results showed that the expression of EZH2 and its downstream, methylation of Histone H3 at lysine 27 (H3K27me3), were significantly enhanced after high Pi medium stimulation while the osteogenic markers Runx2, Osteopontin (OPN) and Msh homeobox 2 (Msx2) protein levels were upregulated and the expression of VSMC differentiation markers α-SMA, Calponin (CNN) and Smooth muscle protein 22 (SM22) were downregulated.

3. In vitro, the osteogenic markers Runx2, OPN and Msx2 were significantly upregulated in high Pi treated VSMCs compared to control VSMCs. Moreover, the epigenetic markers EZH2 and H3K27me3a were markedly repressed in calcifying VSMCs by time.
4. 3-DZNep treatment reduced the calcium deposition in a concentration dependent manner. Western blotting showed that 3-DZNep treatment blocked the increased expression of osteogenic markers Runx2, Bone morphogenetic protein 2 (BMP2) as well as epigenetic markers EZH2 and H3K27me3a by high Pi treatment, indicating that inhibition of EZH2 attenuates VSMCs Calcification.

**Conclusion:** Our study revealed that EZH2 is highly expressed in calcified vascular tissues of CRF patients and CRF mice, rat aorta culture and VSMCs calcification models, and EZH2 inhibitor 3-DZNep attenuated calcification of VSMCs. EZH2 could be a promising target for treatment of vascular calcification in CRF patients.
Figure 2. A. 10- to 12-week-old male mice were fed with chow diet or adenine diet of various concentration for 8 weeks. B-F. The levels of serum creatinine (Scr; C), blood urea nitrogen (BUN; D), uric acid (UA; E), phosphate (Pi; E) and alkaline phosphate (ALP; F) were measured. G. Quantification of calcium deposition in aortas of mice fed with chow diet or adenine diet for 8 weeks. H. Representative von Kossa staining and Runx2, EZH2 staining. I. Quantitative PCR analysis of mRNA levels of Runx2 and EZH2. Data represent mean ± SE.
Figure 3. EZH2 promotes aortic ring calcification with high phosphate (ex vivo study). A. Histological analysis of aortic rings with Von kossa staining (Bar=100μm). B. Time course analysis of vascular calcification induced by phosphate stimulation. C. Representative Western blot analysis and quantification of EZH2, H3k27me and osteogenic genes (Runx2, Mx2, OPN) and VSMC differentiation markers (α-SMA, CNN and SM22) protein levels. At least 3 independent experiments were performed. *P<0.05 by one-way ANOVA followed by the Student-Newman-Keuls test for post-hoc comparison.
Figure 4: EZH2 promotes VSMC calcification in vitro. A-B. Quantification of calcium (Ca) deposition and Alizarin Red staining in A7r5 cells under Pi stimulation for 3, 5, 7 days. The data presented as the means±SEM from at least 3 independent experiments in triplicate. *P<0.05 by two-way ANOVA followed by the Bonferroni test. C. Representative Western blot analysis and quantification of EZH2, H3k27me and osteogenic genes (Runx2, Msx2, OPN) protein levels β-GP stimulation for 1-3 days (D).
EFFICACY OF PAXLOVID WITHIN 5 DAYS VERSUS 5 DAYS AFTER DIAGNOSIS IN COVID-19 PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background
Paxlovid is a commonly used antiviral drug for patients with COVID-19. There are few studies in patients with CKD. Therefore, we conducted a retrospective cohort study to compare the drug efficacy of Paxlovid in patients with CKD at different time points after COVID-19 infection.

Methods
70 CKD patients
4 weeks follow-up

Results
Use Paxlovid
After 5 days

Conclusion
Early use of Paxlovid to inhibit virus replication has a good therapeutic effect on CKD patients.
Background and Aims: With the liberalization of COVID-19 control policies in mainland China, the majority of the Chinese population has experienced Omicron infection since mid-December 2022. Paxlovid is a commonly used antiviral drug for patients with COVID-19, but there are few studies in patients with chronic kidney disease (CKD). Therefore, we conducted a retrospective cohort study to explore the drug efficacy of Paxlovid in patients with CKD at different time points after COVID-19 infection.

Method: 70 CKD patients who were admitted to the Department of Nephrology, the Third Affiliated Hospital of Southern Medical University before January 07, 2023 and diagnosed with COVID-19 were included. The patients were divided into three groups: No Paxlovid group, Paxlovid group within 5 days of diagnosis, Paxlovid group after 5 days of diagnosis, each patient was followed-up for at least 4 weeks. The primary outcome measures included all-cause mortality, length of hospital stay, PCR positive duration and the aggravation of the disease requires ICU admission or mechanical ventilation, or the initiation of renal replacement therapy, and re-hospitalization. The t test or non-parametric test was used to compare the quantitative data, the chi-square test was used to compare the rates, and the K-M curve and Cox regression model were used for survival analysis.

Results: Among the 70 patients (mean age 65.8±15.90 years, male sex 67.7%), Paxlovid was not used in 35 patients (50%), used in 16 patients (22.9%) within 5 days of diagnosis, Paxlovid group after 5 days of diagnosis, each patient was followed-up for at least 4 weeks. The primary outcome measures included all-cause mortality, length of hospital stay, PCR positive duration and the aggravation of the disease requires ICU admission or mechanical ventilation, or the initiation of renal replacement therapy, and re-hospitalization. The t test or non-parametric test was used to compare the quantitative data, the chi-square test was used to compare the rates, and the K-M curve and Cox regression model were used for survival analysis.

Results: Among the 70 patients (mean age 65.8±15.90 years, male sex 67.7%), Paxlovid was not used in 35 patients (50%), used in 16 patients (22.9%) within 5 days of diagnosis, and in 19 patients (27.1%) after 5 days. At the start of follow-up, there were no significant differences in age, gender, eGFR, comorbidities, COVID-19 severity and laboratory parameters between patients who used Paxlovid within 5 days and after 5 days of diagnosis. However, patients who used Paxlovid had more severe disease than those who did not use Paxlovid (P<0.001), and patients were more likely to use glucocorticoids (74.3% vs 17.1%, P< 0.001), as well as lower lymphocyte count (0.54*10^9/L vs 0.85*10^9/L, P = 0.016) and percentage (9.5% vs 14.2%, P = 0.009). Higher levels of IL-6 (68.57 pg/ml vs 14.66 pg/ml, P = 0.015) and CRP (113.36 mg/L vs 24.57 mg/L, P = 0.001). After a median follow-up of 45 days, we found that patients used Paxlovid had significantly longer hospital stays and higher rehospitalization rates, with subgroup analysis finding that the increased length of stay and rehospitalization rates were mainly attributable to Paxlovid use after 5 days of diagnosis. Patients who used Paxlovid after 5 days had longer nucleic acid positive time (25 days vs 7 days, P = 0.001) and longer hospital stay (16 days vs 10 days, P = 0.008) compared with those who used Paxlovid earlier. At the end of follow-up, a total of nine patients had died. The K-M survival curve was drawn after the exclusion of mild patients, which showed that patients who used Paxlovid within 5 days had the lowest risk of death, those who did not use Paxlovid had the highest risk of death, and those who used Paxlovid after 5 days fell in between. However, due to the small sample size, the difference was not statistically significant (P = 0.155). The Cox regression analysis showed that IL-6 (HR 1.009; 95% CI: 1.004-1.014, P = 0.001) was the best predictor of death risk in COVID-19 patients with CKD after adjusting other factors.

Conclusion: The risk of death in CKD patients infected with COVID-19 is significantly higher than that in the general population. Early use of Paxlovid to inhibit virus replication has a good therapeutic effect on these patients, which can greatly reduce the risk of death, admission to ICU or emergency renal replacement therapy. Delayed use of Paxlovid may increase the time of nucleic acid positive and the length of hospital stay.

Figure 1: K-M curves for different treatment groups.
EFFECTS OF EMPAGLIFLOZIN ON KIDNEY AND CARDIAC MRI MEASURES IN PATIENTS WITH CHRONIC KIDNEY DISEASE
Parminder Judge and on behalf of the EMPA-KIDNEY collaborative group
University of Oxford, Oxford, United Kingdom

Background and Aims: EMPA-KIDNEY demonstrated empagliflozin reduced the risk of kidney disease progression or cardiovascular death in patients with CKD at risk of progression, but the mechanisms of benefit are uncertain. MRI was used to assess whether empagliflozin modified the structure and function of the kidneys and heart at around 18 months after randomization.

Method: Randomized participants from 8 sites in UK and Germany without a contraindication to MRI scanning, were eligible and invited to participate in this substudy. MRI scans were performed using a standardized protocol. Renal T1 mapping (MOLLI 5[3]3 scheme which measures fibrosis and inflammation) was computed by first segmenting MOLLI data using a U-net and then applying the masks to both kidneys. Cardiac MRI included cine steady-state free precession imaging to assess biventricular volumes, mass and function, and T1 mapping to assess myocardial inflammation and fibrosis. The primary outcome was kidney cortical T1 mapping measured by MOLLI. Secondary outcomes included LV ejection fraction, myocardial T1 MOLLI and LV mass index. Differences in MRI measurements between treatment groups were analysed using linear regression adjusted for baseline age, sex, eGFR, UACR and diabetes status. 172 participants were required to provide 90% power at 2p = 0.05 to detect a 50 ms difference in T1.

Results: 172 participants had an MRI scan around 18 months after randomization. 93 (54%) were allocated empagliflozin and 79 (46%) placebo. Mean (SD) age was 60 (16) years, 26% were female and 23% had diabetes. Mean eGFR was 37 (14) ml/min/1.73m² and geometric mean (95% CI) UACR was 242 (182-322) mg/g (Table 1). Adjusted mean (SE) cortical T1 mapping by MOLLI was 1623 (10) ms in those allocated empagliflozin versus 1634 (11) ms in those allocated placebo, difference in means (95% CI) −11 (−41 to 18), P = 0.45 (Table 2). Medullary T1 MOLLI scores were similar. Empagliflozin had no significant effect on cardiac MRI measures: difference (95% CI) in LV ejection fraction 1% (−1 to 4); myocardial T1 MOLLI −3 ms (−16 to 10); LV mass index −3 g/m² (−5 to 0) (Table 2).

Conclusion: Empagliflozin had no significant effect on MRI-based measures of fibrosis within the kidney cortex or myocardium in people with CKD at risk of progression. There was no effect of treatment on measures of cardiac structure or function. Further MRI measures will be available for presentation by the time of the ERA congress.

Funding: Boehringer Ingelheim, Eli Lilly and others; Clinicaltrials.gov:NCT03594110.
### Table 2: Effect of allocation to empagliflozin versus placebo on kidney and cardiac MRI parameters at 18 months.

<table>
<thead>
<tr>
<th>Outcome (units)</th>
<th>Empagliflozin (n = 93)</th>
<th>Placebo (n = 79)</th>
<th>Difference in means (95% CI)†</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal cortical T1 MOLLI (ms)</td>
<td>1623 (10)</td>
<td>1634 (11)</td>
<td>-11 (-41, 18)</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Kidney</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medullary T1 MOLLI (ms)</td>
<td>1930 (11)</td>
<td>1923 (11)</td>
<td>7 (-24, 37)</td>
<td>0.67</td>
</tr>
<tr>
<td>Corticomedullary difference in T1 MOLLI (ms)</td>
<td>307 (7)</td>
<td>289 (8)</td>
<td>18 (-2, 39)</td>
<td>0.08</td>
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<tr>
<td><strong>Cardiac</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Myocardial T1 MOLLI (ms)</td>
<td>1275 (5)</td>
<td>1278 (5)</td>
<td>-3 (-16, 10)</td>
<td>0.67</td>
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<tr>
<td>LV ejection fraction (%)</td>
<td>52 (1)</td>
<td>51 (1)</td>
<td>1 (-1, 4)</td>
<td>0.37</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>45 (1)</td>
<td>48 (1)</td>
<td>-3 (-5, 0)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

†Values are absolute differences in arithmetic means (95%CI). The estimates and p values were derived from linear regression with adjustment for elements included in the minimization algorithm which determined treatment allocation (age, sex, prior diabetes, eGFR, and uACR [but not region as the MRI substudy was only conducted in Europe]).

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**EFFECTS OF EMPAGLIFLOZIN ON FLUID OVERLOAD IN CHRONIC KIDNEY DISEASE: AN EMPA-KIDNEY BIOIMPEDANCE SUBSTUDY**

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**Background and Aims:** The EMPA-KIDNEY trial showed that, compared to placebo, empagliflozin 10 mg once daily reduced the risk of kidney disease progression or cardiovascular death in 6609 patients with chronic kidney disease at risk of progression. We aimed to assess effects of empagliflozin on bioimpedance-measured fluid overload and adiposity in a subset to better understand the mechanisms of cardiovascular benefits of sodium glucose co-transporter-2 inhibitors.

**Method:** This EMPA-KIDNEY substudy added Body Composition Monitor (BCM) measurements at randomization and the 2 and 18 month follow-up visits to the trial’s main protocol-specified procedures. The primary outcome was Absolute Fluid Overload (a parameter reflecting overhydration, derived from extracellular and intracellular resistance). Pre-specified subgroup analyses of the primary outcome were by sex, diabetes status, estimated glomerular filtration rate (eGFR) and N-terminal pro-brain-type natriuretic peptide (NT-proBNP) at baseline. The key secondary analysis was a composite of death from heart failure, heart failure hospitalisation or development of new moderate (>7%, ≤15%) or severe (>15%) BCM-measured Relative Fluid Overload. Tertiary outcomes included weight, anthropometry, and other BCM-measurements of body water and adiposity. The primary outcome was analysed using mixed-model repeated measures (MMRM) methods. The key secondary outcome used time-to-first event methods.

**Results:** A total of 660 EMPA-KIDNEY participants were recruited into this substudy. Mean age was 64 years, 205 (31%) were female and 245 (37%) had diabetes. Mean (SD) eGFR was 36 (12) ml/min/1.73m² and median (Q1-Q3) NTpro-BNP was 211 (93-581) ng/L. Mean (SD) Absolute Fluid Overload at baseline was 0.4 (1.6) L, 19% had moderate fluid overload and 5% fulfilled criteria for severe fluid overload at baseline. Compared to placebo, the mean study average absolute difference in Absolute Fluid Overload was -0.24L (95% CI -0.38, -0.11), with similar differences at 2 months and 18 months (Figure 1). This difference was similar in men and women, in people with and without diabetes, and across the spectrum of eGFR and NT-proBNP studied (Figure 2). The number of key secondary outcomes was low and there was no significant difference in the risk of this outcome between treatment groups (35/332 [10%] vs 38/328 [12%], hazard ratio 0.91 [95% CI 0.57, 1.45], p = 0.69).

**Conclusion:** In patients with chronic kidney disease, empagliflozin reduced bioimpedance-measured fluid overload irrespective of diabetes status or level of eGFR. This effect persisted for at least 18 months with no evidence of attenuation over time.

**Funding:** Boehringer Ingelheim, Eli Lilly and others; Clinicaltrials.gov:NCT03594110.
Figure 1: Effect of Empagliflozin versus Placebo on Mean Absolute Fluid Overload by Time. Mean Absolute Fluid Overload in litres at randomization is plotted separately for empagliflozin and placebo groups at time 0. The estimated marginal means (and standard errors) for the Absolute Fluid Overload value (from the MMRM model) within the time window surrounding the 2-month and 18-month follow-up visits are plotted at the median follow-up day in each treatment group. The estimated means are adjusted for baseline Absolute Fluid Overload and for any differences in key baseline characteristics (age, sex, diabetes, eGFR and uACR) between treatment groups.

Figure 2: Effect of Empagliflozin versus Placebo on Mean Absolute Fluid Overload (in Litres) By Pre-specified Subgroups. Analyses using MMRM methods excluded 40 consenting participants with no valid follow-up measurements (3 deaths before first follow-up measurement, 28 with no measurement performed and 9 excluded due to inadequate data quality as pre-specified in the Data Analysis Plan).
BIO-CONDUCTIVITY MEASUREMENTS ENABLE PORTABLE AND SELF-ADMINISTERED CHRONIC KIDNEY DISEASE SCREENING AND MONITORING

Pak To Cheung1, Fedi Zouari1, Adrien Touboul1, Cheuk Man Ho1, Venice Sin1, Eddie C. Wong1,2, Iris Zhou3, Desmond Yap1,4 and Russell Chan1

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Background and Aims: Chronic kidney disease (CKD) is an escalating health concern. The identification of CKD during mass public screening by laboratory tests constitutes important resource implications. Home-based and self-administered approach to screen and monitor disease severity in both healthy and CKD subjects are eagerly awaited. Frequency-difference electrical impedance tomography (fDEIT) reconstructs the interior of a body by measuring the electrical responses to a small alternating current applied at the surface of the subject at various frequencies. Kidney fibrosis is a cardinal feature of CKD, which is associated with alterations in renal molecular composition and hence electrical conductivity. Therefore, this study aims to investigate the feasibility of a portable, self-administered approach to assess CKD severity using fDEIT in the kidney region.

Method: Clinical subjects are recruited at Queen Mary Hospital, Hong Kong. EIT data was collected via a PVC belt acting as an electrode holder placed circumferentially on the upper abdominal region of the subject. The belt was connected to a portable console to collect EIT data. 24 frequencies ranging from 10KHz to 300KHz are used to stimulate electrical responses in the body. (Figure 1A) Paired blood and urine samples were collected for measured of eGFR. Group source separation was implemented to extract the kidney region of interest (ROI) and extract conductivity features (Figure 1A); these features, together with the age of the subject, are then input into a regression model to estimate the eGFR and the CKD stage of the subject according to the following classification scheme: stage 1 CKD (eGFR > 90) as healthy subjects, stages 3, 4, 5 CKD (eGFR < 60) as unhealthy subjects, stage 2 CKD (60 < eGFR < 90) as borderline cases.

Results: 75 subjects were recruited (54 with CKD and 21 were healthy volunteers). We obtained an eGFR estimation model with R2 score of 0.40. We also obtained a CKD stage classifier with sensitivity of 87.5% and specificity of more than 99.9%. (Figure 1C) The mean conductivity in the extracted kidney signal comprises 40% weighting in the regression model (Figure 1B), showing comparable importance as the age in predicting the eGFR.

Conclusion: The results demonstrate that measuring bio-conductivity anomalies through fDEIT is highly accurate and non-invasive, and can be developed into a portable and self-administrable device to screen and monitor CKD

FINERENONE ADDED TO RAS/SGLT2 BLOCKADE FOR NON-DIABETIC CHRONIC KIDNEY DISEASE: RESULTS OF A PRECLINICAL DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL

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Background and Aims: Inhibitors of the renin-angiotensin system (RAS), sodium-glucose transporter (SGLT)-2, and the mineralocorticoid receptor (MR) have all demonstrated renoprotective effects in large clinical trials of diabetes-related CKD. Furthermore, dual RAS/SGLT2 blockade showed additive renoprotective effects also in non-diabetic CKD. We hypothesized that triple RAS/SGLT2/MR blockade would be even superior to dual RAS/SGLT2 blockade in non-diabetic CKD.

Method: We performed a “no touch” preclinical randomized controlled trial in Col4a3-deficient mice with spontaneous and progressive CKD (registry ID: PCTE0000266). Treatments were administered as food admix from 6-14 weeks of age at the following estimated doses: 10 mg/kg ramipril, 30 mg/kg empagliflozin, 10 mg/kg finerenone. The prespecified primary endpoint was total lifespan up to uremic death. Ancillary studies addressed baseline histology, and mechanistic studies on a subset of mice after 2.5 weeks of treatment.

Results: At the time of randomization, Col4a3−/− mice had albuminuria, elevated serum creatinine, glomerulosclerosis, tubular atrophy, and interstitial fibrosis. Total lifespan was 63.7 ± 9.99 days (vehicle), 77.25 ± 5.34 days (ramipril), 80.3 ± 10.98 days (ramipril+empagliflozin), and 103.05 ± 20.28 days (triple therapy), respectively. Artificial intelligence-based histopathology and RNA sequencing analysis documented a potent anti-sclerotic, -inflammation and -fibrotic effect of the triple combination.

Conclusion: Adding finerenone to dual RAS/SGLT2 blockade significantly prolongs uremia-free lifespan even when started at an advanced stage of Alport nephropathy. Triple RAS/SGLT2/MR blockade could be a potent treatment strategy to prolong uremia-free lifespan in patients with CKD related to Alport syndrome and possibly other progressive kidney disorders.
Figure 1: Finereone added to a dual RAS/SGLT2 inhibition substantially prolongs lifespan of Col4a3-/- mice with progressive CKD due to Alport nephropathy. (A) Kaplan-Meier graph of survival. (B) Effects of RASi, RASi/SGLT2i, and RASi/SGLT2i/MRA treatments on kidney function (GFR) in Col4a3-/- mice. All quantitative data are means ± SD.

Table 1: Evolution of GFR in Col4a3-/- mice.

<table>
<thead>
<tr>
<th>Group (n = 20)</th>
<th>6 weeks (μl/min)</th>
<th>7 weeks (μl/min)</th>
<th>10 weeks (μl/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD-veh</td>
<td>180.64 ± 32.11</td>
<td>146.95 ± 62.77</td>
<td>0.00 ± 0.00</td>
</tr>
<tr>
<td>CKD-RASi</td>
<td>187.61 ± 33.01</td>
<td>191.47 ± 44.36</td>
<td>54.46 ± 28.42</td>
</tr>
<tr>
<td>CKD-RASi/SGLT2i</td>
<td>187.25 ± 38.49</td>
<td>178.55 ± 30.48</td>
<td>55.43 ± 52.72</td>
</tr>
<tr>
<td>CKD-RASi/SGLT2i/MRA</td>
<td>185.27 ± 35.70</td>
<td>176.75 ± 39.21</td>
<td>125.40 ± 54.70</td>
</tr>
<tr>
<td>P</td>
<td>0.936</td>
<td>0.022</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

GFR, glomerular filtration rate; CKD, Chronic kidney disease.

#3382 REASONS FOR DIALYSIS INITIATION AND SAFETY OF DAPAGLIFLOZIN AMONG DIALYSIS PARTICIPANTS: NEW INSIGHTS FROM DAPA-CKD

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Background and Aims: The DAPA-CKD trial demonstrated that dapagliflozin reduced the risk of kidney failure in patients with chronic kidney disease (CKD) with or without type 2 diabetes. In contrast to most other trials, participants who reached dialysis were allowed to continue study medication with dapagliflozin or placebo. In this pre-specified analysis of the DAPA-CKD trial, we assessed reasons for dialysis initiation and serious adverse events (SAEs) among participants who initiated dialysis and continued the study medication.

Method: The DAPA-CKD trial randomized 4304 patients with CKD (estimated glomerular filtration rate [eGFR] 25–75 mL/min/1.73m²) and albuminuria (urinary albumin-to-creatinine ratio 200–5000 mg/g) to dapagliflozin 10 mg daily or placebo in addition to standard of care. Chronic dialysis was defined as the need for dialysis for at least 28 days. Investigator reported reasons for dialysis and SAEs were summarized by treatment groups.

Results: During median 2.4 years follow-up, 68/2152 (3.2%) and 99/2152 (4.6%) participants in the dapagliflozin and placebo groups respectively required chronic dialysis. Reasons for dialysis initiation are shown in the Table below, with volume overload being the most frequently reported. Roughly one-third of patients in both groups had discontinued study drug in advance of dialysis initiation; in the dapagliflozin and placebo groups, 25/68 (37%) and
41/99 (41%) continued the blinded study medication while receiving chronic dialysis. Among these, SAEs were reported in 8/25 (32%) and 11/41 (27%), respectively.

**Conclusion**: Participants who continued dapagliflozin or placebo after dialysis initiation experienced similar rates of SAEs. To determine whether dapagliflozin provides cardiovascular or other benefits to patients with kidney failure on chronic dialysis, will require a dedicated prospective trial. Based on our prespecified exploratory analysis, we observed no safety concerns that might discourage the conduct of such a trial.

**Funding**: This study was funded by AstraZeneca

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### 4296

**EFFECTS OF FERRIC CITRATE HYDRATE ON FIBROBLAST GROWTH FACTOR 23 AND PLATELET COUNT IN CKD AND NON-CKD PATIENTS WITH IRON DEFICIENCY ANAEMIA**

**Kyoko Ito**, **Kojo Arita**, **Yuko Mitobe**, **Tadao Akizawa** and **Norio Komatsu**

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**Background and Aims**: Iron deficiency increases the transcription and cleavage of the peptide hormone, fibroblast growth factor 23 (FGF23). Elevated FGF23 has been associated with increased risk of cardiovascular events and mortality. Iron deficiency also increases platelet count (PLT) in part, and higher levels PLT are associated with arterial thrombosis in the brain. Ferric citrate hydrate (FC, Riona®, Torii Pharmaceutical Co., Ltd. Tokyo, Japan) is an oral iron-based phosphate binder for patients with chronic kidney disease (CKD) and also an iron preparation approved for treatment of iron deficiency anaemia (IDA) in Japan. A phase 3 study was conducted to investigate the efficacy and safety of FC in CKD and non-CKD patients with IDA. This study aimed to evaluate the effects of FC on intact FGF23 and c-terminal FGF23 levels, and the proportion of patients with high PLT (exceeding upper limit: >35.2 × 10^4/μL).

**Method**: A randomized, open-label, multicentre, uncontrolled, 24-week study was conducted at 31 centres in Japan from July 2018 to December 2019 (JapicCTI-184000) in CKD and non-CKD patients with IDA (Hb: < 8.0 g/dL and < 11.0 g/dL, serum ferritin < 50 ng/mL in CKD (eGFRcre < 60 mL/min/1.73 m^2) and < 12 ng/mL in non-CKD). CKD patients scheduled to initiate maintenance dialysis were excluded. Dynamic allocation was used to randomise subjects (CKD and non-CKD with Hb at baseline) to the FC-low group (500 mg [approximately 120 mg elemental iron]/day) or FC-high group (1000 mg [approximately 240 mg elemental iron]/day) (1:1). Notably, if investigators determined that sufficient iron replacement had been achieved from week 8 onwards, the study treatment was completed. For this reason, changes from baseline to week 8 were evaluated.

**Results**: Of 73 patients (CKD n = 42, non-CKD n = 31), 36 were allocated to the FC-low group (CKD n = 21, non-CKD n = 15) and 37 to the FC-high group (CKD n = 21, non-CKD n = 16). Baseline levels of serum ferritin, transferrin saturation (TSAT), c-terminal FGF23, intact FGF23, and PLT are shown in Table 1. Regardless of CKD status, serum ferritin and TSAT increased. After FC-low treatment, mean changes from baseline to week 8 (95% CI) in serum ferritin and TSAT were 18.8 (13.3, 24.2) ng/mL and 8.1 (4.4, 11.8) % in CKD, 17.5 (13.8, 21.3) ng/mL and 13.8 (8.7, 18.9) % in non-CKD, they were 28.1 (13.4, 42.7) ng/mL and 8.8 (5.4, 12.1) % in CKD, 15.9 (12.1, 19.8) ng/mL and 19.9 (9.8, 30.1) % in non-CKD. After administration of FC, in both groups, intact FGF23 levels did not change, whereas c-terminal FGF23 levels decreased. Median changes (interquartile range) from baseline to week 8 of c-terminal FGF23 were -58.00 (-227.50, -12.25) RU/mL in CKD and -725.00 (-1124.00, -168.50) RU/mL in non-CKD, and -66.00 (-265.70, -27.00) RU/mL in CKD and -649.50 (-1127.00, -326.65) RU/mL in non-CKD. Serum phosphate did not change regardless of CKD status. At baseline, high PLT was observed in all these patients, PLT reduction to below 35.2 × 10^4/μL was observed until week 8.

**Conclusion**: In patients with IDA, administration of FC increased serum ferritin and TSAT, decreased c-terminal FGF23, and normalized PLT in patients with high PLT at baseline regardless of CKD status. FC may decrease the potential risk of cardiovascular events in CKD or non-CKD patients with IDA.

<table>
<thead>
<tr>
<th>Variables</th>
<th>FC-low (N = 36)</th>
<th>FC-high (N = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFRcre (mL/min/1.73 m^2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD (n = 21)</td>
<td>41.22 (12.40)</td>
<td>41.82 (14.72)</td>
</tr>
<tr>
<td>non-CKD (n = 15)</td>
<td>84.48 (14.30)</td>
<td>89.94 (14.70)</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD (n = 21)</td>
<td>10.15 (0.84)</td>
<td>10.22 (0.63)</td>
</tr>
<tr>
<td>non-CKD (n = 15)</td>
<td>9.40 (0.55)</td>
<td>9.40 (0.60)</td>
</tr>
<tr>
<td>Serum ferritin (ng/mL)</td>
<td></td>
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<tr>
<td>CKD (n = 21)</td>
<td>16.87 (9.07)</td>
<td>15.88 (8.12)</td>
</tr>
<tr>
<td>non-CKD (n = 15)</td>
<td>5.17 (2.63)</td>
<td>4.91 (1.89)</td>
</tr>
<tr>
<td>TSAT (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD (n = 21)</td>
<td>12.4 (6.7)</td>
<td>12.5 (7.8)</td>
</tr>
<tr>
<td>non-CKD (n = 15)</td>
<td>4.3 (3.5)</td>
<td>3.6 (1.3)</td>
</tr>
<tr>
<td>Serum phosphate (mg/dL)</td>
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<tr>
<td>CKD (n = 21)</td>
<td>3.56 (0.72)</td>
<td>3.32 (0.48)</td>
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<tr>
<td>non-CKD (n = 15)</td>
<td>3.69 (0.30)</td>
<td>3.34 (0.69)</td>
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<tr>
<td>Intact FGF23 (pg/mL)*</td>
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<tr>
<td>CKD (n = 21)</td>
<td>64.00 (48.10, 82.20)</td>
<td>58.20 (45.10, 72.50)</td>
</tr>
<tr>
<td>non-CKD (n = 15)</td>
<td>40.80 (37.30, 47.20)</td>
<td>35.90 (30.10, 48.75)</td>
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<tr>
<td>C-terminal FGF23 (pg/mL)*</td>
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<td></td>
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<td>CKD (n = 21)</td>
<td>159.00 (135.00, 390.00)</td>
<td>188.00 (136.00, 361.00)</td>
</tr>
<tr>
<td>non-CKD (n = 15)</td>
<td>1010.00 (260.00, 1240.00)</td>
<td>775.00 (394.00, 1285.00)</td>
</tr>
<tr>
<td>PLT (10^11/μL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD (n = 21)</td>
<td>24.27 (7.17)</td>
<td>26.56 (8.58)</td>
</tr>
<tr>
<td>non-CKD (n = 16)</td>
<td>33.25 (9.02)</td>
<td>36.99 (8.38)</td>
</tr>
</tbody>
</table>

mean (SD), *median (Q1, Q3)
DIALYSIS

D1 - EXTRACORPOREAL TECHNIQUES & ADEQUACY

#4195
CAN A BLOOD TEST FOR MIDDLE MOLECULES BE USED TO MEASURE RESIDUAL kidney FUNCTION TO PERFORM INCREMENTAL DIALYSIS?

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Background and Aims: Incremental dialysis involves combining residual kidney functions (RFK) with dialysis dose to individualise treatment, increasing the dialysis dose as RFK falls. Potential benefits include quality of life benefits, less treatment burden and health economic benefits. Kidney Disease Outcome Quality Initiative (KDOQI) recommends incremental haemodialysis may be performed when renal urea clearance (KRU) is > = 2 ml/min. To avoid underdialysis, incremental approach requires frequent interdialytic urine collections to monitor RFK, which can be inconvenient.

An easier assessment of RFK would likely increase the uptake of incremental dialysis. Blood levels of middle molecules (e.g Beta 2 Microglobulin (Beta2M) and Beta Trace Protein (BTP)) have been studied as predictors of RFK. However, their role in identifying patients for incremental dialysis have not been tested. There are a few published methods of predicting RFK using middle molecules. A proposed simple method is identification of patients with KRU > = 2 ml/min, based on having a blood middle molecule level below a certain cut-off. Alternatively direct prediction of KRU from middle molecule levels can be performed with an algorithm/equation.

We set out to establish if these methods may identify patients with significant RFK who can benefit from incremental dialysis.

Method: We conducted a retrospective analysis on the data from a multicentre feasibility randomised controlled trial to assess the impact of incremental versus conventional haemodialysis initiation. As a part of this trial 55 participants were followed up for up to 12 months with monthly RFK measurement using interdialytic urine collections. Monthly Beta2M and BTP measurements were also performed. We used (1) a published middle molecules-based KRU equation (2) published Beta2M cut-off levels, to predict RFK. We, then, compared the predicted RFK with conventionally measured RFK from urine collection. The focus was to establish reliability of these methods in identifying patients with KRU > = 2 ml/min, which is the recommended cut-off for incremental dialysis, and to identify where underdialysis might occur if these methods were used in clinical practice.

Results: The middle molecules-based KRU equation had 62% sensitivity and 84% specificity to identify those with KRU > = 2, whereas a beta2M cut-off level of < 19.15 mg/L had 78% sensitivity and 82% specificity. 6/55 (10.9%) participants would have had underdialysis whilst performing incremental dialysis guided by a middle molecules-based KRU equation and 7/55 (12.7%) would underdialyse using the Beta2M cut-off level to predict KRU. The predicted mean underdialysis that would occur using these methods was 0.2 – 0.3 standard kt/v units. Combining these methods with urine volume improved specificity and sensitivity. Beta2M level of < 19.15 mg/L and Urine volume of > 0.5 litre/day combined predicted KRU > = 2 with 70% sensitivity and 98% specificity. In other words, only 1/55 (1.8%) patients would have had underdialysis if incremental dialysis were performed based on a combination of Beta2M cut-off and urine volume.

Conclusion: Blood Beta2M level, when combined with urine volume assessment reliably predicts adequate RFK to perform incremental dialysis safely. If dialysis patients can reliably estimate or measure their urine volume, this tool can potentially replace the need for cumbersome interdialytic urine collection to determine RFK and offer an easy way to perform incremental dialysis.

D2 - VASCULAR ACCESS & COMPLICATIONS

#5528
FIBROBLAST GROWTH FACTOR 21 PREDICTS ARTERIOVENOUS FISTULA FUNCTIONAL PATENCY LOSS AND MORTALITY IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS

Xinhui Hu, Qing Wei, Bin Wang and Hong Liu
Zhongda Hospital, Southeast University School of Medicine, Institute of Nephrology, Nanjing, P.R. China

Background and Aims: Arteriovenous fistula (AVF) dysfunction is a common complication in patients undergoing maintenance hemodialysis (MHD). Elevated serum level of fibroblast growth factor 21 (FGF21) was associated with atherosclerosis and cardiovascular mortality. However, its association with vascular access outcomes remains elusive. In this study, we aimed to evaluate the relationship of serum FGF21 levels with AVF dysfunction and all-cause mortality in patients undergoing MHD.

Method: We performed a study of patients undergoing MHD who received AVF creation at a tertiary medical center in China from January 2018 to December 2019. Serum FGF21 concentration was detected by enzyme-linked immunosorbent assay (ELISA). Patients were followed-up to record two clinical outcomes, including AVF functional patency loss and all-cause mortality. The follow-up period ended at April 30, 2022. Kaplan-Meier curves were used to analyze AVF dysfunction events and mortality. Univariate and multivariate Cox proportional risk model analyses were used to calculate risk ratios (HR) and 95% CI and independent prognostic factors. The receiver operating characteristic (ROC) curve and area under the curve (AUC) were used to analyze the predictive value of FGF21 in AVF functional patency loss and all-cause mortality.

Results: Among 147 patients, the mean age was 58.49 ± 14.41 years, and 58.50% of them were males. The median serum level of FGF21 was 150.15 (70.57-318.01) pg/ml. During median follow-up period of 40.83 months, the serum level of FGF21 was an independent predictor for AVF functional patency loss (per 1 pg/ml increase, HR 1.002 [95% CI: 1.001-1.003, P = 0.003]), and all-cause mortality. The follow-up period ended at April 30, 2022. Kaplan-Meier curves were used to analyze AVF dysfunction events and mortality. Univariate and multivariate Cox proportional risk model analyses were used to calculate risk ratios (HR) and 95% CI and independent prognostic factors. The receiver operating characteristic (ROC) curve and area under the curve (AUC) were used to analyze the predictive value of FGF21 in AVF functional patency loss and all-cause mortality.

Conclusion: Serum FGF21 level was an independent risk factor and predictor for AVF functional patency loss and all-cause mortality in patients undergoing MHD.
Figure 1: Kaplan-Meier estimate of AVF functional patency in patients undergoing maintenance hemodialysis with low levels of serum FGF21 ($\leq 150.15 \text{pg/ml}$) and high levels of serum FGF21 ($>150.15 \text{pg/ml}$) ($P < 0.001$; log-rank test).
Figure 2: Kaplan-Meier estimate of overall survival in patients undergoing maintenance with low levels of serum FGF21 ($\leq$150.15pg/ml) and high levels of serum FGF21 (>150.15pg/ml) ($P = 0.016$; log-rank test).

#5803
ARTERIOVENOUS FISTULA BLOOD FLOW ESTIMATION THROUGH AI MODEL EXPLOITING THE PATIENT'S ROUTINELY COLLECTED DATA
Francesco Bellocchio¹, Mario Garbelli¹, Len Usvay², Stefano Stuard¹ and Luca Neri¹

¹Fresenius Medical Care Italia SpA, Italy, ²Fresenius Medical Care, United States of America and ³Fresenius Medical Care Deutschland GmbH, Germany

Background and Aims: Clinical monitoring and surveillance are key pillars of Arteriovenous Fistula (AVF) management in hemodialysis patients. They are aimed at limiting the risk of suboptimal dialysis dose and Vascular Access (VA) failure. AVF blood flow (Qa) is commonly used to assess VA function. Several methods have been proposed for the measurement of Qa including doppler
Abstracts

Confusion matrix (CM) of the estimation. The diagonal elements of CM represent the number of right matches between predicted and actual (true) label, while off-diagonal elements are those that are mislabeled. The CM values are normalized over actual label (by row).

<table>
<thead>
<tr>
<th>precision</th>
<th>recall</th>
<th>F1-score</th>
<th>MAE</th>
<th>support</th>
</tr>
</thead>
<tbody>
<tr>
<td>very low</td>
<td>0.9</td>
<td>0.8</td>
<td>0.84</td>
<td>0.25</td>
</tr>
<tr>
<td>low</td>
<td>0.57</td>
<td>0.7</td>
<td>0.63</td>
<td>0.30</td>
</tr>
<tr>
<td>normal</td>
<td>0.79</td>
<td>0.75</td>
<td>0.77</td>
<td>0.27</td>
</tr>
</tbody>
</table>

ultrasound, and Body Thermal Monitor, among others. All these diagnostic tests are, in general, time-consuming for clinical staff, operator dependent, and costly for healthcare providers. To overcome limitations in the uptake of current Qa measurement techniques, we used data automatically recorded by dialysis machine sensors and medical information captured in electronic charts to estimate Qa using a machine learning technique.

**Method:** For this historical cohort study, we analyzed electronic health records (EHR) of adult patients from four different European countries (Czech Republic, Portugal, Slovakia, and Spain), receiving in-center hemodialysis therapy in Fresenius Medical Care dialysis clinics between January 1st, 2015 and June 30th, 2022 registered in the European Clinical Database (EuClinD®). All patients consented their pseudo-anonymized data be used for secondary data analysis. The input dataset included 49 variables representing the health status of the patients, functional parameters of AVF function and the HD treatment parameters. The input variables were collected in the 90 days before the Qa measure. We constructed metrics representing the 90-day average and trend of each functional and medical parameter. Qa was classified in three levels: < 525 ml/h (very low), 525 ml/h - 925 ml/h (low), > 925 ml/h (normal).

We estimated Qa as ordinal classification problem. Therefore, we used 2 binary classifiers based on the XGBoost algorithm. The estimation of the first-class, P(Qa ≥ 525), is given by the first classifier and the estimation of the third class, P(Qa ≥ 925), is given by the second classifier. The probability of the middle class is computed as P(Qa ≥ 525) - P(Qa ≥ 925). The Qa estimation accuracy was assessed computing mean absolute error (MAE), precision and recall, F1-score and confusion matrix.

**Results:** Our dataset included 46,292 Qa measurements referred to 5,940 different hemodialysis patients. We obtained an overall precision of 0.77, a recall of 0.76, a F1-score of 0.76, a MAE of 0.27. The same metrics for each class are shown in Table 1. The model was able to detect fistula with “very low flow” with a precision of 0.9 and 16% of the missed “very low flow” AVFs are predicted as “low flow” and 4.7% are predicted as normal flow. The Confusion Matrix for each class is shown in Figure 1.

**Conclusion:** In this study we showed that clinically relevant Qa classes can be accurately predicted by resorting to routinely collected clinical data extracted from an electronic health record without any additional effort from healthcare professionals, training or instrumentation. Qa assessment is an important parameter in the evaluation of AVF function. Our algorithm accurately

discriminated patients with “very low flow” that may be referred to vascular surgeon evaluation. It might help the AVF surveillance process, without adding time-consuming procedures for clinical staff or costs for healthcare provider.

**#3408 A META-ANALYSIS OF VASCULAR ACCESS OUTCOMES IN HEMODIALYSIS PATIENTS OVER 75 YEARS OF AGE**

Alexandra Ntemka1, Christos Argyriou2, Parthena Kyriklidou1, Miltiadis Lazaridis2 and Georgios Georgiadis2

1 General Hospital Of Thessaloniki “Papageorgiou”, Thessaloniki, Greece and 2 University Hospital of Alexandroupolis, Greece

**Background and Aims:** The age of patients with end-stage renal disease is constantly growing, but evidence for the best vascular access for hemodialysis is scarce and controversial for elderly. A meta-analysis was performed in hemodialysis patients over 75 years old to compare the outcomes of different vascular access procedures in the sub-group of elderly ESRD patients ≥ 75 years of age.

**Method:** A literature search was performed using the electronic databases MEDLINE and SCOPUS up to October 2021. Twelve eligible articles fulfilled the inclusion criteria and were finally selected in the meta-analysis (Table). Three of these studies including ESRD patients >70 years of age were exceptionally included as the mean age was well above 75 years. First step analysis was focused on studies that reported the primary patency rates of autologous vs. prosthetic vascular accesses (5 studies). Second step analysis was focused on articles comparing the results of primary and secondary patency rates of distal (forearm) vs. proximal (upper arm) fistulas in elderly patients (8 studies). All these studies were retrospective cohort studies, none was randomized controlled trial.

**Results:** Regarding the first step analysis, primary failure rate at 24 months was in favor of AVFs (OR: 0.56, 95% CI: 0.38-0.83, p = 0.003, Fig. 1). Although several studies have shown that AVG patency is not affected by age, this meta-analysis showed patency benefit of AVF in this subgroup of elderly patients ≥ 75 years of age. In a second step, the 12-month primary failure rate was by far in favor of proximal AVFs (OR: 2.14, 95% CI: 1.53-2.78; p <.00001, Fig. 2). The 12-month secondary patency rate of the forearm AVFs was also inferior compared to the proximal AVF (OR: 1.76, 95% CI: 1.12-2.78; p <.01, Fig. 3). These findings favor the use of proximal AVFs as first choice access in this subgroup of elderly patients, especially when they are late referrals or have low life expectancy.

**Conclusion:** The question of the right access in elderly ESRD patients does not have an easy answer. The present study shows that patients ≥75 years old should not be excluded from creation of an autologous access, with proximal AVFs having better patency rates.
Table 1: The included studies in meta-analysis.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study</th>
<th>Data extraction</th>
<th>Age</th>
<th>NOS (number of stars)</th>
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<tbody>
<tr>
<td>Staramos et al</td>
<td>2000</td>
<td>Retrospective</td>
<td>Graph</td>
<td>&gt;70 (MA 78)</td>
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</tr>
<tr>
<td>Borzumati et al</td>
<td>2013</td>
<td>Retrospective</td>
<td>Text</td>
<td>&gt;75</td>
<td>6</td>
</tr>
<tr>
<td>De Leur et al</td>
<td>2013</td>
<td>Retrospective</td>
<td>Table</td>
<td>&gt;75</td>
<td>7</td>
</tr>
<tr>
<td>Cui et al</td>
<td>2016</td>
<td>Retrospective</td>
<td>Graph</td>
<td>&gt;75</td>
<td>6</td>
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<tr>
<td>Olisha et al</td>
<td>2015</td>
<td>Retrospective</td>
<td>Text</td>
<td>&gt;80</td>
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</tr>
<tr>
<td>Jadlowiec et al</td>
<td>2016</td>
<td>Retrospective</td>
<td>Table</td>
<td>&gt;70 (MA 78.7)</td>
<td>5</td>
</tr>
<tr>
<td>Bae et al</td>
<td>2018</td>
<td>Retrospective</td>
<td>Graph</td>
<td>≥80</td>
<td>7</td>
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<tr>
<td>Misskey et al</td>
<td>2018</td>
<td>Retrospective</td>
<td>Table</td>
<td>&gt;80</td>
<td>6</td>
</tr>
<tr>
<td>Hwang et al</td>
<td>2019</td>
<td>Retrospective</td>
<td>Graph</td>
<td>&gt;70 (MA 75.9)</td>
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<td>Lee et al</td>
<td>2019</td>
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<td>Graph</td>
<td>&gt;85</td>
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<td>&gt;75</td>
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<tr>
<td>Drouven et al</td>
<td>2020</td>
<td>Retrospective</td>
<td>Table</td>
<td>&gt;80</td>
<td>7</td>
</tr>
</tbody>
</table>

MA: Mean age, NOS: Newcastle-Ottawa Scale

Figure 1: Differences (forest plot) in the unassisted 2 years failure rate between the autologous AVFs and AVGs in patients' ≥75 years old.

Figure 2: Differences (forest plot) in the unassisted 1 year failure rate between the autologous forearm AVFs and upper arm proximal AVFs in patients' ≥75 years old.

Figure 3: Differences (forest plot) in the secondary 1 year failure rate between the autologous forearm AVFs and upper arm proximal AVFs in patients' ≥75 years old.
THE CHANGING HAEMODIALYSIS POPULATION IN A SINGLE UK CENTRE: A POST PANDEMIC PHENOMENON?
Joanna Mckinnell1, Zoe Pottman1, Kirsty Swinscoe1, Nahedh Abdulifa1, Liberty Berino1 and Nick Selby1,2
1University Hospitals Derby and Burton NHS Foundation Trust, Renal, Derby, United Kingdom and 2University of Nottingham, Nottingham, United Kingdom

Background and Aims: Following the Covid-19 pandemic, UK dialysis centres have seen a sharp increase in numbers of patients requiring renal replacement therapy (RRT) particularly haemodialysis (HD). This has resulted in pressures on dialysis capacity and staffing. There may also have been negative effects on other aspects of quality of care, such as a fall in the proportion of patients dialysing via an Arterio-venous fistula (AVF) or worsening anaemia. To study this further, we conducted a retrospective observational study to describe the incident and prevalent HD populations in the post-Covid pandemic period and compare these against pre-pandemic patterns, in a single UK dialysis centre.

Method: We reviewed data on prevalent HD patient numbers across our service. We specifically collected data from all patients commencing HD between January 2021 and December 2022 using electronic medical records. We collected information on time known to renal prior to starting dialysis, clinic data including which types of clinic attended, documentation of pre-dialysis decisions about modality as well as vascular access referrals, vascular access clinics and vascular access surgery as well as haemoglobin (Hb) at first dialysis. We compared figures with published pre-pandemic data from the 23rd annual UK Renal Registry report on data collected to December 2019 for our centre. We defined a planned start to dialysis as patients who were known to renal >90 days. This aligns with the registry definition. We compared proportional data using the chi square test.

Results: Comparing prevalent data in Dec. 2022 with Dec 2019, there was a 17% increase in the prevalent HD population from 298 to 349. The proportion of patients dialysing via an AVF fell from 88% to 80% (p = 0.006). The spread across different types of HD in Dec.2022 remained static at 71% In-Centre HD (72% in Dec 2019), 11% Satellite HD (9% in 2019) and 17% HDHD (18% 2019) with overall numbers rising across all HD modalities (p for trend = 0.37). PD numbers also rose from 58 to 71 keeping the total percentage on home therapies stable at 31% in our unit. From Jan. 2021- Dec. 2022 inclusive 147 people commenced HD of whom 115 (78%) had planned starts. This compares to 58 starting HD in 2019 and 79% planned (p = 0.85). There was a significant fall in the proportion of planned start HD patients who commenced dialysis with an AVF/AVG, from 81% in 2019 to 56% in 2021-22 (p = 0.003). Themes emerged in planned starters who did not start HD with an AVF/AVG and are detailed in Figure 1. Median Hb level of planned starts on HD was lower at only 94 AVF/AVG, from 81% in 2019 to 56% in 2021-22 (p = 0.003). Using the electronic patient records, we identified patients with significant vascular access events (thrombosis, angiographic stenosis requiring angioplasty or doppler with > 50% stenosis) without vascular access event. Information for clinically detected malfunctioning fistula was retrieved from the last clinic letter and the last vascular access multidisciplinary meeting notes prior to the vascular event. For the event positive patients, we included in the analysis the Vasc-alert data 2 months prior to the event. For the negative group, we included Vasc-alert data for 5 consecutive months with 1 month follow up. For the analysis we used the number of events per patient for the Vasc-alert data 2 months prior to the event. For the negative group, we included Vasc-alert data for 5 consecutive months with 1 month follow up. For the analysis we considered HRS positive if ≥ 2 HRS were generated.

Results: Out of 141 patients with available Vasc-alert data there were 60 patients dialyzing via a tunneled line. Amongst 81 patients with arteriovenous fistula or graft, 58 had available Vasc-alert data for ≥ 2 months. Out of 12 event positive (4 patients with thrombosed access, 6 patients with stenosis requiring angioplasty and 2 patients with < 50% doppler referred and awaiting fistulogram),10 (83%) had ≥ 2 HRS generated 2 months prior to the vascular event (Median 8, IQR 6.75-8). Out of the 46 patients without vascular events, 15 patients (32.6%) had ≥ 2 HRS and 2 patients had only one HRS score.

Patient characteristics by vascular event are presented in Table 1. The sensitivity and specificity of HRS ≥ 2 for detecting future vascular events were 83.3% and 67.4%, respectively. The positive and negative predictive value of HRS ≥ 2 were 40% and 93.9% respectively. History of prior access stenosis and clinically detected malfunctioning fistula were significantly associated with vascular access events (P value 0.002, < 0.001 respectively), and HRS > 200 discrete values (P value 0.007 and 0.005 respectively). Within the patients with thrombosed access, 2 patients (50%) detected by HRS were not detected with clinical monitoring.

Conclusion: Our results suggest that vascular access risk score can be a useful screening tool to assist clinical decision making for VA risk stratification. Prospective studies are required to evaluate its utility in the VA surveillance pathway.
Table 1: Patient characteristics and vascular events.

<table>
<thead>
<tr>
<th>EVENTS</th>
<th>Total (N = 58)</th>
<th>Yes (N = 12)</th>
<th>No (N = 46)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE¹</td>
<td>Mean ± SD</td>
<td>58.2 ± 15.7</td>
<td>58.7 ± 15.0</td>
<td>58.0 ± 16.0</td>
</tr>
<tr>
<td>SEX²</td>
<td>Male</td>
<td>44 (74.6%)</td>
<td>11 (84.6%)</td>
<td>33 (71.7%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>15 (25.4%)</td>
<td>2 (15.4%)</td>
<td>13 (28.3%)</td>
</tr>
<tr>
<td>BMI¹,³</td>
<td>Mean ± SD</td>
<td>25.6 ± 4.8</td>
<td>26.1 ± 4.9</td>
<td>25.5 ± 4.8</td>
</tr>
<tr>
<td>HTN²,⁴</td>
<td>Yes</td>
<td>58 (98.3%)</td>
<td>13 (100.0%)</td>
<td>45 (97.8%)</td>
</tr>
<tr>
<td>DM²,⁵</td>
<td>Yes</td>
<td>21 (35.6%)</td>
<td>5 (38.5%)</td>
<td>16 (34.8%)</td>
</tr>
<tr>
<td>CVS²,⁷</td>
<td>Yes</td>
<td>25 (42.4%)</td>
<td>6 (46.2%)</td>
<td>19 (41.3%)</td>
</tr>
<tr>
<td>PRIOR STENOSIS²</td>
<td>Yes</td>
<td>19 (32.2%)</td>
<td>9 (69.2%)</td>
<td>10 (21.7%)</td>
</tr>
<tr>
<td>CLINICAL SURVEILLANCE²</td>
<td>Yes</td>
<td>13 (22.0%)</td>
<td>8 (66.6%)</td>
<td>5 (10.9%)</td>
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<tr>
<td>ACCESS RISK SCORE³</td>
<td>Yes</td>
<td>25 (42.4%)</td>
<td>10 (83%)</td>
<td>15 (32.6%)</td>
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<tr>
<td>HD VINTAGE⁸</td>
<td>Median [IQR]³</td>
<td>3.0 [2.0 - 6.0]</td>
<td>6.0 [3.0 - 7.0]</td>
<td>3.0 [2.0 - 5.0]</td>
</tr>
</tbody>
</table>

¹T: independent samples T-test; ²FE: Fisher’s exact test; ³BMI: Body mass index (Kg/m²); ⁴HTN: Hypertension; ⁵DM: Diabetes mellitus; ⁶X²: Pearson’s Chi-square test for independence of observations; ⁷CVS: Cardiovascular events; ⁸Z: Mann-Whitney test; ⁹IQR: interquartile range (25th 75th percentiles); ¹⁰significant at p < 0.05

REFERENCE

D3 - EPIDEMIOLOGY & OUTCOME

#4199
PSYCHOSOCIAL ASSESSMENTS AND HOSPITAL ADMISSION RATES IN ELEVATED OR HIGH ACUITY HEMODIALYSIS PATIENTS
Joanna Willetts¹, Sceetl Chaudhuri¹, Len Usavat², Kathleen Belmonte², Felicia Speed², Anna Rutherford² and Jeffrey Hymes³
Background and Aims: Using data routinely captured in electronic medical records of a large dialysis organization (LDO) in close collaboration with social workers (MSW), we developed a weekly patient acuity score to identify the level of need for psychosocial support in hemodialysis patients to help social workers optimize visits to deliver timely personalized care. We evaluated how interventions by a MSW affected future hospital admission rate in in-center hemodialysis (ICHD) patients with Elevated or High acuity in an LDO.

Method: Using data from prevalent (vintage >90 days) ICHD patients from Mar-2022 through Dec-2022, a weekly acuity score was computed using 95 routinely captured variables considered critical (e.g., psychosocial, cognitive, clinical, treatment, hospitalization). Each variable was assigned points based on a priori criteria which were summed and categorized based on population distribution for each week. Patient acuity was assigned as Low, Moderate, Elevated, or High based upon percentile distribution. We defined MSW interventions as the number of assessments completed (0, <1, 1, or >1 per month) during the baseline period (BL, Mar-2022 through May 2022). Next, we compared hospital admission rate in the BL period to that in a follow-up period (FU, June 2022 through Dec 2022) for patients whose acuity at start of BL was Elevated or High (E/H), stratified by monthly MSW assessment exposure. This analysis focuses on prevalent ICHD patients in the Elevated and High acuity categories at baseline (BL, March 2022 through May 2022) as they were expected to have been prioritized for MSW assessment.

Results: We identified 29,665 prevalent ICHD patients whose acuity was E/H at the start of BL; 8.2%, 24.8%, 20.9%, and 46.2% had 0, <1, 1, and >1 MSW assessments per month during BL, respectively. As expected, hospital admission rate was generally high for patients with E/H acuity. Likewise, for patients with E/H acuity, hospital admission rate increases as the number of monthly interventions in BL increases (Figure 1). For patients with E/H acuity, in each category of BL MSW assessment exposure, the hospital admission rate in FU is lower than in the BL period and the magnitude of the decrease is larger when there are more MSW assessments in the BL period; for 0, <1, 1, and >1 respective MSW assessments, the respective rate ratios were 0.99, 0.99, 0.98, and 0.90, and rate ratio was significantly lower for patients with >1 MSW assessment in BL.

Conclusion: Our results suggest that acuity is helping MSW to identify patients with requiring more psychosocial and other needs as 46.2% of patients with E/H acuity had >1 MSW assessment. Our results also suggest that >1 MSW assessments in E/H acuity patients results in a larger magnitude in the decrease of hospital admission rates compared to other levels of MSW assessment exposure. Future analyses are needed to confirm these results.

Determination of Predictors of Outcomes Following Vascular Access Conversion: Which Patients Benefit Most?
Amun Hofmann1, Suman Lama2, Hanjie Zhang3, Ashin Assadian4, Murat Sor5, Peter Kotanko1 and Jochen Raimann6

Method: We studied prevalent incident HD patients undergoing conversion from CVC to non-CVC, between Jan. 2016 and Dec. 2019. Predictors included demographic and clinical variables such as comorbidities, drug history, and lab parameters. First, feature importance was assessed to separate weak from strong predictors using the Boruta algorithm. Second, important and tentative features were utilized in a subsequent machine learning workflow. Our main outcome was the predictive performance of different machine learning classification algorithms to predict re-conversion to central venous catheter and mortality within 1 year after conversion. Performance was quantified as accuracy, sensitivity, and AUC ROC. We compared insights from Machine learning algorithms to multivariate logistic regression models with selected inputs based on published literature (sex, age, BMI, diabetes, inflammation, blood pressure).

Results: After exclusions of patients with missing data, 38,151 out of 73,031 incident HD patients were studied. Of these, 25,470 (66.8%) experienced no major adverse outcome within 1 year after access conversion, 3,683 (9.7%) underwent re-conversion, and 7,779 (20.4%) did not survive the observational period, and 1,219 (3.2%) required re-conversion and did not survive the follow-up period. Post HD systolic blood pressure, history of a previous non-CVC that failed, and anthropometric characteristics (height, weight) had most weight in
Table 1: Prediction performance regarding adverse outcomes within the first year after conversion.

<table>
<thead>
<tr>
<th>Model</th>
<th>Accuracy</th>
<th>AUC</th>
<th>Recall</th>
<th>Prec.</th>
<th>F1</th>
<th>Kappa</th>
<th>MCC</th>
<th>TT (Sec)</th>
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<td>0.6149</td>
<td>0.3572</td>
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<td>0.2375</td>
<td>1.3720</td>
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<tr>
<td>lr</td>
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</tr>
<tr>
<td>ridge</td>
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<td>0.2375</td>
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<tr>
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<td>1.3720</td>
</tr>
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</table>

The prediction of re-conversion to CVC, according to the Boruta algorithm. Ethnicity and age were found to be the most important predictors of mortality. Classification based on the absence/presence of any major adverse outcomes resulted in a predictive accuracy between 0.70 and 0.54, depending on the respective algorithm. Sensitivity and ROCAUC had maxima of 0.58 and 0.69, respectively. However, information gain by including all additional values had no remarkable effect on the predictive qualities (Table 1).

Logistic regression for re-conversion in survivors only resulted in an accuracy of 0.78 and sensitivity of 0.29. Limiting predictors to 6 published predictors of our studied outcomes in the context resulted in an accuracy of 0.77 and sensitivity of 0.22 (Figure 1a and b).

**Conclusion:** Prediction of re-conversion and mortality within 1 year after catheter-to-arteriovenous access conversion is accurately feasible based on demographic and clinical features but discrimination of those benefiting most comes with low predictive accuracy. It remains reasonable to assume that not all patients will truly benefit from conversion, the inability to identify those that do not based on retrospective medical records data, again emphasizes “Fistula first” (if surgically feasible) and the need for investigation into molecular and genetic risk determinants.

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#4088

**IMPACT OF DYSMAGNESEMIA ON ATRIAL FIBRILLATION IN MAINTENANCE HAEMODIALYSIS PATIENTS: A NATIONWIDE STUDY**

Tatsunori Toida, Noriaki Kurita, Abe Masanori, Norio Hanafusa and Nobuhiko Joki

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BACKGROUND AND AIMS: The dose-response relationship between serum magnesium (sMg) and atrial fibrillation (AF) and the contribution of dysmagnesemia to AF remain unknown among haemodialysis patients.

METHOD: This was a nationwide cross-sectional study on the Japanese Society for Dialysis Therapy registry as of the end of 2019. Eligible participants were adult patients undergoing haemodialysis thrice a week. The main exposure was sMg, categorised into seven categories (<1.5, 1.5–<2, ≥2–<2.5, ≥2.5–<3, ≥3–<3.5, ≥3.5–<4, and ≥4.0 mg/dL). The outcome was AF reported by dialysis facilities. The independent contribution to AF was assessed via logistic regression to generate population-attributable fractions, assuming a causal relationship between sMg and AF.

RESULTS: A total of 165,926 patients from 2,549 facilities were analyzed. The prevalence of AF was 7.9%. Compared with the reference (>2.5–≤3 mg/dL), lower sMg was associated with increased AF (adjusted ORs [95%CI] of 1.49 [1.19–1.83], 1.24 [1.17–1.32], and 1.11 [1.05–1.16] for sMg of <1.5, 1.5–<2.0, and >2.5 mg/dL, respectively). The slightly high sMg was associated with fewer AF (adjusted OR 0.87 [95%CI 0.79–0.96] for sMg of >3.0–≤3.5 mg/dL). The adjusted population-attributable fraction of lower sMg and higher and lower sMg for AF was 7.4% and 6.9%, respectively.

CONCLUSION: An association does indeed exist between lower sMg and AF, with the fewest percentages of AF at sMg levels above the reference range for the general population. Dysmagnesemia may be an important contributor to AF among adult haemodialysis patients. Further longitudinal studies are warranted to determine whether correction of sMg reduces the incidence of AF.

#4543

EFFECT OF COMORBIDITIES ON HEALTHCARE EXPENDITURES FOR PATIENTS ON KIDNEY REPLACEMENT THERAPY IN A FRENCH COHORT

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BACKGROUND AND AIMS: End stage kidney disease (ESKD) is associated with a substantial economic burden. In France, the cost of care for such patients represents 2.5% of the total French healthcare expenditures, but serves less than 1% of the population. These patients’ healthcare expenditures are high because of the specialized and complex treatment needed as well as the presence of multiple comorbidities. This study aims to describe and assess the effect of comorbidities on healthcare expenditures (direct medical cost and non-medical costs including transportation and compensatory allowances) for patients with ESKD in France, while considering the modality and duration of renal replacement therapy (RRT).

METHOD: This retrospective observational study included adults who started RRT for the first time between 2012 and 2014 in France and were followed for 5 years. Linear models were built to predict mean monthly cost (MMC) by integrating first the time duration in the cohort, then patient characteristics and finally the duration of use of each treatment modalities. A complementary analysis stratified on age group was also performed. The variables included in these analyses were: body mass index, age, sex, RRT modality, time in the cohort, coronary artery disease, heart failure, chronic respiratory disease, active cancer, diabetes, lower-limb arterial disease, HIV/AIDS, abdominal aneurism, rhythm disorders, stroke or transient ischemic attack, liver disease, mobility limitations. All RRT modalities available in France were also included: renal transplant (RT), hemodialysis (HD) in center, HD in self-care unit, HD in out-center, HD at home, assisted continuous ambulatory peritoneal dialysis (aCAPD), non-assisted continuous ambulatory dialysis (naCAPD), assisted automated peritoneal dialysis (aAPD), non-assisted automated peritoneal dialysis (naAPD).

RESULTS: A total of 22,506 patients were included in the study. The mean MMC was 6,391€ (95% CI 6,345–6,438 €). The comorbidities with the highest effect on MMC were inability to walk (95% CI 291–291 €), HIV positivity (95% CI 594–594 €), and diabetes (95% CI 1,434–1,434 €), followed by the presence of diabetes, cancer, and respiratory disease, which had a great impact on MMC in younger patients.

CONCLUSION: This study confirms the importance of considering patient characteristics, comorbidities and type of RRT when assessing healthcare expenditures for patients with ESKD. Better care of comorbidities prior to RRT could reduce cost for individual patients as well as potentially reduce the incidence of patients in ESKD. Even though the Euro value is specific to France, other countries might benefit from evaluating and anticipating healthcare costs for patients in RRT by assessing patient comorbidities.
RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS ACROSS DIALYSIS MODALITY
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Background and Aims: Among dialysis patients, cardiovascular events are the leading cause of death. Little is known about difference in the frequency of cardiovascular events between various dialysis modalities. Glucose load may contribute to a metabolic burden in peritoneal dialysis (PD). On the other hand, hemodialysis can cause intradialytic hypotension, cardiac stunning, and arrhythmias, which are associated with increased risk of death. We compared risk of major cardiovascular events in patients who started continuous ambulatory PD (CAPD), automated PD (APD) and home HD with in-center HD patients.

Method: We included 968 patients who entered dialysis in the Helsinki-Uusimaa healthcare district in Finland from 2004 to 2017, of whom 162 were on CAPD, 229 on APD, 145 on home HD and 432 on in-center HD at day 90 from the start of dialysis. Patients were followed up for 5 years or until the end of 2019. Major adverse cardiovascular event (MACE) was defined as acute myocardial infarction, stroke or death due to cardiovascular disease. The cumulative incidence of the first MACE was calculated by taking other causes of death into account as competing risk events and censoring at time of kidney transplantation. Cox regression was used to compare risk of MACE between dialysis modalities with adjustment for age, gender, primary renal disease, prior comorbidities (coronary heart disease, left ventricular hypertrophy, heart failure and stroke), and laboratory data (plasma albumin, phosphate and ionized calcium). Imputation was performed to replace missing values of comorbidities and laboratory data.

Results: Of all 968 patients, 195 (20%) experienced a MACE during the entire follow-up and 62 (6.4%) during the first year of follow-up. The cumulative incidence of first MACE was similar in in-center HD and CAPD patients and higher than that in APD and home HD patients (Figure 1). Without adjustments, the hazard ratio of MACE was 0.83 [95% CI 0.56–1.2] for CAPD, 0.49 [95% CI 0.31–0.77] for APD and 0.42 [95% CI 0.23–0.78] for home HD in comparison to in-center HD. After adjustment for possible confounders, the hazard ratio of MACE was 1.1 [95% CI 0.70–1.6] for CAPD, 0.88 [95% CI 0.53–1.5] for APD and 0.80 [95% CI 0.41–1.6] for home HD and not statistically significantly different in comparison to in-center HD.

Conclusion: We observed a lower risk of MACE among patients who entered APD or home hemodialysis compared to in-center hemodialysis, but after adjusting for potential confounding factors, the difference diminished and was no longer statistically significant.

Figure 1: Cumulative incidence of the first MACE according to dialysis modality.
components to patients’ risk, we included both DCa and serum calcium level (SCa) in the models. We observed significant associations with all outcomes and SCa, but not with DCa and the interaction between them. In a subgroup analysis of patients with iPTH levels below 130 pg/ml (n = 7,438), we did not find any significant association between DCa and the outcomes.

**Conclusion:** In this observational study, no differences in all-cause or cardiovascular mortality were observed with the prescription of DCa 1.50 as compared to 1.25 after adjustment for confounders, whereas the risk of SCD appeared to be lower in the group of DCa 1.50. The association between the SCa-DCa gradient and outcomes appears to be predominantly related to the effect of SCa.

**REFERENCE**


**#3282**

ASSOCIATION OF PROLONGED QT INTERVALS WITH MORTALITY IN HEMODIALYSIS PATIENTS: A NATIONWIDE RETROSPECTIVE COHORT STUDY

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**Background and Aims:** The prevalence of prolonged QT intervals is known to be prevalent among hemodialysis patients. In the general population, prolonged QT intervals are linked to increased mortality, however, the correlation between prolonged QT intervals and prognosis in hemodialysis patients remains uncertain. The objective of this study was to investigate the association between prolonged QT intervals and mortality and cardiac death among hemodialysis patients.

**Method:** We conducted a retrospective cohort study using the JSDR2019-2020, a nationwide registry of hemodialysis patients in Japan. We excluded from these subjects those younger than 18 years, with QT interval deficit, dialysis less than 3 times a week, atrial fibrillation, peritoneal dialysis, and home dialysis. In 2019, we collected data on various factors and basic patient information, and subsequently monitored outcomes in 2020. QT intervals were corrected using Bazett’s formula. Our primary and secondary outcomes were death and cardiac death which we defined as a composite of heart failure, pulmonary edema, arrhythmia, ischemic heart disease, and acute myocardial infarction, respectively. We performed univariate and multivariate analyses of the relationship between QT interval categories and outcomes using logistic regression models, adjusting for age, gender, cause of end-stage renal failure, serum concentrations of iron, potassium, magnesium, calcium, and phosphorus, history of dialysis, and history of cardiovascular disease. We also created a restricted cubic spline to visualize the relationship between QT intervals and outcomes. We employed multivariate imputation by chained equations to complement missing values. We set the significance level at 5%.

**Results:** Of the 332,599 patients in the database, 198,624 were included in the analysis of this study. The mean (standard deviation: SD), median (quartiles), and actual number (%) of subjects were: age 69.8 (12.4), 130,735 (65.8) male, 101,988 (51.3) with diabetes, and 66.0 (29.0, 128.0) months of dialysis history. The mean QT interval (SD) was 450.7 msec (30.5). During the 1-year observation period, there were 29,705 deaths, 7,247 cardiac deaths, and 12,166 new cases of ischemic heart disease. The odds ratios (95% confidence intervals: 95%CI, p value) for death within 1 year in the three QT interval categories (<460 [reference], 460 < = & <500, 500 < ) were 1(−), 1.58 (1.52-1.64, p<0.001), and 2.49 (2.35-2.62, p<0.001), respectively. In multivariate analysis, the adjusted odds ratios for death within 1 year in each QT interval category were 1(−), 1.44 (1.37-1.21, p<0.001), and 1.98 (1.87-2.09, P <0.001), respectively. Our analysis of cardiac death as an outcome also revealed a statistically significant increase in cardiac death with increasing QT intervals.

**Conclusion:** QT intervals were prolonged in hemodialysis patients, and prolonged QT intervals were significantly associated with increased mortality and cardiac death.
**Figure 1:** Association between QT intervals and death. The model was adjusted for age, gender, cause of end-stage renal failure, serum concentrations of iron, potassium, magnesium, calcium, and phosphorus, history of dialysis, and history of cardiovascular disease.

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**#3794**

**AUTOPHAGY PATHWAY ACTIVATION IN IMMUNE-INFLAMMATORY CELLS OF PERITONEAL DIALYSIS PATIENTS**

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**Background and Aims:** The better understanding of the biological pathways related to chronic kidney disease (CKD) may be useful for the identification of new therapeutic targets to improve the management of CKD patients. High-throughput technologies with innovative bioinformatics approaches for data analysis are very useful to achieve this objective.

**Method:** We reinterrogated our previous gene expression microarray data obtained from peripheral mononuclear cells (PBMCs) of 5 healthy subjects (HS), 9 chronic kidney disease patients with KDOQI stage II-III (CKD) and 10 CKD patients undergoing peritoneal dialysis treatment (PD). Advanced statistical and machine learning methods, including support vector machine learning and partial least squares discriminant analysis, were used for bioinformatics. Western blot and flow cytometry, then, was used to validate these results in an independent study group (10 HS, 10 CKD and 15 PD).

**Results:** Statistical analysis revealed that the transcriptomic profile of PD was significantly different from HS and CKD. Instead, no significant differences were observed between HS and CKD. A total of 348 genes (p < 0.0001, FDR < 5%) were able to differentiate PD patients from the other two study groups. Autophagy resulted one of the most up-regulated pathways in PD and the autophagy related 5 (ATG5), a gene encoding for a key protein involved in autophagic vesicle formation, was the top discriminative transcript (as demonstrated also by the VIP score). Western blot for ATG5 and LC3BII, main phagosome proteins, performed on the validation cohort, confirmed the activation of autophagy pathway only in PBMC of PD patients.

**Conclusion:** Our high-throughput data demonstrated, for the first time, that the autophagy pathway is activated in immune-cells of PD patients. This condition may significantly impact their immune-response and -homeostasis and, probably, it represents the last attempt of these circulating cells to avoid apoptosis.

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**#4787**

**VITAMIN D AND PARATHYROID HORMONE PREDICT INCIDENT MAJOR ADVERSE CARDIAC EVENTS IN PATIENTS STARTING HAEMODIALYSIS: A REAL-WORLD ANALYSIS**

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**Background and Aims:** Despite its advantages, haemodialysis (HD) is associated with increased cardiovascular mortality and morbidity, with some studies reporting 48% higher mortality, within 2 years of starting treatment. HD patients are known to suffer from vitamin D deficiency which has been linked to excess CV mortality and morbidity. We aimed to investigate the prognostic significance of vitamin D in predicting incident Major Adverse Cardiovascular Events (MACE) within 5 years of commencing HD.

**Method:** A retrospective cohort study was performed using electronic medical records from a global federated research network from the US (TriNetX). The TriNetX network was searched on 31st January 2023. The cohorts commenced HD post-diagnosis of End-Stage Kidney Disease. Data censoring for MACE was invoked prior to the index event of HD. Vitamin D (25-hydroxyvitamin D and 1,25 dihydroxy Vitamin D) concentrations were the first reported result within 3 months of starting HD. Cohorts were grouped according to biomarker-specific thresholds and 1:1 propensity-score matched for age, gender, and co-morbidities (hypertension, diabetes mellitus and smoking status). Logistical regression produced odds ratios with 95% CI for 5-year MACE. MACE was defined, a priori, as a composite of ischaemic heart disease, angina pectoris, acute myocardial infarction, heart failure, AF, stroke, and all-cause mortality. All statistical analysis was performed on the TriNetX online platform.

**Results:** The results are shown below. There was no association between outcome and PTH at 55 pg/ml threshold. Only results that reached statistical significance (p<0.05) are shown. Patients with a 25-OH Vitamin D
concentration <24 ng/ml or 1,25-diOH Vitamin D at <35 pg/ml had significantly more events, as shown below.

**Conclusion:** Circulating plasma levels of cholecalciferol and calcitriol are predictive of CV outcomes in patients commencing HD; however, the risk profile is different between low levels of active and inactive vitamin D. As the incident HD population are at increased risk of CV mortality and morbidity, cholecalciferol and calcitriol should be included in assessing overall risk.

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**D5 - PERITONEAL DIALYSIS & HOME THERAPIES**

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#### #3482

**IN VIVO EVALUATIONS OF THE PROTECTIVE EFFECTS OF NEW FORMULATIONS FOR PERITONEAL DIALYSIS ADOPTING A POWERFUL MULTI-PHOTON MICROSCOPY BASED APPROACH**

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**Background and Aims:** Peritoneal dialysis (PD) is a renal replacement therapy that enables metabolic waste products and excess fluids to be eliminated through the peritoneal membrane. Exposure to conventional dialysates at high glucose concentrations is considered critical for the pathogenesis of peritoneal fibrosis, angiogenesis, and epithelial-mesenchymal transition (EMT). These events largely contribute to peritoneal membrane aging, resulting in ultrafiltration failure. Preclinical research in this field suffers from the lack of valid and reproducible *in vivo* systems and so far has been limited to *in vitro* systems of mesothelial or endothelial cell lines. *In vitro* studies on mesothelial cell monolayers have validated the significant protective effects of dialysates with alternative osmo-metabolic agents. With their better biocompatibility these novel formulations could provide a valid substitute for conventional solutions (1,2). The method proposed, based on multi-photon microscopy, aims to study the physiology of the peritoneal membrane during dialysis exchange and to validate the effects of biocompatible dialysates in animal models of fibrosis as observed in the course of dialysis treatment.

**Method:** We have implemented a surgical procedure to optimize the stability of a flap of parietal peritoneum to allow direct microscope observation. The innovative technology of multi-photon microscopy enables one to observe the vessels of microcirculation *in vivo* and provides a 3D rendering of the peritoneal membrane, giving an overview of all the single layers without the use of specific markers (Figure 1). One may also assess specific phenomena induced by the fibrotic process, such as the thickening of the sub-mesothelial interstitium, exploiting the autofluorescence signal from excited collagen fibers caused by the physical phenomenon of Second Harmonic generation. *In vivo* microscopy evaluation of peritoneal membrane senescence parameters was conducted in rats subjected to one daily intraperitoneal injection (10 mL/day) for 15 days with one of the following PD solutions: a commercially available glucose-based neutral-pH, low-GDP, PD solution (Physioneal 3.86%, Baxter Healthcare, Italy), and a new single-chamber low glucose PD solution containing osmo-metabolic agents such as L-carnitine and xylitol (XyloCore HS, Galenica Senese, Italy). XyloCore HS is a lactate-buffered PD solution with glucose (1.5%), L-carnitine (0.02%) and xylitol (2.0%). The osmotic strength of the two PD solutions tested was comparable.

**Results:** Treatment with XyloCore HS was associated with a significant reduction in thickness of the sub-mesothelial interstitium (p = 0.013), the density of collagen fibers (p = 0.012) and the vascular composition (p = 0.006), as well as the number of branch points (p = 0.0335), when compared to rats treated with a commercial glucose-based PD solution, Physioneal. Figure 2 shows the different thicknesses of sub-mesothelial strata upon treatment with the PD solutions under investigation.

**Conclusion:** Previous *in vitro* studies have shown that XyloCore (1,2), a novel glucose-sparing PD solution currently in Phase III clinical development (ELIXIR - NCT03994471), is able to counteract the glucotoxic effects on the peritoneal membrane induced by conventional dialysates. Our pre-clinical *in vivo* methodology not only confirms our previous *in vitro* findings, but also

<table>
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<th>Outcome</th>
<th>Number with outcome</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
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<td>1.07-1.32</td>
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<td>Angina Pectoris</td>
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<td>1.22</td>
<td>1.05-1.41</td>
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<td>Ischaemic Heart Disease</td>
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<td>1.27</td>
<td>1.15-1.41</td>
<td>&lt;0.0001</td>
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<tr>
<td>1, 25 dihydroxy Vitamin D &lt;35 pg/ml = ref group (N = 2418/cohorts; mean age 56[16]; 52% male)</td>
<td>135</td>
<td>1.41</td>
<td>0.99-2.02</td>
<td>0.05</td>
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</tbody>
</table>

**Figure 1**

Multi-photon microscopy as a new frontier for *in vivo* imaging of the peritoneal membrane

Graphical and histological representation of the parietal peritoneum

3D rendering of membrane
suggests that long-term protective effects may be achieved with XyloCore. Further studies are in progress in a diabetic animal model to extend the favorable peritoneal in vivo findings of XyloCore treatment to a systemic level, possibly by improving glycemic control.

**REFERENCES**


#5664

**PERITONEAL DIFFUSE PODOPLANIN EXPRESSION IS ASSOCIATED WITH SEVERE ARTERIOLOPATHY IN CHILDREN ON PERITONEAL DIALYSIS**

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**Background and Aims:** Podoplanin is a transmembrane glycoprotein binding chemokines and modulating inflammatory reactions. In healthy peritoneum, it is expressed in mesothelial cells and in lymphatic endothelium, expression beyond these structures (diffuse podoplanin staining, DPS) has been observed in adult patients with encapsulating peritoneal sclerosis (EPS).

**Method:** Parietal peritoneal tissues from 71 children on PD fluids with low glucose degradation product (GDP) content underwent digital histomorphometry. DPS and pathomechanisms of peritoneal membrane transformation and vasculopathy were hierarchically clustered. A panel of 13 peritoneal cell markers was selected and tissue sections were stained with metal conjugated markers to evaluate podoplanin signals. Single-cell analysis was used to characterize peritoneal cells with positive podoplanin signals.

**Results:** DPS was present in 22% of the PD patients, all devoid of any clinical, radiological or histological feature of EPS. DPS positive patients were younger, had higher dialytic glucose exposure (median 103 vs. 154 g/m²/day, p = 0.002), and lower peritoneal arteriolar lumen to vessel (L/V) ratio, i.e. exhibited more arteriolar lumen narrowing. PD duration [median 20 (14.5, 48) months] and peritonitis incidence were similar as in non-DPS patients. In multivariable analysis, glucose exposure, PD duration, epithelial-to-mesenchymal transformed (EMT) cells and lower patient body surface area (BSA) independently predicted the presence of DPS. DPS and lower mesothelial surface coverage predicted lower arteriolar L/V ratio. In subgroups matched for BSA, PD duration and dialytic glucose exposure, DPS patients had a lower L/V ratio, (0.44 ± 0.13 vs. 0.31 ± 0.18, p = 0.003) and higher submesothelial CD45 leucocyte, CD68 macrophage and EMT cell count. Submesothelial lipopolysaccharide and hyaluronic acid receptor CD44 were increased in DPS positive patients, hyaluronan synthase 1 and 2 were similar. Among DPS positive patients, DPS intensity grade was higher in those with history of bacterial or fungal peritonitis (7 out of 15). Two patients had three and four peritonitis episodes respectively, their PD pattern did not differ from patients with history of only one peritonitis episode. Hierarchical clustering demonstrated highest similarity of DPS positive areas with CD68 positive areas. In IMC analysis of DPS positive areas, highest podoplanin signals were derived from M2 classified macrophages (CD68+CD163+) and fibroblastic cells [αSMA positive/non-endothelial/non-macrophage (αSMA+PROX1-CD31-CD68-CD163-)], signals derived from M1 classified macrophages (CD68+CD163-) were lowest.

**Conclusion:** Peritoneal DPS in pediatric patients on low-GDP PD is associated with lower BSA, higher dialytic glucose exposure, history of infectious peritonitis and peritoneal inflammatory and EMT cell invasion, and predicts obliterating peritoneal vasculopathy. We identified M2 macrophages as major source of extra-lymphatic peritoneal podoplanin accumulation, suggesting their role in severe peritoneal transformation.

#5668

**PERITONEAL DIALYSIS ADDITIVE REDUCES TRANSPERITONEAL LOSS OF BLOOD MICROPARTICLE AND EXTRACELLULAR MATRIX PROTEINS IN A CONTROLLED CROSSOVER TRIAL**

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**Background and Aims:** About 11% of patients requiring dialysis worldwide are treated with peritoneal dialysis (PD). With each PD exchange high amounts of protein are removed from the peritoneal cavity stemming from the systemic circulation (reflecting toxin removal, loss of serum proteins, inflammatory processes) and local inflammatory processes. Thereby, the clinically measured peritoneal protein loss (PPL) is the result of transperitoneal serum loss, lymphatic drainage, transmesothelial reabsorption, local production, and cellular components. Although high PPL has been found to be predictive of mortality and cardiovascular morbidity, the pathophysiological concept is still poorly understood.

**Method:** Peritoneal dialysis effluent (PDE) samples were obtained from peritoneal equilibrium tests during a prospective, multicenter, double-blinded, controlled, randomized, dual-period, 2-treatment, crossover, phase II, proof-of-concept study in Austria. PDE samples were submitted to proteomic analysis by tandem mass tag (TMT) labeling and 2D reversed phase liquid chromatography mass spectrometry. To disentangle transmembrane serum protein loss from local protein production we developed a novel and unique analytical approach. Briefly, partitioning around medoids and proximity in the Euclidean space for between visit (non-treatment visits only) single-protein kinetics was utilized to achieve this separation. A multivariate mixed-effects model was calculated to identify treatment (intraperitoneal alanyl-glutamine administration) effects.
Results: We identified 2,624 different proteins within the PDE of 12 patients across two time-points. A large cluster of proteins with stable abundance in collinearity with well-established clinical characteristics of transperitoneal transport (e.g., dialysate-to-plasma-albumin) in accordance with the three-pore-model was identified. After clustering and separation, the proteins resembling similar time-course kinetics to clinical transperitoneal membrane transport characteristics (one of five clusters) were all identified to be able to theoretically traverse through the small peritoneal pore (< 4-6 nm). Of these 549 proteins lost from the systemic circulation via transperitoneal small pore diffusion, the appearance of 51 in the PD effluent was significantly reduced by intraperitoneal administration of alanyl-glutamine. The affected proteins are mainly involved in extracellular matrix organization, part of extracellular exosome signaling and blood microparticles, e.g., high density lipoprotein (HDL) formation (Apollipoprotein A1).

Conclusion: PPL is an important but poorly understood undesired effect of PD associated with cardiovascular morbidity and mortality. Our novel analytical approach enables us to disentangle the complexity of transperitoneal serum protein loss and local protein production on single-protein level across the peritoneal proteome. Furthermore, we were able to delineate the potential beneficial effects of intraperitoneal alanyl-glutamine treatment on PPL and peritoneal health which might even suggest potential beneficial effects on cardiovascular morbidity (e.g., HDL formation).

KIDNEY TRANSPLANTATION

E2 - EPIDEMIOLOGY & OUTCOME

#5504
EXTENDED VALIDATION OF THE IBOX IN REAL LIFE SETTING, DIFFERENT TRANSPLANT SYSTEMS AND CLINICAL TRIALS: THE IBOX EXTENDED TRIAL

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GRAPHICAL ABSTRACT

Extended validation of the iBox in real-life settings, different transplant systems and clinical trials: the iBox extended trial

Background

The iBox is a validated prognostication system predicting long-term kidney allograft failure. It received regulatory endorsement by EMA, for surrogate endpoint for clinical trials. As the iBox system was primarily built using a deep phenotyped cohort, there is a need for proof-of-principle in extended clinical scenarios, geographically diverse centers, national and international transplant allocation systems.

Methods

- 10,851 transplant recipients
- 17 academic medical centers
- Europe, North America and South America

Results

Destination cohort: 6,000 recipients
- Banff with donor risk index (MDRD186, MDRD175, CKD-Epi)0.81; 2) iBox + structural (absence of histology); 3) iBox + functional (without DSA measurements); 4) iBox to risk evaluation, functional parameters (eGFR, proteinuria), allograft histological lesions (IFTA, g+ptc, i+t, cg Banff scores), and circulating anti-HLA DSA. We stratified the performances of the iBox according to several real-life scenarios, including: 1) iBox + different eGFR formulas (MDRD186, MDRD175, CKD-Epi); 2) iBox + urinary dipstick; 3) iBox Functional + Structural (absence of DSA measurements); 4) iBox functional + Immunological (absence of histology); 5) iBox in response to treatment in T-cell mediated rejection (TCMR); 6) iBox for in response to treatment antibody mediated rejection (ABMR) clinical trials. The performances of the iBox system were assessed with the discrimination (C-index) and calibration.

Results: The derivation cohort included 4,000 recipients from Europe (France, Belgium, Spain, Germany, Finland n = 4,643), the United States (n = 1,537) and South America (Brazil, Argentina n = 671). The mean recipient age was 50.26 years (14.05) with a median follow-up after evaluations of 5.41 years [IQR: 3.26 to 7.13]. 1336 patients (12.3%) lost their graft during the study follow-up. The performances of the iBox were confirmed in the different real-life setting with the following C-Index: 1) iBox + different eGFR formulas (MDRD186, MDRD175, CKD-Epi): 0.81; 2) iBox + urinary dipstick: 0.80; 3) iBox Functional + Structural (histology): 0.80 (derivation) and 0.84 (validation); 4) iBox functional + Immunological: 0.80 (derivation) and 0.83 (validation); 5) iBox in response to treatment in T-cell mediated rejection: 0.81; 6) iBox for in response to treatment antibody mediated rejection trials 0.81. The score showed an accurate calibration in every scenario.

Conclusion: The iBox extended trial confirms in various medicos-economic settings the performances transportability and surrogacy of the iBox system, further reinforcing its use as a surrogate end point for clinical trials including TCMR and ABMR.

#5237
RACIAL DISPARITY AND KIDNEY FUNCTION IN LIVING KIDNEY DONORS

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GRAPHICAL ABSTRACT

Racial disparity and kidney function in living kidney donors

Background

Kidney disease disproportionately affects some races and ethnicities. Whether this disparity exists in living kidney donors is unknown. We aimed to evaluate the association between racial/ethnic and kidney function after living kidney donation.

Methods

- (OPTN/SRDB, January 1977–Aug 2022)
- 166,845 living kidney donors

Results

- Age (1% to 99%)
- race (AA, CA, NH)
- race (AA, CA, NH)

Conclusion

- Kidney donors disproportionately affect some races and ethnicities. Whether this disparity exists in living kidney donors is unknown. We aimed to evaluate the association between racial/ethnic and kidney function after living kidney donation.
Method: A retrospective cohort study utilizing Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR) database includes living kidney donors undergoing donation between June 1972 and September 2022. Time-to-event of >35% rising post-donation serum creatinine from pre-donation serum creatinine among different races and ethnicities was examined by multiple Cox proportional hazard regression analyses.

Results: Of 136,814 living kidney donors, the mean ± SD age was 42 ± 12 years and 61% were female. The majority were White (70%) followed by Hispanic (14%), Black (11%), Asian (4%), multiracial (0.61%), American Indian/Alaska Native (0.47%), and native Hawaiian/other Pacific islander (0.25%). Among 103,938 living kidney donors with post-donation serum creatinine, 78,344 (75%) living kidney donors had the event over a median time to follow-up of 6.27 months (interquartile range 4.07, 8.67). The incidence rate of the event was 0.09 person-months. Mean pre-donation serum creatinine was 0.85 ± 0.19 mg/dL and post-donation serum creatinine during routine follow-up visits at 6, 12, and 24 months were 1.22 ± 0.30, 1.194 ± 0.30, and 1.16 ± 0.27 mg/dL, respectively (Figure 1A). Mean percentage of elevated serum creatinine from pre-donation serum creatinine were 46, 43, and 41%, respectively (Figure 1B). Compared to White, Blacks had a significantly higher; while Hispanics and multi-racial groups had a significantly lower risk of increased post-donation serum creatinine >35% (hazard ratio (HR) Black 1.03, 95% confidence interval (CI) 1.01, 1.06, P = 0.008; HR Hispanic 0.95, 95% CI 0.93, 0.97, P < 0.0001; HR Multiracial 0.92, 95% CI 0.84, 0.99, P = 0.049; Figure 2). After adjusting for age, gender, U.S. citizenship, education level, pre-donation body mass index, systolic blood pressure, diastolic blood pressure, serum creatinine, post-donation proteinuria, history of pre-donation hypertension, and the interaction term between race/ethnicity and age (<70 or ≥70), Black remained at greater risk for the event and Asians still had a lower the risk (HR Black 1.22, 95% CI 1.13, 1.31, P < 0.001; HR Asian 0.88, 95% CI 0.83, 0.94, P < 0.001). Other races/ethnic had no significant difference in the risk. Age was an effect modifier with attenuated risk for increased serum creatinine >35% observed in older Hispanic, Asian, and multiracial groups (P interaction 0.037, 0.001, and 0.006, respectively).

Conclusion: Blacks are at risk of increased post-donation serum creatinine >35%; while Asian is protective compared to White independent of pre- and post-donation factors. Elderly Hispanic, Asian, and multiracial living kidney donors do not have worsened kidney outcome compared to their younger living kidney donors with the same races/ethnicities.
Next Generation Sequencing: From Banff Score Molecular Signatures and Classifiers to Predicted Histological Archetypes of Kidney Biopsies

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Background and Aims: To improve risk stratification in kidney transplantation, molecular diagnostic tools are increasingly investigated for their feasibility and gain in diagnostic power. Nonetheless, previously published studies focused on sequencing technologies and gene panels with limited vision of the transcriptome (pathogenesis-based transcripts [PBTs], Banff Human Organ Transplant [BHOT] panel). The EU-TRAIN consortium was built to discover new predictive and informative biomarkers for kidney transplant histology and rejection diagnoses, leveraging a next generation sequencing technology.

Method: EU-TRAIN (NCT03652402) is a prospective multicentric study including unselected kidney transplant cohorts from 11 centres from 4 countries (France, Spain, Germany, Switzerland). We performed a bulk RNA sequencing on the polyadenylated probes of 770 kidney biopsies (n = 540 kidney recipients) collected between 2018 and 2021. Differential gene expression analyses were computed to obtain a molecular signature for all Banff score lesions. We then derived three different feature selections by either i) training an ElasticNet model on all differentially-expressed genes (DEGs), or by taking the top 30 ii) overall DEGs or iii) the top 30 DEGs focusing on transcripts included in the BHOT gene panel. From them, we trained four machine learning (ML) classifiers through a 10-times repeated 3-fold cross-validation. Models’ performances were assessed on a hold-out test.
set accounting for 30% of the total samples. Finally, we derived prototypic histological profiles using an archetypal analysis on the samples’ predicted Banff score probabilities from the best classifier. 

**Results:** The ElasticNet feature selection lowered the number of DEGs to be predicted accurately the Banff score lesions and 8 profiles were identified among these predictions. External validation and archetypes’ association with graft loss will be addressed in the future.

**Conclusion:** In addition to the previously described factors usually related to worse evolution of IgA nephropathy in the native kidney and after post-transplant recurrence, we observed that cellular inflammation influences worse evolution after rIgAN. We suggest to considering the Banff criteria for acute cellular inflammation to better understand the subsequent evolution of patients with rIgAN.

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**#6257**

**PROGNOSTIC VALUE OF A POSITIVE CROSSMATCH BEFORE DESENSITIZATION IN A COHORT OF HIGHLY-SENSITIZED PATIENTS**

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**GRAPHICAL ABSTRACT**

**Prognostic value of a positive crossmatch before desensitization in a cohort of highly-sensitized patients**

**Background:** Human Leukocyte antigen (HLA) sensitization in patients is a barrier for Kidney Transplantation (KT) access, and highly-sensitized patients remain on the waiting list longer than other patients which results in a higher morbidity and mortality. Desensitization may be an option to increase their access to KT. All patients transplanted in this context have a negative Complement-Dependent Cytotoxicity crossmatch (CDC-CM) the day of KT. However, the stratification of the long-term risk of graft loss according to flow cytometry crossmatch (FC-CM) and to CDC-CM during the desensitization period remains unknown.

**Method:** In this retrospective study, all highly-sensitized patients (Panel Reactive Antibigen (PRA) ≥ 85) in our center were included. CDC-CM and FC-CM were performed on samples before and during the desensitization period and clinical follow-up data were retrieved. Pre-KT desensitization strategy consisted in two Rituximab infusions (375mg/m²) and a variable number of apheresis (mostly semi-specific immunoadsorption) associated with a classical immunosuppression-based regimen (tacrolimus, mycophenolate and steroids).

**Results:** A total of 183 highly-sensitized recipients received a KT between 2014 and 2022. Of these, 23 were desensitized prior to KT and among them 18 had a positive FC-CM before KT and 5 had no positive FC-CM on all assessed serum samples. Mean age was 52.9 ± 13 years. Mean follow-up was 5.2±4 and 3±2 years for non-desensitized and desensitized patients respectively. PRA before desensitization was higher in desensitized patients (98%) versus non-desensitized patients (95%) and the mean time on the waiting list was 5.8±4 versus 7.5±4 years respectively. Death-censored graft survival and patient’s survival, using cox-survival analysis, were not statistically different between the desensitized kidney transplanted patients and the highly-sensitized patients without desensitization (p = 0.77 and p = 0.57 respectively). In sub-group analyses, the positivity of FC and/or CDC-CM did not add an additional risk of graft loss or patient mortality.

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**#5393**

**INFLUENCE OF CELLULAR INFLAMMATION ON THE OUTCOME OF KIDNEY TRANSPLANTATION AFTER RECURRENT OF IgA NEPHROPATHY**

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**Background and Aims:** The recurrence of IgA nephropathy (rIgAN) worsens the prognosis of renal transplantation, representing the third cause of loss in these recipients. Several variables at the time of recurrence, such as worse renal function, greater proteinuria, previous steroid withdrawal, and MEST-C histological findings have been associated with a higher risk of graft loss after recurrence. The presence of clinical or subclinical inflammation has been associated with a higher risk of kidney graft loss, but it is not precisely known how it influences the outcome of patients with rIgAN.

**Method:** A multicenter retrospective study was carried out including renal transplant recipients with biopsy-proven IgA nephropathy as the underlying disease in which the recurrence of the primary disease had been verified by means of graft biopsy and in which the Banff criteria were available or could be reviewed. Cellular inflammation was defined according to Banff scores as “t” or “i” ≥ 2. The main endpoint was progression to CKD stage 5 or death censored-graft loss (DCGL).

**Results:** 118 kidney transplant recipients were included with an age of 47 ± 14 years at recurrence, 80% male, with a mean time to biopsy of 65 ± 69 months and a post-transplant follow-up of 118 ± 70 months. After recurrence, 34 (28.8%) transplants were lost after 35 ± 28 months, excluding death. Using univariate Cox regression, the factors related to CKD stage 5 or graft loss were systolic blood pressure (HR 1.039, 95% CI 1.016-1.064, p = 0.001), glomerular filtration rate (HR 0.948, 95% CI 0.922-0.974, p < 0.001), the logarithm of proteinuria (HR 15.836, 95% CI 5.504-45.565, p < 0.001), Oxford-C score (HR 3.490, 95% CI 2.137-5.699, p < 0.001), interstitial fibrosis (HR 2.173, 95% CI 1.362-3.468, p = 0.001) and cellular inflammation (HR 2.458, 95% CI 1.237-4.884, p = 0.010). After multivariate analysis, cellular inflammation remained significantly related to CKD stage 5 or DCGL (HR 2.338, 95% CI 1.077-5.075, p = 0.032), independently of systolic blood pressure, glomerular filtration rate, the logarithm of proteinuria and Oxford-C score.

**Conclusion:** There is a significant impact of cellular inflammation on the adverse evolution of rIgAN in the native kidney and in the post-transplantation period. This finding is important to better understand the evolution and make accurate decisions regarding the treatment strategy in these patients.
Conclusion: Desensitization allows highly-sensitized patients to access KT with an HLA-incompatible graft (with a positive CDC or FC-CM on the serum collected prior to desensitization), with the same graft survival as similarly sensitized patients transplanted with an HLA-compatible graft without desensitization.

#3973
EXCELLENT EFFICACY AND BENEFICIAL SAFETY DURING FIVE YEAR FOLLOW-UP OF RAPID STEROID WITHDRAWAL AFTER RENAL TRANSPLANTATION (HARMONY STUDY)
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Background and Aims: We previously reported excellent efficacy and improved safety aspects of rapid steroid withdrawal in the randomized controlled one year “Harmony” trial with 587 predominantly deceased-donor kidney transplant recipients randomized either to basiliximab or rabbit antithymocyte globulin induction therapy and compared to standard immunosuppressive therapy consisting of basiliximab, low tacrolimus once daily, mycophenolate mofetil, and corticosteroids. The five-year post-trial follow-up (FU) data reported here were obtained in an observational manner to evaluate, how these excellent short-term surrogate parameters will translate into hard long-term outcome parameters like patient death/graft loss.

Method: The five-year post-trial follow-up data were obtained in an observational manner at a three and a five-year visit for patients who consented to participate and covered clinical events that occurred from the second year onwards.

Results: Biopsy-proven acute rejection and death-censored graft loss rates remained low and independent of rapid steroid withdrawal (see Figure 1). Rapid steroid withdrawal was an independent positive factor for patient survival (adjusted hazard ratio 0.554, 95 % confidence interval 0.314 to 0.976; p = 0.041, see Table 1). The reduced incidence of post-transplantation diabetes mellitus in rapid steroid withdrawal patients during the original one-year study period was not compensated by later incidences during follow-up. Incidences of other important outcome parameters such as opportunistic infections, malignancies, cardiovascular morbidity/risk factors, donor specific antibody formation, or kidney function did not differ during follow-up period.

Abstracts
Belatacept outcomes in pediatric kidney transplantation: An international multicenter study

Belatacept is a co-stimulation blocker associated with better long-term outcomes in adult patients compared to CNI based regimens. Data on its use in older children and young adults are lacking. We are the 1st to report outcomes for 45 pediatric kidney transplant recipients converted to belatacept.

Method: 45 patients were included from 4 centers (USA and France) between 05/2018 and 12/2021. Patients received an induction with basiliximab (n = 39) or ATG (n = 6). Maintenance immunosuppression included CNI, MMF +/- steroids. Patients' viral status (EBV, CMV) were monitored monthly to report outcomes for 45 pediatric kidney transplant recipients converted to belatacept. All patients were EBV viral at the time of conversion (4 were EBV+ at the time of conversion). 6 patients because of delayed graft function and 1 to avoid CNI toxicity. 38/45 patients were converted after a median of 4.1 years post-transplant (IQR 1.7-6.0). GFR was stable or improved over a median follow-up time of 1.6 years (IQR 1.1-2.4), Fig 1 A. Rejection episodes were observed in 10/45 patients (22%) after a median of 10.2 months (IQR 6.1-15.8) and included 7 TCMR, 2 ABMR and 1 mixed rejection. None of these patients were converted early (<3 m), 5 had been converted for non-adherence, 4 had pre-existing DSA and 4 had prior history of rejection. Evolution of GFR in rejectors is shown in Fig 1 B. CNI were reintroduced for 6/10 and belatacept stopped for 3/10. Regarding viral complications, 1 severe BKV nephropathy required the discontinuation of belatacept. All patients were EBV+ at conversion (4 were EBV- at the time of transplantation). No EBV replication was observed.

Conclusion: Selected pediatric kidney recipients benefit from long-term CNI toxicity avoidance, but selection criteria need to be refined to avoid rejection under costimulation blockade.
Figure 1:

A  Evolution of graft function (eGFR Schwartz formula) after initiation of belatacept

N = 45 patients

- Early conversion
  (-3 months post transplant)
- Standard conversion
  (-3 months post transplant)

B  Evolution of graft function (eGFR Schwartz formula) and outcomes in patients who developed rejection on belatacept

N = 10 patients

<table>
<thead>
<tr>
<th>Rejection type</th>
<th>Patient</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed rejection</td>
<td>Patient 3</td>
<td>BELA stopped</td>
</tr>
<tr>
<td>AEMR</td>
<td>Patient 7</td>
<td>BELA stopped</td>
</tr>
<tr>
<td>Patient 10</td>
<td>BELA stopped</td>
<td></td>
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<tr>
<td>Patient 11</td>
<td>Patient 22</td>
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<tr>
<td>Patient 28</td>
<td>Patient 39</td>
<td>CHI restarted</td>
</tr>
<tr>
<td>Patient 41</td>
<td>Patient 44</td>
<td>CHI restarted</td>
</tr>
</tbody>
</table>

Median time to rejection: 19.2 months (IQR 1.15-1.8)
#6402

**IMPACT OF DARATUMUMAB AND BELATACEPT ON HLA ANTIBODIES IN KIDNEY TRANSPLANT CANDIDATES WITH 100% CPRA: EARLY RESULTS OF ATTAIN (ITN090ST)**

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**Background and Aims:** Despite high allocation priority, <10% of kidney transplant candidates with cPRA 100% can find a compatible donor. Current desensitization strategies are ineffective due to antibody rebound. Adding costimulation blockade to plasma cell (PC) depletion prevents antibody rebound in nonhuman primates by countering nodal B cell and Tfh expansion.

**Method:** ATTAIN is a pilot, phase I/II trial of daratumumab, a CD38 mAb used in multiple myeloma, plus belatacept, a high affinity CTLA4-Ig, to desensitize kidney transplant candidates with cPRA ≥99.9%. Enrolled subjects receive daratumumab (6 doses: 8 mg/kg) and belatacept (4 doses: 10 mg/kg) over 10 weeks with bone marrow and blood assessments pre- and post-treatment. The primary efficacy endpoint (PE) is a composite of (1) elimination of ≥1 HLA antibody specificity, (2) ≥50% reduction in the MFI of ≥3 HLA antibody specificities, or (3) kidney transplant from a previously incompatible donor. Target accrual is 15, enrolled in 2 cohorts (5+10).

**Results:** Cohort 1 (n = 5, mean age 44, 60% with previous transplant) has been enrolled and treated, with 5-31 weeks follow-up to date. The treatment was tolerated well in all 5 patients who showed a significant reduction in most HLA antibodies after treatment without manifestation of rebound. 3 of 5 participants reached the PE and 5 of 5 had >50% bone marrow (BM) PC depletion. One patient received a kidney transplant from a previously incompatible deceased donor and is doing well at 7 months post-transplant without rejection or rebound of HLA antibody. Treatment was temporarily paused in 3 subjects due to AEs (acute cholecystitis and COVID, upper GI bleed, fevers); no cases of opportunistic infection or malignancy occurred.

**Conclusion:** A novel HLA desensitization regimen consisting of PC depletion with Daratumumab and costimulatory blockade with Belatacept appears safe and successful in the ongoing ATTAIN clinical trial. In the initial subject, this regimen led to transplant without HLA antibody rebound or acute rejection. Longer follow-up and additional subjects are needed to confirm these promising results. ATTAIN (NCT04827979) is a trial conducted by the Immune Tolerance Network and sponsored by NIAID (award UM1AI109565).

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**Figure 1:** Study regimen.

**Figure 2:** Change in HLA antibodies with treatment.
DONOR-DERIVED CELL-FREE DNA (DD-CfDNA) AS A NON-INVASIVE BIOMARKER OF KIDNEY ALLOGRAFT REJECTION IN PEDIATRIC KIDNEY TRANSPLANTATION

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Background and Aims: Rejection remains the first cause of allograft loss in pediatric kidney transplant (pKTx) recipients. Detection of rejection currently relies on KTx biopsies performed either because of allograft dysfunction with the risk of late diagnosis or per surveillance protocols allowing early detection of subclinical rejection but resulting in many unnecessary biopsies. Dd-cfDNA was reported as a new non-invasive biomarker with the potential to improve rejection detection and guide biopsy indications. We aim to assess the association of dd-cfDNA levels with biopsy results in a large cohort of pediatric KTx recipients.

Method: All pediatric KTx patients with at least one dd-cfDNA assessment at the time of a biopsy at a single pediatric transplant center were included. Clinical, biological and histological data were collected from medical reports. Dd-cfDNA were retrospectively measured from plasma samples biobanked at the time of allograft biopsy between 2015 and 2020 or collected in patients who received regular dd-cfDNA testing as part as clinical care between 2021 and 2022.

Results: 170 cfDNA measurements in 132 pKTx recipients were available at the time of a biopsy, including 100 performed for surveillance. Mean age at biopsy was 16 years with a median time from KTx of 21 [11;38] months. Median eGFR was 62 [48;83] mL/min/1.73 m², median UPCR 0.21 [0.14;0.36] g/g, and 20% had DSA at the time of the biopsy. Biopsy findings included: 109 normal, 30 borderline, 15 TCMR, 11 AMR and 5 mixed rejections. Median cfDNA level was 0.64 [0.31;1.80] %. We found a strong association between cfDNA levels and active tubule-interstitial and microvascular Banff lesions (Figure 1). cfDNA levels were significantly increased in cases with rejection (Figure 2).

Using the proposed cut-off of 0.5%, performances of the test to detect rejection were Se 84%, Spe 51%, PPV 33%, NPV 92%. Among the borderline cases, 17 (57%) had cfDNA >0.5%.

Conclusion: We confirm in the largest pediatric KTx cohort to date, the association of dd-cfDNA levels with allograft rejection and its potential interest as a non-invasive biomarker in children. Further studies are needed to assess the added value of dd-cfDNA monitoring to the current standard of care and its ability to reduce unnecessary surveillance biopsies and improve outcomes.

Figure 1: Association between dd-cfDNA levels and active tubule-interstitial and microvascular Banff lesions.
Background and Aims: Antibody induction therapy is frequently used as an adjunct to the maintenance immunosuppression in adult kidney transplant recipients (KTRs). There are few comparisons of antibody induction therapy allowing early glucocorticoid withdrawal in KTRs. The purpose of the present study was to compare induction therapy involving tocilizumab with the most commonly used induction regimens in patient populations at either high immunologic risk or low immunologic risk.

Method: In this prospective study, we randomly assigned patients to receive tocilizumab or conventional induction therapy such as basiliximab. Patients were stratified according to acute rejection risk, with a high risk defined by a repeat transplant, a peak or current value of panel-reactive antibodies of 30% or more. The 102 high-risk patients received tocilizumab (one dose of 8 mg/kg, in 52 patients) or basiliximab (a total of 40 mg over 4 days, in 50 patients). The 113 low-risk patients received tocilizumab (one dose of 8 mg/kg, in 62 patients) or basiliximab (a total of 40 mg over 4 days, in 51 patients). All patients received tacrolimus and mycophenolate mofetil and underwent a 10-days glucocorticoid (prednisone) taper in a regimen of early steroid withdrawal. The primary endpoint was biopsy-confirmed acute rejection at 6 months and 12 months. Patients were followed for 2 years for safety and efficacy endpoints.

Results: The rate of biopsy-confirmed acute rejection was significantly lower in the tocilizumab group than in the basiliximab group at both 6 months (5.3% vs. 10.9%, P<0.01) and 12 months (7.9% vs. 12.9%, P<0.01). At 2 years, the rate of biopsy-confirmed acute rejection in low-risk patients was lower with tocilizumab than with basiliximab (9.7% vs. 17.7%, P<0.05), but among high-risk patients, no significant difference was seen between tocilizumab and basiliximab (19.2% vs. 16.0%, P = 0.68). Adverse-event rates were similar among all four treatment groups.

Conclusion: By the first year after transplantation, biopsy-confirmed acute rejection was less frequent with tocilizumab than with conventional therapy. The apparent superiority of tocilizumab with respect to early biopsy-confirmed acute rejection was restricted to patients at low risk for transplant rejection; among high-risk patients, tocilizumab and basiliximab had similar efficacy. Further randomized and controlled studies are needed to support these results.
Circulating nephrin autoantibodies could be a possible candidate for CF in the specimens were observed in all 14 patients with post-transplant recurrent punctate deposition of IgG colocalized with nephrin in grafted kidney biopsy

**Conclusion:** The autoantibodies to nephrin in plasma samples and the deposition of IgG colocalized with nephrin in all 14 recurrent patients. The IF staining of graft biopsy specimens showed punctate

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**#6771**

**HEPATITIS B VIRUS REACTIVATION IN KIDNEY TRANSPLANT RECIPIENTS TREATED WITH BELATACEPT**

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**Background and Aims:** Hepatitis B virus (HBV) reactivation in kidney transplant recipients may be associated with liver failure and graft loss, especially in anti-HBc antibody (HBcAb)-positive HBs antigen (HBsAg)-negative patients. Belatacept, a selective costimulation blocker, has been used in kidney transplantation for some time and has been associated with reactivation of other viruses as BK or CMV. However, there are few data on HBV reactivation among kidney recipients treated with belatacept.

**Method:** We performed a retrospective study in two French kidney transplantation centres including all transplant recipients receiving belatacept. Among HBcAb-positive patients, we analyzed HBV reactivation rate, outcomes and risks factors.

**Results:** 135 patients treated with belatacept were included, and 32 were HBcAb-positive. Seven patients reactivated HBV (21.9% of HBcAb-positive patients), including 5 HBsAg-negative patients (16.7%); reactivation occurred 54.8 (±70.9) months after transplantation. There was no significant difference in survival between patients that reactivated HBV and patients that did not: 5-year patient survival of 100% (28.6; 100) and 83.4% (67.6; 100), respectively (p = 0.363) and 5-year graft survival of 100% (28.6; 100) and 79.8% (61.7; 100), respectively (p = 0.335). No factor, including HBsAb positivity and antiviral prophylaxis, was statistically associated with the risk of HBV reactivation.

**Conclusion:** Compared to the few studies that exist in this area, the HBV reactivation rate was high in patients treated with belatacept in our study. Our findings suggest that systematic antiviral prophylaxis for anti-HBc antibody (HBcAb)-positive HBs antigen (HBsAg)-negative patients should be considered and that there should be close monitoring of HBV serology and viral load in these patients to detect early HBV reactivation.

**Background and Aims:** Diabetic nephropathy (DN), which is one of the most common systemic microvascular complications of diabetes mellitus, is extremely harmful to the patients' health. There were some studies had shown that the disturbance of lipid metabolism was connected with the progression of DN. Therefore, the purpose of our study was to find the lipid metabolism-related hub genes in DN and provide a better reference for the diagnosis of DN.

**Method:** The Gene Expression Omnibus (GEO) database was used to download the gene expression profile data of DN and healthy samples (GSE142153), and we obtained the lipid metabolism-related genes from the Molecular Signatures Database (MSigDB). Differentially expressed genes (DEGs) between DN and healthy samples were analyzed and the weighted gene co-expression network analysis (WGCNA) was performed to examine the connection between genes and clinical traits and screen the key module genes in DN. Next, we utilized the Venn Diagram R package to identify the lipid metabolism-related genes in DN, and the Protein-Protein Interaction (PPI) of these genes was constructed. Then we carried out the Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. Moreover, the hub genes were identified using two machine learning algorithms, and the Gene Set Enrichment Analysis (GSEA) was used to analyze the functions of the hub genes. Furthermore, the immune infiltration discrepancies between DN and healthy samples and the correlation between the immune cells and hub genes were estimated. Finally, quantitative reverse transcription-PCR (qRT-PCR) experiment verified the expression of key genes.

**Results:** A total of 1445 DEGs were found in DN samples compared to healthy samples, and 694 DN-related genes in yellow and turquoise modules were identified by WGCNA. Next, we used the Venn Diagram R package to further identify 17 genes that were related to lipid metabolism and constructed a PPI network. Then GO analysis revealed that these 17 genes were significantly correlated with 'phospholipid biosynthetic process' and 'cholesterol biosynthetic process', while the KEGG analysis showed these lipid metabolism-related genes were enriched in 'glycerophospholipid metabolism' and 'fatty acid degradation'. Moreover, SAMD8 and CYP51A1 were identified through the intersections of two machine learning algorithms. The results of GSEA analysis revealed that the 'mitochondrial matrix' and 'GTPase activity' were the significantly enriched GO terms in SAMD8 and CYP51A1, and the KEGG pathways of them were mainly concentrated in 'pathways of neurodegeneration - multiple sclerosis'. Immune infiltration analysis suggested that there were 9 immune cells expressed differently in DN and healthy samples, and both SAMD8 and CYP51A1 were significantly correlated with activated B cell and effector memory CD8 T cell. Finally, qRT-PCR confirmed the expression of SAMD8 and CYP51A1 in DN was high.

**Conclusion:** In summary, the lipid metabolism-related genes SAMD8 and CYP51A1 may play key roles in DN.
Figure 1: Differentially expressed genes analysis.
Figure 2: Weighted gene co-expression network analysis.
Figure 3: Protein-protein interaction network of hub genes.

Figure 4: GO and KEGG functional enrichment analysis.
Figure 5: Identification of hub genes.
Figure 6: Analysis of immune cell infiltration landscape.

Figure 7: qRT-PCR validation. (A) Higher expression of CYP51A1 in DN blood samples. (B) Higher expression of SAMD8 in DN blood samples. qRT-PCR, quantitative reverse transcription-Polymerase chain reaction.
EXPLORATION OF PROGNOSTIC FACTORS IN DIABETIC NEPHROPATHY WITH NODULAR LESION USING TRANSCRIPTOME ANALYSIS OF HUMAN KIDNEY TISSUES

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Background and Aims: Although the speed of eGFR decline is usually rapid in patients with diabetic nephropathy (DMN) and a nodular lesion (NL), some patients with NL experience a slow eGFR decline. The factors associated with the difference in prognosis remain unknown. In this study, we aimed to explore prognostic factors by performing transcriptome analysis on preserved residual renal biopsy specimens from patients with pathologically diagnosed and prognostically known DMN with nodules.

Method: Patients who had an annual eGFR drop rate > 5 mL/min/1.73 m² were defined as rapid decliners (RD) and the others as slow decliners (SD). Twelve patients (RD = 6 and SD = 6) who underwent kidney biopsy, had no other renal comorbidities, and had been followed up for at least one year were included. Total RNA was isolated from renal biopsy tissues in formalin-fixed, paraffin-embedded blocks, and microarray analysis was done.

Results: At the time of renal biopsy, the eGFR, urine protein, and rate of sclerotic glomeruli were not statistically different between the RD and SD groups, at 49.7±10.1 mL/min/1.73 m² and 57.5±12.4 mL/min/1.73 m² (p = 0.258), 7.5±4.2 g/gCre and 4.0±2.7 g/gCre (p = 0.123), and 19.2±13.4% and 25.5±14.4% (p = 0.450), respectively. In microarray analyses (total 58,341 gene probes), genes with little expression (raw signals <50) and with little differences between RD and SD (processed signals <0.3) were excluded, leaving 14,227 genes for further analysis. A total of 1,496 differentially expressed genes (DEGs) were selected with p-values <0.05 and fold change ≥2 between the RD and SD group for further bioinformatic analysis. Using the Ingenuity Pathway Analysis system, 15 canonical pathways and 9 diseases or functions annotations were found to be enriched. In addition, upstream regulator analysis identified 73 upstream regulators. Among them, only two regulators, CBX5 and CCN5, showed p <0.05 and absolute z-score > 2 as activated and inhibited regulators, respectively, in the RD group. We next performed regulator effects analysis, indicating one regulator network which identified the key upstream regulator CCN5. The regulator network also showed a small number of genes involved in the viral infection, which included CDH1, CD24, and ESR1. Additionally, IPA showed 25 interaction networks ranging from 11 to 38. The fifth-ranked network was associated with Cancer, Organismal Injury, and Abnormalities (score = 32), in which CD24 and ESR1 were included. We, therefore, performed qRT-PCR to compare the expression levels of CDH1, CD24, and ESR1 in the RD group with those in the SD group.

The expression levels of CD24 and ESR1 in the RD group were downregulated compared with those in the SD group (p = 0.004 and p = 0.022, respectively) although there was little difference in the level of CDH1 between them (p = 0.638).

Conclusion: Transcriptomic analysis using renal biopsied tissue revealed that ESR1 and CD24 might be candidates for renoprotective factors in DMN with NL.

#3084

AMINOPEPTIDASE A REGULATES ACUTE ANGIOTENSIN DEPENDENT HYPERTENSION

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Background and Aims: Aminopeptidase A (APA) is an enzyme that cleaves a single aspartate residue from the amino-terminus of several renin-angiotensin systems (RAS) peptides. We have shown that genetic deficiency of APA was associated with increased blood pressure and ultrastructural glomerular pathology in mice. Here we studied the effect of this Aminopeptidase on different peptides of the RAS and its effect on acute hypertension.

Method: We developed an in vitro assay based on Aspartate formation by APA to detect which Angiotensin (Ang) peptides are the substrate of this enzyme. The identified Ang peptides were injected to determine their relative effects on systolic blood pressure (SBP) in anesthetized WT mice. The effect of recombinant Aminopeptidase A on Ang I, Ang II and Ang 1-12 mediated SBP increase was further assessed in APA deficiency using global knockout mice (KO), and after systemic injection of recombinant APA.

Results: In the in vitro assay, the rAPA showed significant cleavage activities for Ang II (22427±3353, n = 12), Ang I (21883±1692, n = 3). Ang I-7 (15833±3395, n = 3), Ang-9 (15773±3395, n = 3) and Ang-1-12 (13170±220, n = 3) as evidenced by the formation of aspartate measured as a readout of enzymatic cleavage. When the five angiotensin peptides were injected into WT mice, only Ang I, Ang II and Ang 1-12 caused a substantial increase in SBP (Figure 1, left). In APA KO mice the bolus administration of Ang II showed an exaggerated increase in SBP compared to WT mice (Figure 1, right). The effect of Ang I and Ang 1-12 in APA KO appeared similar (not shown). When Ang I, Ang II and Ang 1-12 were administrated in WT mice preinjected with APA the increase in SBP was markedly reduced (p<0.001, p = 0.0024 and p = 0.0063, respectively).

Conclusion: Aminopeptidase A can cleave the N-terminal aspartate from Ang II as well as from other RAS peptides upstream [Ang 1-12, Ang I (1-10) and Ang I-9] and downstream of Ang II (Ang 1-7). Aminopeptidase A deficiency is associated with exaggerated SBP response to Ang I, Ang II and Ang 1-12 whereas the recombinant enzyme restores the effect on acute hypertension caused by infusion of these peptides. This suggests that APA could be used to treat hypertension due to RAS overactivity.
URINARY OROSOMUCOID IS ASSOCIATED WITH ALL-CAUSE MORTALITY IN THE GENERAL POPULATION
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Background and Aims: Urinary albumin excretion (UAE) is considered a risk factor for cardiovascular (CV) disease and all-cause mortality, but the pathophysiological mechanisms are not known, and studies are not consistent with regards to the effect of pharmacological UAE reduction on endpoints. Another protein, orosomucoid (41-43kDa), is a non-specific acute inflammatory protein and is a part of the glycolax that covers the endothelium. Under normal conditions the concentration in urine is low, but a marked increase is demonstrated under both acute and chronic inflammation and in cardiovascular disease. In patients with diabetes urinary orosomucoid excretion (UOE), was an independent predictor of all-cause and cardiovascular mortality even in normoalbuminuric patients. In this longitudinal study, our aim was to study both UAE and UOE in a middle-aged cohort from the general population. We hypothesized that UOE, but not UAE, is an independent predictor for all-cause mortality.

Method: The Tromsø Study is a population-based, prospective study with repeated health surveys of inhabitants of Tromsø (Northern Norway), and the first took place in 1974. From the sixth wave (Tromsø6, 2007/2008) we included all participants with urinary samples. Follow-up time was assigned from the attendance date of Tromsø6 until 31.08.2022. The associations between urinary markers and all-cause mortality were assessed by Cox regression analysis.

Results: The cohort included 7180 subjects (4094 women and 3086 men) with a mean (SD) age 63.5 (±9.2) years. Median urinary orosomucoid to creatinine ratio (UOCR) was 0.44 g/g, median albumin to creatinine ratio (UACR) was 0.36 mg/mmol, mean (SD) eGFR was 88.1 (±14.0) ml/min/1.73m² and 1689 died during follow-up. UOCR was independently associated with all-cause mortality (hazard ratio (HR) per g/g increase 1.02, 95% CI 1.01, 1.03, p < 0.001) adjusted for sex, age, UAE, eGFR and CV risk factors (diabetes, hypertension, smoke, cholesterol, BMI). The HR for UOCR above vs. below median adjusted for the same variables was 1.13 (95% CI 1.01, 1.27, p = 0.032). UACR above median with the same adjustments was not associated to all-cause mortality (hazard ratio 1.04, 95% CI 0.93, 1.15, p = 0.484).

Conclusion: In this study, we showed for the first time that UOE, but not UAE, was an independent predictor of all-cause mortality in a large cohort from the general population. Thus, UOE may be an earlier marker of vascular damage
than UAE. Whether UOE is clinically useful as an early marker of CV disease should be further studied.

F3 - PREVENTION, TREATMENT & CLINICAL TRIALS

#3000
EFFICACY AND SAFETY OF COTADUTIDE, A DUAL GLP1-GLUCAGON RECEPTOR AGONIST, IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND T2DM

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Background and Aims: Cotadutide is a dual GLP1-glucagon receptor agonist under development for NASH and CKD with T2DM. Incretin-based therapies have been shown to promote improvements in albuminuria while the addition of glucagon has been suggested to provide hepatic benefits; the renal benefits of dual GLP1-glucagon receptor agonism are unknown but kidney and liver are the organs with highest expression of glucagon receptor. We sought to evaluate the efficacy and safety of cotadutide in patients with CKD and T2DM.

Method: In this randomised, double-blind, phase 2b study, patients with T2DM and CKD on insulin and/or oral therapy including ≥40% treated with SGLT-2i (HbA1c ≥ 6.5 and < 10.5%), eGFR ≥ 20 and < 90 ml/min/1.73m² and BMI ≥ 25 (23 in Japan) kg/m² were treated for 26 weeks. Participants were randomised (n = 45 per arm) to receive once-daily SC cotadutide titrated up to 100, 300 or 600 μg, or placebo. The primary endpoint was percentage change in albumin creatinine ratio (UACR) at 26 weeks. Safety and tolerability. Changes in renal function was evaluated as an exploratory endpoint.

Results: A total of 248 Participants were randomised. Approximately 47% were on SGLT-2i and 97% were on ACE inhibitors or ARBs at baseline. The primary endpoint was met. Dose dependent reductions in UACR from baseline were observed after 26 weeks treatment with 300 and 600 μg of cotadutide, -39.9% (95 CI -52.5, -23.9) and -46.0% (95% CI -57.1, -32.1) vs placebo (P <0.001). In patients on background SGLT2i therapy, similar reductions in UACR from baseline were observed after 26 weeks treatment with 300 and 600 μg of cotadutide, -31.2% (95% CI -51.9, -1.5) and -48.7% (95% CI -64.1, -26.6) vs placebo (P = 0.01 and <0.001 respectively). There was no observed change in eGFR early in dosing. At 26 weeks, an increase in eGFR (+5.5 ml/min/1.73m²) was observed with 600 μg of cotadutide (p = 0.028). A statistically significant, modest reduction in serum uric acid was observed as an exploratory endpoint at 26 weeks in the 100 and 600 μg arms (-0.54 mg/dL, p = 0.03 and 0.76 mg/dL, p = 0.001 respectively) but not the 300 μg arm (-0.32 mg/dL, p = 0.17). No significant changes in urine KIM-1 were observed. A significant increase in pulse rate was observed (+4.8 bpm), alongside a numerical reduction in systolic BP (-8.3 mmHg) at 600 μg on office-based measures. SAEs were balanced across all arms and there were fewer AE-related discontinuations at 100 and 300 μg versus placebo, but more discontinuations at 600 μg.

Conclusion: In patients with CKD with T2DM, cotadutide promoted clinically important effects on UACR on top of standard of care with an acceptable tolerability profile. The results suggest cotadutide has potential to provide benefit to patients with CKD and T2DM. Larger studies will be required to evaluate this.

#5699
IS GFR DECLINE INDUCED BY SGLT-2 INHIBITOR OF CLINICAL IMPORTANCE?

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Background and Aims: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are associated with better cardiovascular outcome and with nephroprotection independent of diabetes status. However, the use of SGLT2i often cause an initial decline in estimated glomerular filtration rate (eGFR). This study addresses the question whether there is a relationship between vascular improvement and GFR dipping.

Method: We measured GFR (mGFR) and calculated GFR (eGFR) in 65 patients with T2D at baseline and after 12 weeks of treatment with either a combination of Empagliflozin (E) + Linaagliptin (L) (n = 34) or Metformin (M) + Insulin (I) (n = 31). mGFR was measured using the gold standard clearance technique by infusion of inulin. In addition, pulse wave velocity (PWV) was obtained at office and under ambulatory conditions. We splitted the study cohort according to the median change of mGFR after 12 weeks and compared the baseline characteristics.

Results: mGFR and eGFR decreased significantly with E-L and with M+I (Ott C et al. Cardiavasc Diabetol. 2021). However, no correlation was noticed between the change of mGFR and change of eGFR for either treatment cohorts (E-L: p = 0.404; M+I: p = 0.460). We found a significant decrease in office PWV in the E-L group only (8.2±1.6 to 7.8±1.5, p = 0.028) without any change in 24-h PWV. The change of office PWV correlated with the change of mGFR (p = 0.009) in E-L group only and remained significant after adjustment for the change of office systolic BP (p = 0.018). In addition, we observed a correlation between the change of high sensitive C reactive protein (hsCRP) and change in mGFR (p = 0.031). We identified patients with higher albumin excretion (p = 0.044), higher fasting plasma glucose (p = 0.014) and high hsCRP (p = 0.057) to have a greater decline in mGFR with E-L.

Conclusion: First, eGFR may not be an appropriate parameter to assess the true change in renal function after receiving E-L in a single patient. Second, after E-L medication a high decrease in mGFR goes in parallel with vascular improvement and less inflammation thereby reflecting the pleiotropic pharmacologic effects of SGLT 2 inhibitors.
Background and Aims: Immunosenescence, or aging process of the immune system, leads to either defective immune response or increased systemic inflammation. Previous studies have shown that kidney immune system may coordinate the process of kidney inflammation, resolution, or progressive fibrosis in kidney diseases. However, the exact role of individual immune cell type has not been systematically characterized, especially in the context of ageing kidneys.

Method: Firstly, we induced acute and chronic aristolochic acid nephropathy (AAN) in 15-month-old mice. At different stages of AAN (Steady state, acute inflammation, recovery from acute injury, and chronic fibrosis), mice were then sacrificed, and kidneys were harvested for further processing. We flow-sorted kidney CD45+ immune cells (live cells) and applied to 10 x Genomics platform for single cell isolation and cDNA library construction. Illumina NovaSeq 6000 system was used for RNA sequencing. Finally, we performed downstream bioinformatics analysis through CellRanger and Seurat pipelines.

Results: Utilizing AAN mouse model, we successfully conducted flow sorted kidney immune cells single-cell RNA sequencing (scRNAseq) from 15 M/O kidneys with AKI and CKD. We clearly identified 25 distinctive immune cell types, representing distinctive lymphoid and myeloid populations (Figure 1a). We showed dynamic change of immune cell compositions upon different phases of AAN (i.e., CCR2+ monocytes and proliferative macrophages increased during acute inflammation, activated T cells expanded during recovery phase, CD206+CCL8+ macrophages enriched within the fibrotic kidneys) (Figure 1b). By analysis of differentially expressed genes (DEG), we identified 30 top-ranked genes, which uniquely enriched in specific cell subset (Figure 1c).

Conclusion: We have successfully unveiled the immune cell landscape in ageing kidneys with AKI and CKD. Our preliminary data has demonstrated that distinct immune cell subsets at different phases of injury may have unique roles. Future work will focus on the cell-cell interactions and immune cell activation/differentiation.
Figure 1: (1a) UMAP plot of 25 kidney immune cell clusters were performed. Total 45,005 cells were analyzed using 10x CellRanger and Seurat pipelines. (1b) UMAP plot of 25 kidney immune cell clusters, split into “steady state”, “acute inflammation”, “recovery”, and “fibrosis”. Notably, we found that CCR2+ monocytes and proliferative macrophages increased during acute inflammation, activated T cells expanded during recovery phase, and CD206+CCL8+ macrophages enriched within the fibrotic kidneys. (1c) Dot plot showing top 30 differentially expressed genes, enriched in specific kidney immune cell types. Data were analyzed by Seurat package.
RECOMBINANT HIGH-DENSITY LIPOPROTEIN MODULATES INFLAMMATORY RESPONSE AND RENAL DYSFUNCTION IN A SWINE MODEL OF SEPSIS-INDUCED ACUTE KIDNEY INJURY

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Background and Aims: Sepsis is a severe and dysregulated inflammatory disease that often precedes the development of acute kidney injury (AKI) with consequent worsening outcome. Although clinical data demonstrate that high-density lipoprotein (HDL) levels drop in septic patients with a poor prognosis, little is known about the molecular basis of HDL’s role in systemic inflammation and renal function. Here we investigate the possible effects of a novel engineered HDL-mimetic (CER-001) in a swine model of lipopolysaccharide (LPS)-induced AKI.

Method: Sepsis was induced by intravenous infusion of a saline solution containing 300 μg/kg of LPS in a porcine model. The animals were randomized into three groups: LPS (endotoxemic pigs, n=6), CER20 (endotoxemic pigs treated with a single dose of CER-001 20mg/kg; n=6), and CER20 × 2 (endotoxemic pigs treated with two doses of CER001 20mg/kg; n=6). Animals were sacrificed after 24h from the start of experimental procedure. Renal histologic and biochemical changes were analyzed. Endothelial dysfunction biomarkers, circulating pro-inflammatory mediators, LPS and Apolipoprotein A-I (Apo A-I) levels were quantified with ELISA assay. Systemic complement activation was evaluated by Wieslab kit.

Results: Untreated animals were highly susceptible to LPS challenge and usually succumbed before completing the study protocol (LPS group 16.7%). CER-001 treatment increased the survival rate of endotoxemic pigs, compared to the LPS group (CER20, 50%; CER20 × 2, 66.7%). Furthermore, as shown in Figure 1A, LPS injection led to a time-dependent increase of IL-6 in endotoxemic animals respect to basal condition (T0). CER-001 treatment was able to reverse LPS effects. In particular, the second infusion of CER-001 three hours after the first dose (T3) strongly reduced IL-6 serum levels back to basal level (LPS p < 0.05). Similarly, we found high levels of TNF-α and MCP-1 in endotoxemic pigs that were significantly decreased in both CER-001 treatment arms (T24, CER20 × 2 vs LPS group, IL-6, p = 0.0086; TNF-α, p < 0.0001; MCP-1, p = 0.0009). In addition, CER-001 treatment ameliorated systemic endothelial dysfunction by reducing VCAM and ICAM serum levels. A significant activation of classical and alternative complement pathway (vs T0 p < 0.05) was observed at 1h, 3h and 24h after LPS infusion. CER001 treatment significantly prevented systemic complement activation in both treated groups (vs LPS p < 0.05). We also investigated whether CER001 infusions significantly prevented renal tissue damage. Endotoxemic pigs presented oliguric AKI with increased tubulo-interstitial infiltrate, extensive collagen deposition, and glomerular thrombi; CER-001 treatment preserved renal parenchyma, recovered urine output, decreased creatine levels, and reduced the biomarkers of tubular damage, Cystatin C and KIM-1, both in serum and urine samples. Considering that HDL has a very high affinity for LPS, we evaluated the circulating LPS concentration in treated animals. We observed that LPS levels were greatly reduced in treated animals and the effects are more evident after the second infusion of CER-001(Figure 1B). Therefore, we also examined LPS levels in bile samples and we observed a dose-dependent increasing amount of endotoxin in the CER001 treated septic pigs.

Conclusion: This preclinical data indicates that CER001 treatment prevents systemic inflammation thereby limiting renal damage. The mechanism of action is two-fold consisting of both the scavenging of endotoxin and a direct anti-inflammatory effect of CER-001.
#5645

**SHORT-CHAIN FATTY ACIDS, PROPIONATE AND BUTYRATE, RESEMBLE THE BENEFICIAL EFFECTS OF VITAMIN D DURING ACUTE KIDNEY DAMAGE**

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**Background and Aims:** The vitamin D receptor (VDR) is a nuclear receptor that acts as a ligand-induced transcription factor regulating the renal expression of numerous genes with anti-inflammatory and anti-fibrotic effects, among others. For that, VDR requires the binding of its ligand, 1,25(OH)2D3, to further heterodimerize with its co-activator, RXR, and translocate into the nucleus. Vitamin D deficiency in patients with renal disease leads to a decrease in VDR-mediated signaling and, consequently, of its beneficial functions. Additionally, these patients have intestinal dysbiosis, which leads to alterations in the production of microbial metabolites. Short-chain fatty acids (SCFAs) are metabolites with a clear anti-inflammatory and immunoregulatory role. Until now, some studies have studied their role as regulators of the inflammation and oxidative stress during the renal damage.1,2 However, their role in the VDR-mediated signaling in the kidney and the potential consequences to prevent the progression of the disease have not yet been explored in detail.

**Method:** The tubular epithelial cell line, HK2, was used to analyze the effect of the SCFAs, Propionate (Prop, 1-15mM) and Butyrate (But, 0.5-3 mM), in the VDR expression and their target-genes. In vitro treatment with histone deacetylases (HDACs) inhibitors and specific HDAC1 and HDAC3 siRNAs were used to determine the role of both SCFAs as epigenetic remodelers. The binding of VDR to HDAC1/3 and RXR was determined by ChIP and co-immunoprecipitation assays. The in vivo effect of these SCFAs was evaluated in an acute kidney injury mice model induced by folic acid (250 mg/kg) and administration of Prop (200mg/kg) or But (500mg/kg) at different time points. The expression of VDR and its target genes, inflammatory cell infiltration, renal damage markers and renal function parameters were evaluated at shorter (24h) and longer times (40 days).

**Results:** Treatment of tubular cells with Prop and But induces, in a dose-dependent manner, the VDR gene transcription. This effect is similar to the one obtained by using specific inhibitors and siRNA treatments against HDAC1/3. We determine using ChIP assay, that HDAC1/3 are recruited to the promoter regions of the VDR gene, blocking its expression. In presence of Prop and But, these HDACs are displaced, increasing the acetylation levels and VDR transcription. Moreover, Prop and But prevent the degradation of VDR by the proteasome, increasing its stability and enhancing VDR protein levels. In the presence of both SCFAs, VDR dimerizes with RXR initiating its translocation to the nucleus and allowing the transcription of its dependent genes, such as Cyp24a1 and E-cadherin. Of note, VDR activation by Prop and But is additive to the effect achieved by the vitamin D alone. In vivo studies reported that administration of Prop or But prevents the loss of VDR expression 24h after induction of the damage, leading to its activation and to the expression of its target genes. Additionally, a decrease in the recruitment of neutrophils to the kidney was observed associated to a reduced expression of IL-6. These changes are accompanied by a decrease of the kidney damage markers (KIM-1 and NGAL) and a significant reduction of the creatinine and blood urea nitrogen serum levels. In a second model of AKI-to CKD transition, administration of both SCFAs shows a decrease in the inflammatory (Cd20, Cd12, Lifi, Lth, C52SF2, Ifn, C515, Tief-a) and pro-fibrotic markers (Fip1, a-Sma, Coll1a1, Fn1) and a partial recovery of the glomerular filtration rate at long term.

**Conclusion:** Propionate and Butyrate, not only induce the VDR gene transcription in renal tubular cells but are also able to stabilize and activate the VDR protein. Accordingly, both metabolites are able to restore the loosened expression and activation of VDR due to induced renal damage, reduce the infiltration of immune cells, and partially recover the renal function. Thus, strategies aimed to increase the propionate and butyrate levels with postbiotics could be useful to ameliorate the AKI renal damage and CKD transition.
#6496
CYCLIN D1 AMELIORATES ACUTE KIDNEY INJURY BY IMPROVING FATTY ACID OXIDATION VIA AMPK PATHWAY
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Background and Aims: Acute Kidney Injury (AKI) is a critical condition that is caused by the absence of oxygen during the acute ischemic phase, leading to energy metabolism disturbance and kidney tubular epithelial cell damage. Fatty Acid Oxidation (FAO) is the main source of energy production of renal proximal tubular epithelial cells. Timely promoting FAO, increasing supplies of energy, and promoting cell proliferation are essential to improve kidney injury. However, there is no clinically recognized effective treatment for this. Cyclin D1 (CCND1), a member of the cell cycle family, plays a vital role in cell proliferation. Our previous study showed that CCND1 improved AKI by increasing FAO. This study aimed to investigate the role and molecular basis of CCND1 involvement in fatty acid oxidation of AKI.

Method: CCND1 was evaluated in human kidney proximal tubular epithelial cells (HK-2 cells) and in male C57BL/6J mice (wild type). We investigated the protective role of CCND1 in AKI using a mouse model of ischemia-reperfusion injury, which was treated by transferring CCND1-expressing plasmids in male C57BL/6J mice (wild type) by ultrasound and microbubble-mediated delivery. Eight-week-old male C57BL/6J mice (wild type) were subjected to bilateral renal artery occlusion for 30min followed by 24h of reperfusion. We evaluated FAO, proliferation, and autophagy in vitro and in vivo. In addition, we evaluated the concentrations of blood urea nitrogen and creatinine, evaluated kidney ultrastructure and so on.

Results: In vivo studies showed that activation of CCND1 prevented AKI-induced lipid accumulation, kidney tubule injury and kidney function declined after ischemia-reperfusion injury. Compared to test control, the treatment significantly (p < 0.05) reduced the concentrations of blood urea nitrogen and creatinine. Kidney-specific overexpression of CCND1 increased FAO, promoted proliferation and reduced apoptosis. Mechanistically, CCND1 activated the AMPK pathway, which increased the expression of phosphorylation AMP activated protein kinase (p-AMPK) and upregulated FAO. On the other hand, inhibiting the expression of CCND1 worsened the impairment of FAO and disturbed energy metabolism.

Conclusion: CCND1 improved FAO and reduced lipid accumulation through the active AMPK pathway in kidney proximal tubular epithelial cells (PTECs). Hence, restoring of the expression of CCND1 may offer a novel therapeutic strategy for treating AKI.
MICROPLASTICS: FIRST EXTENDED PROTEOMIC ANALYSIS ON KIDNEY TUBULAR CELLS

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1IRCCS Istituto Giannina Gaslini, Nephrology Dialysis and Transplantation, Italy, 2Scientific Institute for Research and Health Care, IRCCS Istituto Giannina Gaslini, Laboratory of Molecular Nephrology, Italy, 3IRCCS Istituto Giannina Gaslini, Core Facilities - Clinical Proteomics and Metabolomics, Italy, 4Translational Transplant Research Center, Icahn School of Medicine, Department of Medicine, United States of America, 5Ospedale Policlinico San Martino, Unit of Nephrology, Dialysis and Transplantation, Italy and 6University of Genoa, Department of Internal Medicine, Italy

Background and Aims: Several studies have shown the ubiquitous presence of microplastics (plastic fragments between 5 mm and 1 μm in diameter) and nanoparticles (<1 μm) in the environment and their toxicity. Furthermore, microplastics (MPs) absorb a lot of environmental pollutants, such as bisphenol A (BPA), and release them into tissues increasing their toxicity; this is the so-called “Trojan Horse” effect. Recent studies have also proved their presence in human blood and human tissues of healthy people, such as placenta and lung, and in cirrhotic liver. Most frequent biological effects of MPs are inflammation, oxidative stress and alteration of metabolic pathways. In this study proteomic analysis was performed to evaluate the toxicity of polyethylene (PE) and bisphenol-A (BPA) MPs on renal tubular cells (HK2) in vitro. This is the first extended proteomic study on human cells.

Method: HK-2 cultures were exposed for 5-24-48 hours to BPA, PE Microspheres (PE-MP) and MP combined with BPA. Then it was performed a proteomic analysis by mass spectrometry (MS). MS data were obtain by Orbitrap Fusion Tribrid mass spectrometer (ThermoScientific). Analysis of data were performed using unsupervised hierarchical clustering using multidimensional scaling, non-linear support vector machine (SVM) learning, and partial least squares discriminant analysis. In SVM learning, a fourfold cross-validation approach was applied to estimate the prediction and classification accuracy.

Results: The proteomic analysis showed a clear differentiation of the HK2 proteome based on conditioning and identified a “core” of proteins, significant at ANOVA and above the 95th percentile for “fold increase” and significant at T-test compared with controls, highly discriminatory between groups. Finally, among these, a final set of 6 proteins was selected to be validated for distinguishing features: Nephronectin, GDF15, Vasorin, IGFBP7, Midkine, Tissue factor-F3. Nephronectin is a structural membrane's protein involved in cellular adhesion. GDF15, tissue factor F3 and midkine are markers of stress conditions, including inflammation and oxidative stress. IGFBP7 is a biomarker of acute kidney damage. Vasorin is a transmembrane glycoprotein that protects against apoptosis and fibrosis.

Conclusion: MP and BPA significantly modify the protein expression in renal tubular cells. These findings highlight the urgent need for additional research into the toxic effects of plastic debris on human kidneys and the eventual link to kidney diseases.
G2 - EPIDEMIOLOGY & OUTCOME

#6321
ELECTRONIC CREATININE ALERT SYSTEM. A FIRST STEP TOWARDS PREVENTING HOSPITAL ACQUIRED ACUTE KIDNEY INJURY

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GRAPHICAL ABSTRACT

Background and Aims: Acute kidney injury (AKI) is a common complication in the critically ill and non-critically ill patient. There is currently no specific treatment for patients who develop AKI, so early recognition may help prevent progression to more advanced stages and the need for kidney replacement therapies (KRT). Electronic Alert Systems (EAS) emerge as a useful tool in different clinical scenarios to alert the clinician to potentially harmful situations. One of the utilities of the EAS is the AKI scenario, in which the clinician can be alerted early to serum creatinine (SCr) changes in real time and thus establish early intervention protocols to avoid the poor outcomes described above. The aim of the present study is to analyze the incidence of AKI in a tertiary hospital using an EAS based on SCr changes (Electronic Creatinine Alert System -ECAS-).

Method: Retrospective study conducted in a tertiary referral hospital. All discharges of patients over 18 years of age, which were issued from 1 January 2019 to 31 December 2021, were analyzed. Exclusion criteria were: discharges from critical care units, patients admitted to the emergency room, patients with AKI criteria on admission, patients admitted to the nephrology department and patients with CKD G5 or on KRT. The ECAS was developed with the aim of alerting patients with an increase of ≥ 0.3mg/dL of SCr or an elevation of ≥ 1.5 times the baseline creatinine value, based on AKI SCr from the KDIGO guidelines. The aims of the present study were: 1. Number of hospitals discharges that activated the ECAS, as well as the severity of AKI; 2. Categorize the departments in which ECAS was common; and 3. Assessing length of hospital stay, survival and kidney recovery during admission defined as SCr less than 1.5 times baseline.

Results: A total of 69,002 discharges were analyzed over 3 years. Finally, 46,149 discharges were included in the analysis, of which 5,593 (13.5%) discharges activated the ECAS. The distribution by year in which the ECAS was activated was 1,788 (11.8%) of all discharges in 2019, 1,860 (12.4%) in 2020 and 1,945 (12.1%) in 2021. The median age was 75 years (65 – 83), 62% were male. The 5 departments with the highest number of ECAS activations were: Geriatric (14.2%), Cardiology (11.9%), General Surgery (9.9%), Infectious Diseases (9.2%) and Cardiac Surgery (7.6%). Baseline SCr was 1.12mg/dL (0.80-1.79), maximum SCr was 1.99mg/dL (1.40 - 3.19) and SCr at discharge was 1.39 (0.96 - 2.23). 69.7% of patients had AKI stage 1, 21.3% had AKI stage 2 and finally 9% had AKI stage 3. Length of hospital stay was significantly elevated in patients who activated the ECAS [6 days (3-11) vs. 13 (8 - 22); p: <0.001], the survival distributions for the ECAS activation were statistically different, X² (2) = 5.522, p: 0.019. Finally, kidney recovery at discharge was significantly lower in AKI.
2 (18.5%) and AKI 3 (8.5%) patients compared to AKI 1 patients (73%) (p: <0.001 for all).

Conclusion: The ECAS is a suitable electronic alert system that allows rapid identification of patients with AKI. The activation of ECAS is associated with poor outcomes. This study led to the adoption of a nephrology rapid response team for early detection of AKI before creatinine elevation using among others Point-of-care ultrasonography and acute kidney stress biomarkers.

ACCURACY OF PLATELET INDICES AS PREDICTOR OF IN-HOSPITAL MORTALITY IN PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING RENAL REPLACEMENT THERAPY
Melvy June Balasa
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Background and Aims: Acute kidney injury (AKI) is a major medical complication associated with a markedly increased risk of death, particularly in patients admitted to the ICU where in-hospital mortality exceeds 50%. This study aimed to determine the accuracy of MPV, platelet count, and PDW as predictors of adverse outcomes in patients with AKI who received initiation renal replacement therapy (RRT).

Method: A retrospective cohort single-center study was done in a local private tertiary hospital in Cebu. Four hundred ninety-one patients with AKI who underwent RRT between January 2018 and December 2021 were enrolled. A retrieval of data on demographic and clinical parameters during the initiation of RRT was done. The impact of mortality-related factors were identified using univariate and multivariate logistic regression analysis. Determination of optimal cut-off values of platelet indices for in-hospital mortality was done.

Results: This study showed that the in-hospital mortality of patients was 58.45%, with a mean age of 68.6 ± 16.28 years among non-survivors. Among the platelet indices, platelet count and PDW were good predictors of in-hospital mortality in patients who received initiation renal replacement therapy. The optimal cut-off value of platelet count was 173 × 10^3/uL (sensitivity 56.45%, specificity 62.25%, PPV 67.78%, NPV 50.40%, AUC 0.604). The optimal cut-off value of PDW was 16.45% (sensitivity 50.87%, specificity 71.57%, PPV 71.57%, NPV 50.87%, AUC 0.611).

Conclusion: Platelet indices are feasible parameters that can be used as prognostic markers for mortality in patients with AKI requiring RRT. The in-hospital mortality of patients with AKI requiring initiation RRT is high (58.45%). Low platelet counts, high MPV values, and high PDW values are associated with poorer outcomes and higher mortality risk as compared to patients with normal indices.
ACUTE KIDNEY INJURY DURATION AND 20-YEAR RISK OF CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR DISEASE: A POPULATION-BASED COHORT STUDY
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Background and Aims: Acute kidney injury (AKI) is associated with increased risks of chronic kidney disease (CKD) and cardiovascular disease (CVD). The duration of AKI may be an important clinical marker of individuals at high risk of adverse outcomes; however, the potential links between AKI duration and CKD and CVD remain unresolved. Therefore, we examined the associations between AKI duration and CKD and CVD in a population-based setting.

Method: Using population-based plasma creatinine (pCr) data, we identified individuals with first-time AKI in Denmark from 1 January 1990 to 31 December 2018. AKI was defined in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) creatinine criteria. To allow for assessment of baseline kidney function and AKI duration, analyses were restricted to individuals with an assessment of baseline kidney function by pCr within the prior year and evaluation of AKI duration by pCr within seven days after AKI onset. In accordance with the Acute Disease Quality Initiative (ADQI) 16 Workgroup criteria, AKI duration was categorized as “rapid reversal” if a pCr test within two days after AKI onset did not fulfill the AKI definition, as “persistent” if a pCr test between two and seven days after onset did not fulfill the AKI definition, and otherwise as “acute kidney disease” (AKD). CKD was defined by in- or outpatient hospital diagnoses codes or as ≥2 outpatient eGFR <60 ml/min/1.73 m² separated by at least 90 days. CVD was defined by diagnosis codes and evaluated overall and as individual conditions including atrial fibrillation or flutter, ischemic heart disease, heart failure, stroke, and hypertension. When examining CKD, overall CVD, and specific CVDs only individuals without the condition were included in the analyses. Twenty-year cumulative risks and hazard ratios (HRs) were computed and compared across the three AKI duration groups.

Results: We identified 165,334 individuals with first-time AKI and with an assessment of baseline kidney function and AKI duration. Among these 36,514 (22%) had rapid reversal AKI, 22,619 (13%) had persistent AKI, and 110,499 (65%) had AKD. The median age was 72 years (interquartile range (IQR), 62-80) and 52% were females. The most common comorbidities were CKD (37%) and hypertension (43%). Among the 106,916 individuals without prevalent CKD, the 20-year risks of CKD were 18.9% (95% confidence interval (CI), 18.2-19.6) for rapid reversal AKI, 23.2% (95% CI, 22.1-24.2) for persistent AKI, and 22.0% (95% CI, 21.6-22.5) for AKD. The adjusted HRs for CKD were 1.23 (1.17-1.30) for persistent AKI and 1.33 (1.28-1.39) for AKD when compared with rapid reversal AKI. Among the 59,949 individuals without prevalent CVD, the overall 20-year risks of CVD were 36.0% (95% CI, 34.0-38.0) for rapid reversal AKI, 33.2% (95% CI, 31.6-34.9) for persistent AKI, and 32.2% (95% CI, 31.4-33.0) for AKD. This corresponded to adjusted HRs of 1.02 (95% CI, 0.96-1.09) for persistent AKI and 0.97 (95% CI, 0.93-1.02) for AKD when compared with rapid reversal AKI. Findings were consistent across outcomes of atrial fibrillation or flutter, stroke, and hypertension. For ischemic heart disease and heart failure, persistent AKI was associated with adjusted HRs of 1.10 (95% CI, 1.01-1.20) and 1.13 (95% CI, 1.05-1.20), respectively, and AKD with adjusted HRs of 1.08 (95% CI, 1.02-1.15) and 1.08 (95% CI, 1.02-1.13), respectively, compared with rapid reversal AKI.

Conclusion: In conclusion, longer AKI durations were associated with increased long-term risks of CKD. AKI duration was not associated with rates of overall CVD; however, rates of ischemic heart disease and heart failure increased with longer AKI durations. The distinct increase in rates of CKD and specific CVDs with longer AKI durations illustrates the potential for using AKI duration as a risk marker when planning nephrology follow-up after AKI. Further studies examining whether interventions to shorten AKI duration prevent outcomes are warranted.

REGIONAL VARIATION OF ACUTE KIDNEY INJURY IN COVID-19 IN ENGLAND
Nitin Kolhe1, Richard Fluck2 and Maarten Taal2,3

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Background and Aims: The recent worldwide COVID-19 pandemic has identified acute kidney injury (AKI) as a serious complication of COVID-19. Previous reports suggest that AKI associated with COVID-19 has higher morbidity and mortality compared to AKI due to other causes. Limited data has suggested that regional variation in COVID-19 incidence is related to population density. However, little is known about the effect of region, SARS-CoV-2 strains, steroid treatment and other determinants on incidence and mortality in patients with COVID-19 complicated by AKI. The aim of this study was to determine the regional variation of COVID-19 AKI and predictors of mortality in these patients.
**Method:** This retrospective cohort study used hospital episode statistics. Data were collected from all adult hospitalised patients with COVID-19 infection and AKI (diagnostic code U07.1 and N17 in any of the 20 diagnoses codes) between 1st March 2020 and 31st March 2021 until discharge. We also extracted all available secondary diagnoses and procedure codes. Patients with codes for chronic dialysis were excluded. We divided the observation period as per the dominant SARS CoV-2 variant and in relation to publication of the RECOVERY trial. SARS CoV-2 "Other" strain was prevalent between 1st March 2020 and 21st December 2020, "Alfa" between 22nd December 2020 to 17th May 2021. The end date of each phase was based on more than 50% decline in each variant.

**Results:** We extracted 749,844 unique admission spells in 337,029 patients with U071 code in any of the 20 diagnostic codes from 3,324,748 FCEs and admitted during the study period. We excluded patients not resident in England, multiple and duplicate FCEs within a spell. Out of 749,844 admissions, 63,147 patients had 227,268 admissions with AKI. Population incidence of AKI was highest in London at 6316 pmp and lowest in South West 2394 pmp. Mean length of stay was lowest in North East at 15.6 ± 15.9 days and highest in South West at 19.3 ± 18.3 days. London had highest proportion of patients with Asian (15.1%) and Black ethnicity (16.1%). Proportion of AKI patients dialysed varied from 2.5% in North West to 6.5% in London. Unadjusted mortality was highest in North West at 31.8% and lowest in London at 25.4%. In multivariable analysis, increasing age (OR 1.04, 95%CI 1.04, 1.04), Asian ethnicity (OR 1.13, 95%CI 1.08, 1.17), emergency admissions (OR 1.7, 95%CI 1.51, 1.9), and transfers (OR 1.18, 95%CI 1.03, 1.34), ITU admission (OR 5.16, 95%CI 4.98, 5.34) and acute dialysis (OR 2.74, 95%CI 2.6, 2.89) had higher odds of death (Figure 1a). All regions had higher adjusted odds of death as compared to London (Figure 1b). Post RECOVERY trial, the odds of death was lower with prevalent "Other" SARS CoV-2 (OR 0.78, 95%CI (0.76, 0.8)) and "alfa" variant (OR 0.80, 95%CI 0.78, 0.82).

**Conclusion:** In this large national study of COVID AKI, London had lowest adjusted odds of death despite a higher proportion of patients receiving dialysis. The odds of death were lower after the publication of RECOVERY trial which may have resulted in practice pattern change.
SECONDARY BACTERIAL AND FUNGAL INFECTIONS IN COVID-19 PATIENTS WITH ACUTE KIDNEY INJURY AND RELATION WITH CYTOKINE STORM SYNDROME

Radulescu Daniela1,2, Cristiana David1,2, Elena Cuiban1,2, Simona-Daniela Onofrei1, Feier Larisa Florina3, Flavia Liliana Turcu1,2 and Ileana Adela Vacaroiu1,2

1 Carol Davila’ University of Medicine and Pharmacy Bucharest, Clinical Department no.3, Nephrology, Bucharest, Romania and 2’Sf. Ioan’ Emergency Clinical Hospital, Bucharest, Nephrology and Dialysis, Bucharest, Romania

Background and Aims: Both COVID-19 and acute kidney injury (AKI) are associated with impaired host immunity. Virus-induced immunosuppression, overuse of antibiotics and corticosteroids are COVID-19 related factors, while dysregulation of the inflammatory response, increased volemia, hemodialysis catheters are AKI-related factors which favor secondary infections. We aimed to search the relation between markers of cytokine storm syndrome (interleukin-6 – IL-6; ferritin; C-reactive protein – CRP) and incidence of secondary infections and to identify the microorganisms involved in secondary infections in patients admitted with acute kidney injury and COVID-19 patients.

Method: Patients with both COVID-19 and AKI admitted in the 2nd and 3rd waves of the COVID-19 pandemic (May-December 2021) in an COVID-only hospital were included in this retrospective analysis. Diagnosis of AKI was established according to KDIGO creatinine-based criteria. Obstructive AKI cases were excluded. AKI was classified as A-AKI when it was diagnosed at the moment of admission and HA-AKI when it developed during hospitalization. Bacterial and/or fungal infections and the sites of positive cultures were registered in all patients. Colonizations with nonpathogenic microorganisms were excluded. Median values of IL-6, ferritin and CRP (maximum levels recorded during hospitalization) were compared between infected and non-infected patients.

Results: A total of 247 patients with AKI+COVID-19 were included in the study: 146 had A-AKI and 101 had HA-AKI. Secondary bacterial and fungal infections were registered in 111 patients (44.93%) cumulating 161 positive urine, blood, hemodialysis catheter tip, sputum, wounds, feces and tracheal intubation tubes cultures. Secondary infections were noted significantly more frequent in HA-AKI cases than in A-AKI cases: 61.38% (62 patients) vs 33.56% (49 patients) – Fischer exact test, p<0.001. The responsible microorganisms and the sites of positive culture are presented in Table 1. Median values of IL-6, ferritin and CRP (maximum levels recorded during hospitalization) were significantly higher in infected patients than in non-infected patients (Table 2) in the entire study group. IL-6 was significantly higher in infected HA-AKI patients when compared with infected A-AKI (231.40 pg/mL vs 124 pg/mL; p = 0.015), but no significant difference was found between the two subgroups of infected AKI patients regarding median ferritin levels (2481.5 ng/mL vs 1785 ng/mL; p = 0.324) or regarding median CRP values (206.27 mg/L vs 179.59 mg/L; p = 0.546).

Conclusion: Incidence of secondary bacterial and/or fungal infections in patients admitted with AKI and COVID-19 was very high in our study and it was associated with more severe altered markers of cytokine storm syndrome. Secondary infections in COVID-19 patients are important drivers of hospital-acquired AKI or they can aggravate its evolution.
Method: explored. We here aimed to evaluate the association between developing AKI whether developing AKI associates with the risk of dementia is not well (AKI) leads to biochemical and pathological changes in the brain. However, Background and Aims: Division of Nephrology, Department of Clinical Sciences, Sweden and Caring Sciences, Sweden and 6 Karolinska Institutet, Danderyd Hospital, Division of Nephrology, Department of Clinical Sciences, Sweden.

Results: we included all adults with age ≥65 years, free from dementia. We here aimed to evaluate the association between developing AKI and the subsequent risk of dementia in general population.

Method: we included all adults with age ≥65 years, free from dementia diagnosis and with known kidney function in Stockholm during 2006-2019. The exposure was AKI (time varying): prevalent history of AKI was ascertained by clinical diagnoses, and new/ incidental AKI events during observation by both criteria. The outcome was dementia diagnosis, first via confirmed cases in clinical diagnosis and with known kidney function, history of hypertension, diabetes, and cardiovascular disease. Conclusion: In this region-representative cohort, participants who experienced AKI were at increased risk of receiving a diagnosis of dementia.

Table 1: Microorganisms involved in secondary infections in patients with AKI+COVID-19.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Number of positive cultures</th>
<th>Site of culture – number of cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella pneumoniae</td>
<td>34</td>
<td>Tracheal intubation tube - 19; Urine - 9; Blood - 4; Dialysis catheter - 1; Wounds - 1</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>31</td>
<td>Tracheal intubation tube - 25; Blood - 3; Dialysis catheter - 3</td>
</tr>
<tr>
<td>Candida spp</td>
<td>20</td>
<td>Tracheal intubation tube - 13; Urine - 4; Wounds - 3</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>15</td>
<td>Urine - 13; Blood - 1; Dialysis catheter - 1</td>
</tr>
<tr>
<td>E. Coli</td>
<td>14</td>
<td>Urine - 14</td>
</tr>
<tr>
<td>Aspergillus spp</td>
<td>13</td>
<td>Tracheal intubation tube - 8; Sputum - 5</td>
</tr>
<tr>
<td>Staphylococcus spp</td>
<td>12</td>
<td>Tracheal intubation tube - 8; Blood - 3; Dialysis catheter - 1</td>
</tr>
<tr>
<td>Pseudomonas spp</td>
<td>10</td>
<td>Tracheal intubation tube - 5; Urine - 3; Sputum - 2</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>7</td>
<td>Feces - 7</td>
</tr>
<tr>
<td>Proteus spp</td>
<td>4</td>
<td>Urine - 3; Wounds - 1</td>
</tr>
<tr>
<td>Providencia</td>
<td>1</td>
<td>Urine - 1</td>
</tr>
<tr>
<td>Total</td>
<td>161</td>
<td>Tracheal intubation tube - 78; Urine - 47; Blood - 11; Dialysis catheter - 6; Sputum - 7; Wounds - 5; Feces - 7</td>
</tr>
</tbody>
</table>

Table 2: Comparison of markers of cytokine storm syndrome (CSS) between infected and non-infected patients.

<table>
<thead>
<tr>
<th>CSS marker - median value (IQR)</th>
<th>Infected patients</th>
<th>Non-infected patients</th>
<th>P – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 (pg/mL)</td>
<td>191.5 (494.60)</td>
<td>115.10 (244.58)</td>
<td>0.002</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>2326 (3447)</td>
<td>1327.5 (1870)</td>
<td>0.006</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>193.30 (172.63)</td>
<td>131.37 (134.64)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* Mann-Whitney U Test

#5352 INCIDENT ACUTE KIDNEY INJURY AND THE RISK OF DEMENTIA: IN THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

Hong Xu1, Yang Xu2, Sara Garcia-Ptacek3,4*, Annette Bruchfeld4,5, Maria Eriksdotter1,3 and Juan Jesus Carrero 2,6

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Background and Aims: Preclinical studies suggest that acute kidney injury (AKI) leads to biochemical and pathological changes in the brain. However, whether developing AKI associates with the risk of dementia is not well explored. We here aimed to evaluate the association between developing AKI and the subsequent risk of dementia in general population.

Method: We included all adults with age ≥65 years, free from dementia diagnosis and with known kidney function in Stockholm during 2006-2019. The exposure was AKI (time varying): prevalent history of AKI was ascertained by clinical diagnoses, and new/incident AKI events during observation by both clinical diagnoses and transient creatinine elevations according to KDIGO criteria. The outcome was dementia diagnosis, first via confirmed cases in the Swedish registry of cognitive/dementia disorders (SweDem) and enriched with cases identified by two issued diagnoses of dementia in outpatient care or initiation of specific anti-dementia medications. We considered death, migration, and end of follow-up as censoring events and also explored risk associations with specific dementia subtypes. The association between developing AKI and study outcomes was evaluated through time-varying multivariate Cox regression, accounting for recurring AKI events under the assumption that the lowest sCr would represent baseline kidney function, history of hypertension, diabetes, and cardiovascular disease.

Results: In the selected patients, we defined and graded AKI according to the KDIGO criteria, by comparing the peak sCr to the lowest sCr during hospitalization under the assumption that the lowest sCr would represent baseline kidney function. Then, we divided this cohort into 3 groups: 1) patients with no AKI at all, 2) AKI calculated by sCr changes and formally codified in HDF (diagnosed AKI), 3) AKI calculated by sCr changes but not codified in HDF (i.e., undiagnosed AKI). Finally, we compared the clinical characteristics and outcomes of these groups.

Results: We included 56,820 pts. The incidence of AKI was 24.5% (n = 13,920), evaluating the distribution among the 3 groups, we noticed that a small percentage of AKI was reported in HDF, while in the emergency department, AKI was formally reported in HDF, while in the emergency department, AKI was diagnosed in 78% of cases. Compared with No AKI patients, those with AKI (both diagnosed and undiagnosed) had a higher prevalence of comorbidities (diabetes mellitus, heart failure, atrial fibrillation) and incidence of myocardial ischemia and sepsis (Table 1). Moreover, patients with AKI had a significantly longer hospitalization and major mortality risk, at cox regression (HR 2.6, IC 2.4-2.8, p<0.000) and Kaplan Meier (Fig. 2). The mortality risk augmented in all patients with AKI analyzed by both logistic regression univariate (OR 7.1, IC 6.7-7.6, p<0.001) and multivariate analysis corrected by age, gender, and comorbidities (OR 4.5, IC 4.2-4.9, p<0.001). Interestingly, these findings...
Figure 1: Prevalence of the different patterns of Hospital AKI.

Table 1: Characteristics of patients based on Hospital Acute Kidney Injury (AKI).

<table>
<thead>
<tr>
<th></th>
<th>All pts (56,820)</th>
<th>No AKI (42,900)</th>
<th>Undiagnosed AKI (9,498)</th>
<th>Diagnosed AKI (4,422) *</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>29,653 (52.2)</td>
<td>22,274 (51.9)</td>
<td>5,256 (55.4)</td>
<td>2,123 (48.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>70.0</td>
<td>67.7</td>
<td>76.7</td>
<td>79.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage 1 AKI</td>
<td>5,341 (56.2)</td>
<td>7,38 (79.9)</td>
<td>7,38 (79.9)</td>
<td>7,38 (79.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage 2 AKI</td>
<td>2,677 (28.2)</td>
<td>5,86 (13.2)</td>
<td>5,86 (13.2)</td>
<td>5,86 (13.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage 3 AKI</td>
<td>1,480 (15.6)</td>
<td>5,69 (12.9)</td>
<td>5,69 (12.9)</td>
<td>5,69 (12.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DISCHARGE DEPARTMENT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>34,093 (60.0)</td>
<td>25,528 (59.5)</td>
<td>6,258 (65.9)</td>
<td>2,310 (52.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgical</td>
<td>12,894 (22.3)</td>
<td>10,133 (23.6)</td>
<td>2,222 (23.4)</td>
<td>339 (7.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency</td>
<td>8,876 (15.6)</td>
<td>6,767 (15.8)</td>
<td>464 (4.9)</td>
<td>1,645 (37.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intensive Unit</td>
<td>1,154 (2.0)</td>
<td>472 (1.1)</td>
<td>534 (5.8)</td>
<td>128 (2.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COMORBIDITIES, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>4,536 (8.0)</td>
<td>2,919 (6.8)</td>
<td>1,016 (10.7)</td>
<td>601 (13.6)</td>
<td>0.000</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4,877 (8.6)</td>
<td>3,335 (7.8)</td>
<td>768 (8.1)</td>
<td>774 (17.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>5,237 (9.29)</td>
<td>2,963 (6.9)</td>
<td>1,422 (15.0)</td>
<td>852 (19.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>7,315 (12.9)</td>
<td>5,185 (12.1)</td>
<td>1,586 (16.7)</td>
<td>544 (12.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute myocardial ischemia</td>
<td>1,393 (2.5)</td>
<td>924 (2.1)</td>
<td>328 (3.4)</td>
<td>141 (3.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2,229 (3.9)</td>
<td>744 (1.7)</td>
<td>1,023 (10.8)</td>
<td>462 (10.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OUTCOMES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days of hospitalization, d</td>
<td>12.1</td>
<td>9.5</td>
<td>23.5</td>
<td>13.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death, n(%)</td>
<td>4,720 (8.3)</td>
<td>1,636 (3.8)</td>
<td>2,002 (21.1)</td>
<td>1,082 (24.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* In 2,529 pts (57%) of diagnosed AKI the diagnosis was made considering previous sCr not available for the evaluation of AKI stage.

The results were confirmed also considering only the group of patients with undiagnosed AKI (univariate: OR 5.9, IC 4.2-4.9, p<0.001; multivariate: OR 4.6, IC 4.2-4.9, p<0.001).

Conclusion: Undiagnosed AKI is still very common in hospitalized patients, even if it identifies a category of patients with a high risk of complications and mortality. Proper recognition of H-AKI remains a problem to face.
Background and Aims: COVID-19 has been a significant public health concern for the last three years; however, not much is known about the mechanisms that lead to severe kidney outcomes in patients hospitalized with COVID-19. In this multicenter study, we combine isobaric TMT-tagged urinary proteomics and machine learning to predict severe kidney outcomes in hospitalized COVID-19 patients.

Method: Urine samples from hospitalized COVID-19 patients in two medical centers (Mount Sinai Hospital and University of Michigan) were used in this study in adherence with proper consenting protocols. Urine samples were prepared for LC-MS/MS analysis as previously reported [1]. The obtained spectra were analyzed using Proteome discoverer software and matched against Uniprot human database. For constructing the ML algorithm, the samples were randomly divided into discovery and validation set at a 2:1 ratio. Severe outcomes were defined as ICU admission, mechanical ventilation, acute kidney injury (AKI), death, or length of stay more than 21 days. Limma test was used on the discovery set to identify differentially expressed proteins and then features were selected using Boruta feature selection method. 10-fold cross validation on a random forest model was then applied to obtain receiver operating characteristic (ROC) curves.

Results: Urine samples from 120 PCR-positive COVID-19 patients from two different medical centers were collected within one week of hospitalization. More than 3,000 unique urinary proteins were identified using TMT-tagged mass spectrometry. For constructing a predictive algorithm, patients were stratified into severe and mild outcomes. Using Limma test on the discovery set, we identified differentially expressed proteins (DEPs) in severe outcome cohort vs the mild outcome cohort (Figure 1A). A set of 12 top features were identified using Boruta feature selection method and used for random forest model construction within the discovery set with 10-fold cross validation (Figure 1B). The generated ROC curves show that the algorithm demonstrated good predictive power for both discovery and validation set with 87% and 79% accuracy, respectively and close to 90% specificity (Figure 1C, D). On average, major adverse kidney events were observed in patients within 5-13 days after hospitalization. Enrichment analysis of DEP in COVID-19 patients compared to healthy patients showed significant upregulation of immune related processes and downregulation of proteolytic and metabolic processes. Enrichment analysis of DEPs in severe COVID-19 patients compared to mild COVID-19 patients showed significant upregulation of exocytosis and some immune related processes and downregulation of cell adhesion and extracellular matrix organization related processes (Figure 2A, B). Upregulated proteins were associated with kidney proximal tubular cells in addition to pulmonary alveolar cells (Figure 2C). Downregulated proteins were associated strongly with kidney cells such as podocytes and mesangial cells in addition to endothelial cells (Figure 2D).

Conclusion: Here, we developed an algorithm for prediction of severity in COVID-19 patients within 5-13 days after hospitalization. We further delineate potential mechanisms that drive severe outcomes in COVID-19 patients. Learnings from this study can be used for developing therapeutic options for long COVID, in addition to better preparedness in the event of other respiratory illnesses in the future.
Figure 1: (A) DEPs in severe outcome cases compared with mild outcome cases in the discovery set (B) Top features for prediction of severity selected using Boruta feature selection method. ROC curves generated using a random forest model with (C) the discovery sample set, and (D) the validation set.
Figure 2: Enriched biological processes associated with (A) top 25 upregulated and (B) top 150 downregulated DEPs. Cell types associated with (C) Upregulated proteins (D) downregulated proteins.

REFERENCE

MODERATED ORALS

PHYSIOLOGY, CELL BIOLOGY & GENETIC DISEASES
A1 - CELL SIGNALLING, CELL BIOLOGY & HORMONES

#4394
TACROLIMUS BUT NOT VOCLOSPORIN INHIBITS KIDNEY TUBULAR CALCIUM AND MAGNESIUM REABSORPTION IN RATS AT CLINICALLY THERAPEUTIC DOSES
Kuang-Yu Wei1, Martijn H van Heugten1, Hester van Willigenburg1, A. H. Jan Danser1, Linda M. Rehaume2, Jennifer L. Cross2, John J. Viel2, Jeroen de Baaij3 and Ewout Hoorn1

1Erasmus Medical Center, Department of Internal Medicine, Netherlands, 2Aurinia Pharmaceuticals Inc., Victoria, BC, Canada and 3Radboud University Medical Center, Department of Physiology, Netherlands

Background and Aims: Clinically, the calcineurin inhibitor tacrolimus frequently causes hypercalciuria and hypomagnesemia by inhibiting kidney tubular calcium and magnesium reabsorption. Voclosporin, a novel calcineurin inhibitor approved in the USA and Europe for the treatment of adults with active lupus nephritis, has fewer side-effects including less hypomagnesemia. However, the differences between the kidney tubular effects of tacrolimus and voclosporin are unknown. To address this, we compared the effects of tacrolimus, voclosporin, and vehicle in rats.

Method: Tacrolimus (0.5 mg/kg) and voclosporin (0.5 mg/kg) were administrated by daily intraperitoneal injections in male Wistar rats and were compared against vehicle (Cremophor EL: 95% ethanol:saline (5:5:90, v:v:v)) for 28 days (n = 8–9/group). Dosages were determined based on pharmacokinetic studies in rats and aimed to achieve the area under the concentration-time curve observed in clinical studies. At day 18, blood and 24h urine were collected to measure trough levels of the drugs and to analyze the fractional excretions of calcium and magnesium. At sacrifice, kidneys were harvested for immunoblotting of tubular proteins.

Results: Both tacrolimus and voclosporin reached clinically therapeutic doses with trough levels of 2.4 μg/L ± 0.6 μg/L and 25.8 μg/L ± 9.6 μg/L, respectively. Compared to vehicle, tacrolimus caused significantly higher fractional excretions of calcium (+348% ± 127%, P < 0.001) and magnesium (+60% ± 38%, P < 0.01) and also caused hypomagnesemia (plasma magnesium 0.65 mmol/L ± 0.04 mmol/L vs. 0.81 mmol/L ± 0.02 mmol/L, P < 0.001). Compared to vehicle, voclosporin only caused a slight, but non-statistically significant, increase in fractional calcium excretion (+44% ± 38%, P = 0.08) and did not cause higher fractional magnesium excretion (+5% ± 30%, P = 0.96) or hypomagnesemia (plasma magnesium 0.8 mmol/L ± 0.04 mmol/L, P = 0.9). Compared to vehicle, tacrolimus caused an 11-fold decrease in the protein abundance of the cytosolic calcium-binding protein calbindin-D28K and a 2-fold decrease in the abundance of the sodium-chloride cotransporter (NCC). In contrast, voclosporin did not decrease the protein abundances of calbindin-D28K and NCC. No differences were observed between vehicle, tacrolimus, and voclosporin in the calcium channel TRPV5 and magnesium channel TRPM6 (Figure 1).

Conclusion: In contrast to the calcineurin inhibitor tacrolimus, voclosporin does not inhibit the kidney tubular reabsorption of calcium and magnesium and therefore does not cause hypercalciuria or hypomagnesemia. A possible explanation for this difference is that tacrolimus but not voclosporin affects tubular transport in the distal convoluted tubule, which was further supported by the selective inhibition of calbindin-D28K and NCC by tacrolimus. Our data show that tubulotoxicity of tacrolimus is not apparent with voclosporin treatment, at clinically relevant doses.
Figure 1: Effects of tacrolimus and voclosporin on kidney transporters (A) Immunoblotting of whole kidney homogenates in vehicle, tacrolimus and voclosporin groups. (B) Densitometric analysis of immunoblots. Band intensities are normalized to the mean intensity of the vehicle group defined as 1.0. Values displayed under respective blots are mean ± SD (n = 8 rats per group; ** P < 0.01 vs. vehicle; *** P < 0.001 vs. vehicle; & P < 0.001 vs. tacrolimus; ns, non-significant; one-way ANOVA with Dunnett’s post hoc test).
IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES AND PATHWAYS IN NON-DIABETIC CKD AND DIABETIC CKD BY INTEGRATED BIOINFORMATICS ANALYSIS

Clara Barrios1, Jan Julia2, Jessica Gomez2, Eva Marquez1, Andres Ribas1, Laia Sans1, Eva Rodríguez Garcia1, Marta Crespo1 and Marta Riera1

1 Hospital del Mar, Institut Mar d'Investigacions Mediques, Nephrology, Barcelona, Spain and 2 Anaxomic Biotech, Barcelona, Spain

Background and Aims: Chronic kidney disease (CKD) is a complex genetic-based disease with multiple unclarified molecular pathways involved. Dapagliflozin has shown a clear improvement in the progress of renal function in diabetic and nondiabetic populations. However, we do not really know the molecular pathways that this drug modulates. To overcome this global objective we have first seek similarities and differences in genes and molecular pathways implicated in Non-diabetic (Non-DM) CKD (considering Autoimmune-CKD and Hypertension-CKD) and type2 diabetic nephropathy (DN).

Method: Expression datasets were compiled from databases (ArrayExpress and Gene Expression Omnibus). Differential expression analysis (DEA) and Gene Set Enrichment Analysis (GSEA) were carried out; each cohort was compared with controls, and between them as direct comparison (Non-DM CKD vs. DN).

Results: Non-DM CKD and DN share many similarities when compared to controls. However, some quantitative differences come up in terms of genes and pathways (see Figure 1 for examples). (1) Hypertension-CKD is clearly closer to DN than Autoimmune-CKD in both glomeruli and tubulointerstitium both in gene and pathway analysis. (2) Extracellular matrix remodelling and immune system activation (innate and adaptive) are processes involved in Non-DM CKD and Hypertension-CKD and type2 diabetic nephropathy (DN). (3) Metabolic modulations, regarding metabolic acidosis, reprograming and dyslipidaemia, are more present in DN tubulointerstitium than Non-DM CKD subcohorts, tubulointerstitium specifically. (4) Genes related to complement activation are found overexpressed in DN glomeruli compared to CKD/subcohorts, which then translate to a complement system activation rise in the GSEA analysis.

Conclusion: We raise a series of core genes that may be potential targets for the study of Dapagliflozin mechanism of action.
NOVEL DOMINANT ALG5 VARIANT IN TWO UNRELATED FAMILIES WITH LATE-ONSET ADPKD AND ATYPICAL TUBULOINTERSTITIAL CHANGES

Elhussein Elhassan1,2, Tereza Kmochova3, Katherine Benson4, Kendrah Kidd5, Neil Fennelly6, Anthony Dorman6, Aleš Hnízda3, Anthony Bleyer5, Martina Zivna3, Stanislav Kmoch3 and Peter Conlon1,2

1Department of Nephrology and Transplantation, Beaumont Hospital, Dublin, Ireland, 2Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland, 3Research Unit for Rare Diseases, Department of Paediatrics and Inherited Metabolic Disorders, First Faculty of Medicine, Charles University, Prague, Czech Republic, 4School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons in Ireland, Dublin, Ireland, Dublin, Ireland, 5Section on Nephrology, Wake Forest School of Medicine, Winston-Salem, North Carolina, United States of America and 6Department of Pathology, Beaumont Hospital, Dublin, Ireland

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is a monogenic disorder renowned for its clinical and genetic heterogeneity. Recently, variants in the ALG5 gene have been described as a cause of atypical ADPKD and interstitial fibrosis through the disruption of polycystin 1 maturation and trafficking via underglycosylation. In this report, we investigated genetic cause of the disease in two unrelated Irish families displaying late-onset ADPKD phenotype with atypical tubulointerstitial changes.

Method: Routine clinical and radiological evaluations were carried out. Available kidney biopsy specimens were reassessed. Genetic testing was performed on probands and all relatives with cystic kidneys. First, a custom-targeted gene panel of 227 genes associated with kidney disease was used, but the causal variant was not identified. Then reading frame-changing variants in variable number tandem repeats region of MUC1 were excluded by single-molecule real-time sequencing. Whole exome sequencing revealed a variant in the ALG5 gene, which is not included in the initial custom gene panel. By targeted Sanger sequencing, segregation of the variant with the disease phenotype was confirmed in both investigated families. Multiple bioinformatic tools were employed to predict the effect on protein structure and functions.

Results: The clinical diagnosis was consistent in most of the 20 affected individuals with non-enlarged cystic kidneys and few or no liver cysts. All but 1 individual underwent radiological assessment; 7 had kidney and liver cysts, 7 had only kidney cysts, and 5 had no kidney cysts at ages 68.6±14.4, 55.1±15.8, 46.8±15.6 years, respectively. Polycystic liver phenotype (>20 cysts) was present in two individuals. Biopsy-proven extensive kidney interstitial fibrosis and cystic tubular dilation were evident in four affected individuals with available kidney samples. Of the 20 genetically-defined individuals, 4 had end-stage kidney failure at a mean age of 70.25±3.1 years. Ten individuals were CKD stage 3 or greater, while 6 were CKD stage 4 or lower at ages 43.2±12.6 and 63.1±7.5 years (P value 0.004). A novel heterozygous missense variant in the ALG5 gene (NM_013338.5, c.235C>T, p.Arg79Trp) was identified in affected members from investigated families. Genetic screening of 20 affected and 10 unaffected individuals from both pedigrees revealed segregation of the variant with the disease phenotype. The novel ALG5 variant was classified as likely pathogenic as it was absent in the Genome Aggregation Database (gnomAD), is located in a conserved region and is predicted to be deleterious on protein stability.

Conclusion: This study expands the clinical and genetic spectrum of the identified range of ADPKD, considering the pathogenic ALG5 variants. Establishing a precise diagnosis of atypical cystic and interstitial kidney disease is crucial, with essential implications including follow-up, genetic counselling, prognostication, and therapeutic interventions.

Figure 1: Scattered distribution plot of two families with novel monoallelic ALG5 variant and their renal progression at last follow-up. Solid triangles indicate subjects with monoallelic ALG5 variant identified (p.Arg79Trp). Hallow circles indicate wild-type ALG5, none of whom developed chronic kidney disease. Most affected individuals developed chronic kidney disease stage 3 (horizontal line) after 50 years (vertical line). Four individuals had reached end-stage kidney disease, as depicted with an eGFR value of 5ml/min at various ages (x-axis).
THE KETONE BODY BETA-HYDROXYBUTYRATE IS ASSOCIATED WITH BETTER KIDNEY FUNCTION OUTCOME IN PATIENTS WITH ADPKD: RESULTS OF THE DIAPAK COHORT

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1University Medical Center Groningen, Internal Medicine, Nephrology, Groningen, Netherlands and 2Laboratory Corporation of America (LACO) Holdings (Labcorp), Morristown, United States of America

Background and Aims: A dysregulated energy metabolism is a key feature of Autosomal Dominant Polycystic Kidney Disease (ADPKD), characterized by cystic cells being dependent on glucose and poorly able to use other energy sources such as ketone bodies. Besides providing energy, ketone bodies, especially beta-hydroxybutyrate, can act as signaling metabolites and reduce inflammation and oxidative stress. In experimental studies, raising ketone body concentration reduced disease progression. Therefore, we hypothesized that higher endogenous serum beta-hydroxybutyrate concentration reduces disease progression in patients with ADPKD.

Method: We analyzed data from the DIAPAK cohort, a prospective observational cohort study that included 670 patients with ADPKD. Beta-hydroxybutyrate was measured at baseline using nuclear magnetic resonance spectroscopy. We excluded participants with type 2 diabetes, who used disease-modifying drugs (e.g., tolvaptan, somatostatin analogs), were not fasting, or had missing beta-hydroxybutyrate, leaving 521 participants for the analyses. Linear regression analyses were used to study cross-sectional associations and linear mixed-effect modeling for longitudinal associations.

Results: The median concentration of beta-hydroxybutyrate was 94 (IQR 68–147) μmol/L. Of the participants, 61% were female, the mean age was 47.3 ± 11.8 years, and the mean estimated glomerular filtration rate (eGFR) was 63.3 ± 28.9 mL/min/1.73 m². Cross-sectionally, beta-hydroxybutyrate was neither associated with eGFR nor with kidney volume. Longitudinally, beta-hydroxybutyrate was positively associated with the eGFR slope (B = 0.37% (95% CI 0.11 to 0.62), p = 0.005) but not with kidney growth. After adjustment for potential confounders, every doubling in beta-hydroxybutyrate concentration reduced the annual rate of eGFR loss by 0.34 (95% CI 0.10 to 0.58, p = 0.005) mL/min/1.73 m².

Conclusion: These analyses support the hypothesis that raising the beta-hydroxybutyrate concentration, one of the ketone bodies, reduces the rate of kidney function decline in patients with ADPKD.

GLOMERULAR & TUBULO-INTERSTITIAL DISEASES

B1 - BASIC SCIENCE, EXPERIMENTAL & RENAL PATHOLOGY

SELECTIVE RENAL DISPOSITION OF THE CALCINEURIN INHIBITORS VOCRLOSPORIN, CYCLOSPORINE, AND TACROLIMUS

Simon Zhou1, Krishani Kumari Rajanayake2, Miao He1, Bo Wen2, Anika Lkhagva2, Ernie Yap1, Duxin Sun3, Jennifer L. Cross1, Kory Engelke1 and Robert B. Huizinga1

1Auria Pharmaceuticals, Victoria, Canada and 2University of Michigan, Ann Arbor, United States of America

Background and Aims: The calcineurin inhibitors (CNI) cyclosporine (CSA) and tacrolimus (TAC) were revolutionary immunosuppressants when first introduced for solid organ transplantation in the 1980s. Voclosporin (VCS), a novel CNI, recently became the first oral therapy approved in the United States, Great Britain, and Europe for the treatment of active lupus nephritis based on positive results from Phase 2 and 3 clinical trials. Unlike CSA and TAC, VCS has demonstrated a consistent pharmacokinetic and pharmacodynamic profile, eliminating the need for therapeutic drug monitoring. Further, VCS is associated with a more favorable metabolic profile and has not been associated with electrolyte disturbances. Emerging evidence indicates small molecule therapeutics may display differential disposition within organ tissues. This suggests that CNIs may be differentially distributed and retained in the kidney, potentially explaining the difference in their efficacy and safety profiles. To evaluate renal disposition of CSA, TAC, and VCS, we assessed in mice and humans the disposition of each CNI in the kidney relative to its systemic drug exposure.

Method: Single 30 mg/kg doses of CSA, TAC and VCS were administered intravenously to mice. Following intravenous administration, kidneys were collected at 15 minutes, 30 minutes, 1 hour and 2 hours, flash frozen in liquid nitrogen, and stored at −20 °C until sectioning. Sections of 10 μm kidney tissue were mounted on indium tin oxide coated glass slides. Matrix of 10 mg/mL α-Cyano-4-hydroxycinnamic acid in 85% acetonitrile/13% ethanol + 2% water + 0.1% trifluoroacetic acid was sprayed on the tissue using an HTX tissue sprayer, dried for 10 minutes in the vacuum, and subjected to Matrix-assisted Laser
Table 1: Published pharmacokinetic data in humans.

<table>
<thead>
<tr>
<th>Drug</th>
<th>CL</th>
<th>CL/F</th>
<th>fu</th>
<th>Expected CLr (GFR*fu)</th>
<th>CLr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine A</td>
<td>210-240 mL/min</td>
<td>500-600 mL/min</td>
<td>10%</td>
<td>12.5 mL/min</td>
<td>1.48 mL/min</td>
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<tr>
<td>Tacrolimus</td>
<td>37.5 mL/min</td>
<td>NA</td>
<td>1%</td>
<td>1.25 mL/min</td>
<td>0.014 mL/min</td>
</tr>
<tr>
<td>Voclosporin</td>
<td>NA</td>
<td>1060 mL/min</td>
<td>3%</td>
<td>3.75 mL/min</td>
<td>7.82 mL/min</td>
</tr>
</tbody>
</table>

CL, clearance; CL/F, renal clearance; fu, bioavailability; GFR, glomerular filtration rate; NA, not applicable

Desorption and Ionization Mass Spectrometry Imaging (MALDI-MSI). The systemic and renal clearance in humans of CSA and TAC were obtained from the literature; pharmacokinetic data on VCS was obtained from data on file. Renal secretion of each drug was compared to its expected passive filtration based on glomerular filtration rate (GFR), fraction unbound in plasma (fu), and respective systemic drug exposure.

Results: MALDI-MSI demonstrated significantly higher concentrations of drug and more diffuse tissue disposition of CSA in mouse kidney compared to VCS (Figure 1). CSA was retained in all kidney tissues up to 2 hours post-administration. Higher concentrations and more diffuse disposition of TAC was also noted compared to VCS at 15 and 30 minutes; TAC was distinctively retained in the cortex and medulla. VCS had moderate distribution in the cortex and was rapidly excreted with low levels of drug present in the kidney after 1 hour. According to published data, CSA has a measured renal clearance of 1.48 mL/min in healthy human subjects, representing approximately 10% of expected passive filtration of 12.5 mL/min (Table 1). TAC has a renal clearance of 0.014 mL/min representing <2% of expected passive filtration of 1.25 mL/min. VCS has a renal clearance of 7.82 mL/min representing approximately 200% of its expected passive filtration rate of 3.75 mL/min.

Conclusion: MALDI-MSI revealed differential retention and distribution of CSA, TAC and VCS in mice, consistent with their respective renal clearances in humans. Higher drug exposure and ~90% renal reabsorption was observed for both CSA and TAC in this study, whereas the renal handling of VCS suggested a significant component of tubular secretion. The higher rate of secretion and lower overall exposure of kidney tissue to VCS may be associated with an improved safety profile when compared to the more diffuse distribution and greater renal retention of CSA and TAC.

#4744

MODELIZATION OF THE GUT-RENAL AXIS OF IGA NEPHROPATHY BY DEVELOPING (A1KI+/+ PIGR−−) GENOTYPE IN MICE

Jade Majorel1, Grégoire Bon1, Perrine Jullien1, Stéphane Paul2, Anne Druihne2, Michel Cogne2 and Nicolas Maillard1

1CIRI, Gimap, Saint-Priest-en-Jarez, France and 2CNRS UMR 7276 / INSERM U 1262, Cribl, Limoges, France

Background and Aims: IgA nephropathy is the most frequent primary glomerulonephritis worldwide, responsible for end stage renal disease within 20 years after diagnosis. The origin of the nephritogenic IgA1 in plasma remains poorly understood, but elements accumulate to suspect a mucosal origin after abnormal immune regulation. Herein, we propose a mouse model of IgA nephropathy, based on the modification of mucosal IgA synthesis and transport which drives an excess of polymeric forms of IgA1 in plasma. This model is based on (i) the presence of an IgA1 repertoire produced by mucosal plasma cells (A1KI+/+ mice) and (ii) the absence of mucosal transcytosis of IgA allowed by the knockout of PIGR (PIGR−−). This study aimed at describing the phenotype of such a mouse model which is supposed to
circulate increased polymeric IgA1 derouted from a mucosal origin, which is a key feature of the human IgAN. The present study is aimed at describing the phenotype of this model (A1KI+/+ PIGR−/−) through a mucosa-plasma-kidney axis, in comparison to wild type controls (WT), and A1KI+/+ PIGR+/+.

**Method:** Tissue fragments were used for immunofluorescence. Antibodies anti-IgA humain (Igah) FITC, antibodies anti-IgA mice (IgAm) HRP, antibodies goat anti-IgG alexa fluor and antibodies goat anti mice C3 FITC are used. To determine the concentration of murine IgA in the mice studied, ELISA tests were performed with anti-IgAm antibodies not conjugated or conjugated with HRP. The determination of IgAh in mice, anti-IgAh rabbit antibodies and antibody IgAh AP were used. Electrophoresis was performed in non-reducing conditions on polyacrylamide gel, transferred to a blot and revealed using anti-mouse IgA or anti-human IgA.

**Results:** At mucosal level, the observation of ileal slices of (A1KI+/+ PIGR−/−) mice, revealed that both IgAh and IgAm were strongly localized in the subepithelial chorion of villi and lamina propria, much more than in WT and the A1KI+/+ PIGR−/− conditions (figure 1). In serum, human IgA concentration was higher in sera issued from (A1KI+/+ PIGR−/−) mice than serum from A1KI+/+PIGR+/+ and WT mice (figure 2A). The difference was even more striking for murine IgA with a 2log10 gap (figure 2B). The western blot revealed a marked accumulation of circulating polymeric forms of human IgA1 and murine IgA, mostly dimeric and trimeric (figure 2C). In kidney, immunofluorescence shows the presence of human IgA1, C3 and IgG deposit in renal glomeruli in (A1KI+/+ PIGR−/−) mice (figure 3), with less IgA and C3 in A1KI+/+PIGR+/+ and no deposit in glomeruli of WT mice. It is noticeable that IgG can codeposit with human IgG in both A1KI+/+ conditions.

**Conclusion:** This double genetically altered mouse model of IgA nephropathy (A1KI+/+ PIGR−/−) display the mucosal-kidney axis of the human disease, by derouting polymeric IgA1 from a mucosal origin. Those IgA1 accumulate at a subepithelial stage, increase in serum with marked proportion of polymeric forms and deposit in kidney as pIgA1-IgG-C3 immune complexes. So this new murine model of IgA nephropathy could be helpful to investigate some potential therapeutic targets and increases the conviction of the role of mucosa to drive the pathogeny of the disease.
Figure 2: Detection of IgA1 and IgAm in sera (A) The concentration of IgA1h in sera of mice A1KI+/+(NIGA) and A1KI+/+(A1KI). (B) IgAm concentration in corresponding mice of different genotypes. (Concentration log10). (C) Discriminant and not reducing conditions. Electrophoresis allows the visualization of IgAm and IgA1h monomeric and polymeric.
PROTECTIVE ROLE OF THE PODOCYTE IL-15 / STAT5 PATHWAY IN EXPERIMENTAL FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS

Aissata Niasse¹, Kevin Louis¹, Olivia Lenoir², Laurent Mesnard¹, Juliette Hadchouel¹ and Yosu Luque³

¹Inserm, CoRaKid UMR_S1155, Paris, France, ²Paris Research Center Cardiovascular - Inserm University Paris City, Paris, France and ³Sorbonne Université, AP-HP Néphrologie Hôpital Tenon, Paris, France

Background and Aims: During glomerular diseases, podocyte-specific pathways can modulate the intensity of histological disease and prognosis. The therapeutic targeting of these pathways could thus improve the management and prognosis of kidney diseases. The Janus Kinase/ Signal Transducer and Activator of Transcription (JAK/STAT) pathway, classically described in immune cells, has been recently detailed in intrinsic kidney cells. We previously evidenced a protective role for a podocyte-expressed immune receptor such as the common gamma chain (γC) during glomerulonephritis (1). We also found that STAT5, a transcriptional factor classically described and activated downstream γC in T cells is upregulated in podocytes during glomerulonephritis.

Method: Using a mice model with a podocyte-specific deletion of Stat5, we analyzed the role of STAT5 in two experimental models of glomerular diseases.

Results: Here, we show, for the first time, that STAT5 is activated in human podocytes in focal and segmental glomerulosclerosis (FSGS). Additionally, podocyte-specific Stat5 inactivation aggravates the structural and functional alterations in a mouse model of FSGS (Figure 1). This could be due, at least in part, to an inhibition of autophagic flux and an alteration of mitochondrial function. Finally, Interleukin 15 (IL-15), a classical activator of STAT5 in immune cells, increases STAT5 phosphorylation in human podocytes and its administration alleviates glomerular injury in vivo by maintaining autophagic flux in podocytes.

Conclusion: In conclusion, activating podocyte STAT5 with commercially available IL-15 represents a potential new therapeutic avenue for FSGS.
Abstracts

#5420
A MODULAR INTRACELLULAR HIERARCHICAL-RESPONSIVE NANO CARRIER ENABLES DUAL TARGETING FOR HIGH THERAPEUTIC EFFICACY IN KIDNEY DISEASE
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National Clinical Research Center for Kidney Disease, State Key Laboratory of Organ Failure Research, Nanfang Hospital, Southern Medical University, Division of Nephrology, Guangzhou, P.R. China

**Background and Aims:** Single-loaded nanocarrier that can improve targeting capability and drug toxicity compared with free drugs demonstrates a promising strategy for disease treatment. Due to the heterogeneity of the injured cells during the disease progression, dose-induced drug resistance, and instability of nanocarriers in the blood circulation, it is challenging to achieve dual targeting to different injured cell subsets as well as reducing drug dosage but obtaining efficient treatment. In addition, developing nanocarriers is a complex and time-consuming process; there is a desire to develop a universal nanocarrier for various diseases, especially complex ones. Here, we have successfully designed a modular nanocarrier capable of co-delivery drugs. Meanwhile, the effective dosage was reduced to one-tenth of single-loaded nanocarriers.

**Method:** The dual-loaded drug-targeting nanoparticles consist of four main modules, including a chemical material, an antibody, and two drugs. First, we constructed a mesoscale spherical nanoparticle with a particle size of 400 nm from PLGA and wrapped drug A inside it. Next, the foot cell-specific antibody Nephrin is used as the target material and modified on the nanoparticle surface by the ph-sensitive short peptide. Finally, drug B is coupled to the antibody to obtain the final dual-targeting dual-drug nanoparticles. The dual-targeting dual-drug nanoparticles were injected into mice via the tail vein to evaluate their toxicity to organs and the immune system and compared with free drug. We explored the targeting and mechanisms of dual-targeting nanoparticles by organ imaging, Immunofluorescence, and other experimental methods. In mice, we established the model of acute kidney injury, puromycin aminonucleoside nephropathy (PAN), and ccRCC to compare the protective effects and mechanisms of dual-targeting nanoparticles in different concentrations.

**Results:** Dual targeting nanoparticles loaded with different drugs demonstrated the ability of dual targeting of glomeruli and tubules. In treating acute kidney injury, the nanocarriers were encapsulated with rapamycin and dexamethasone acetate; for puromycin nephropathy, the drugs were changed to rapamycin and captopril; and in the treatment of kidney cancer models, gefitinib and glutathione were chosen as targeted antitumor drugs. For different diseases, the lesions were treated significantly with different drug combinations. We observed a reduction of tubular injury in the acute kidney injury model, a recovery of the foot process of podocytes in the puromycin nephropathy model, and a reduction of cancer foci in the renal cancer model. These results show that dual drug-loaded nanomaterials have an excellent ability to cope with complex situations.

**Conclusion:** Dual drug delivery system can flexibly adapt the treatment of various diseases by changing particle size, surface antibodies, and drugs.

#2689
TRANSPLANTATION OF MESENCHY MAL STEM CELLS - NEW FOCUS OF IMMUNE CORRECTION IN TREATMENT OF LUPUS NEPHRITIS
Natalya Krivoruchko, Lina Zaripova, Manarbek Askarov, Abay Baigenzhin, Temirlan Karibekov, Galiya Shaimardanova and Saltanat Bekturganova
National Scientific Medical Center, Astana, Kazakhstan

**Background and Aims:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterised by the production of organ-specific autoantibodies to components of cell nucleus, immune complex lesions of the connective tissue, and the development of irreversible damage of internal organs. Chronic relapsing course of SLE, resistance to steroid and immunosuppressive therapy, toxic effects of drugs determine the need of search for new therapeutic approaches.

**Objective:** To evaluate the efficacy and safety of bone marrow mesenchymal stem cell (MSC) transplantation with high-dose immunosuppressive therapy (HIST) in SLE patients.

**Method:** A total amount of 15 patients with a diagnosis of SLE (ACR criteria) refractory to classical immunosuppressive therapy was examined. Patients were divided into 2 groups: patients from the main group underwent MSCs transplantation with HIST (n = 10), while the control group was observed on the background of traditional immunosuppressive therapy without cell transplantation (n = 5). Both groups were comparable in age, gender of patients, duration and severity of the disease. The SELENA-SLEDAI was used to determine SLE activity. Cytokines were examined by ELISA (IL-1B, IL-4, IL-10, TNF-A), antibodies to double-stranded DNA (anti-dsDNA) and anti-nuclear antibodies (ANA) by indirect immunofluorescence. Morphological examination of kidney included Masson-trichrome histochemistry for collagen fibers, silvering reaction for elastic and reticulin fibers, immunofluorescent and immunohistochemical methods. The safety assessment included registration of various adverse events during and after transplantation. Statistical analysis was carried out by Kruskal-Wallis test using STATISTICA 6.1.

REFERENCE
Results: Monitoring the effectiveness of autologous stem cell transplantation in SLE patients showed a significant 2-fold decrease in activity by SELENA-SLEDAI score from 14.67 ± 1.15 to 7.33 ± 1.15 points after 12 months (p = 0.03). In the control group, this indicator remained unchanged and amounted to 15.0 ± 0.87 points despite ongoing immunosuppressive therapy. Clinical efficacy was noted in all patients receiving HIST and MSC transplantation, which was confirmed by a significant decrease in daily proteinuria from 2.48 ± 0.77 to 1.06 ± 0.56 g/l, a decrease in the value of antibodies to DNA (from 443.28 ± 547.53 to 187.8 ± 146.60) and blood cytokines (significantly for TNF-Α), and an increase in the level of complement (though insignificantly). According to kidney biopsy data, after MSC transplantation with HIST, positive dynamics consisted in an increase in the number of reticulin fibers in the vascular loops of the glomeruli, as well as a decrease in the immune inflammatory process in the vascular loops of the glomeruli by immunofluorescence analysis for the spectrum of antibodies (Figure 1). In most patients of the main group, the doses of methylprednisolone and immune suppressants were reduced. Chills during transplantation was registered in one patient; no other unwanted adverse events were identified. Conclusion: MSC transplantation in combination with HIST is significantly more effective than traditional immunosuppressive therapy in SLE according to clinical and laboratory data. The method is safe, allows decreasing signs of autoimmune aggression and can be used in cases of refractoriness, low efficiency or intolerance of standard therapy for SLE.

Figure 1: An immunofluorescence of a kidney biopsy demonstrated a decrease in the immune inflammatory process in the vascular loops of the glomeruli: the intensity of IgG, kappa, and C1q staining decreased.
**#4851**

**MOLECULAR FEATURES OF CIRCULATORY B CELLS AND RENAL CELLS AT THE SINGLE-CELL LEVEL IN AUTOANTIBODY-NEGATIVE PRIMARY MEMBRANOUS NEPHROPATHY PATIENTS**

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**Background and Aims:** Primary membranous nephropathy (PMN) is an organ-specific autoimmune disease that is the most common cause of idiopathic nephrotic syndrome in adults. Furthermore, the incidence of PMN is increasing, especially in young adults and children. The landmark discovery of nephritogenic autoantibodies against podocyte antigens such as M-type phospholipase A2 receptor (PLA2R) and thrombospondin type-1 domain-containing protein 7A (THSD7A) has provided a paradigm shift in diagnosis and treatment of PMN. However, there are still few patients with negative serum and renal tissue autoantibodies. This study aims to explore the molecular features of antibody-negative PMN.

**Method:** We sorted CD19+ cells from the peripheral blood of a pediatric patient with seven nephritogenic autoantibodies-negative PMN (NEG) by flow cytometry and performed single-cell transcriptome sequencing (scRNA-seq) and single-cell B cell receptor sequencing (scBCR-seq). Meanwhile, scRNA-seq was performed on renal biopsy tissues from the same patient. In addition, we included the scRNA-seq data of renal from anti-PLA2R antibody positive patients (POS) and healthy controls (CTRL), and the scBCR-seq data of B cell from CTRL for integrative analysis.

**Results:** The NEG patient showed typical nephrotic syndrome and was diagnosed as stage III membranous nephropathy by renal biopsy. There was no evidence of anti-PLA2R or anti-THSD7A antibodies in peripheral blood and seven nephritogenic autoantibodies such as anti-PLA2R antibodies in renal tissue. After excluding secondary factors, the patient was diagnosed with PMN. Through scRNA-seq of CD19+ cells, we found that the number, characteristic gene, function and clonotype of naïve B cells and memory B cells in NEG were significantly changed. Expanded CD38+- naïve B cells in NEG had the molecular characteristics of CD19+CD24-CD27-CD38+, defined as transitional B cells. This group of cells had distinct function features of cell activation, and its up-regulated genes were involved in multiple aspects of the BCR signaling pathway. Pseudotime trajectory analysis suggested CD38+- naïve B cells were highly enriched in the beginning of B cell differentiation. There was a preference in the use of VJ gene segments of B cells between NEG and CTRL, especially an increase of the IGHV3-23 and IGLV2-14 in NEG. The stronger pairing frequencies, IGLV2-14/IGLJ3 and IGK2V2-29/IGK2, were identified in NEG. We identified 14 distinct kidney cell types by marker genes. Through re-clustering of glomerular parietal epithelial cells (PECs), the patients were clearly distinct from their control counterparts, indicating a major shift in gene expression for this cell type. PECs in NEG showed significant up-regulation of cellular communication network factor-related genes (CCN1, CCN2), phospholipase A and acyltransferase-related genes (PLA2TA, PLA2TA), and seiptin protein-related genes (SEPTN2, SEPTN7), accompanied by significant down-regulation of podocyte-related genes. In addition, there are clearly distinct cellular functions and pseudotime trajectory in PECs from NEG and POS, and genes such as CCN2, PLAT4, SEPTN2 might drive the special trajectory of PECs in NEG. For the podocytes, the genes related with extracellular matrix and cell adhesion were significantly enhanced in NEG, which consisted with the functional enrichment analysis of the differentially expressed genes and gene set-based scores. We calculated the gene set-based scores including genes encoding lumen-to-blood sodium transporters. Results indicated the enhanced expression of sodium transporters in distal nephrons of MIN patients. More surprisingly, a group of proximal tubule epithelial cells showed significantly higher expression levels of sodium transporters. Among them, the expression of SLC5A12 encoding SMCT2 increased significantly.

**Conclusion:** We have systematically revealed the cell-type specific molecular features of PMN patients from circulation to renal tissue. Our research provides valuable evidence for the molecular diagnosis of PMN in children and insights into pathogenic mechanism of classical nephritogenic autoantibody-negative PMN.

**#6071**

**RITUXIMAB FOR MAINTENANCE OF REMISSION IN ADULT MINIMAL CHANGE DISEASE**

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National and Kapodistrian University of Athens Medical School, Laiko General Hospital, Department of Nephrology and Renal Transplantation, Athens, Greece

**Background and Aims:** Maintaining remission in a minority of adult patients with minimal change disease remains challenging. Prolonged corticosteroid use is associated with severe adverse effects. A limited number of observational studies suggest that rituximab may be an alternative therapeutic option for remission maintenance, allowing steroid withdrawal.

**Method:** We retrospectively analysed the data of all adult patients with minimal change disease, who received rituximab in our centre between 2017 and 2022.

**Results:** A total of 14 adults with minimal change disease were treated with rituximab, six of whom had childhood-onset nephrotic syndrome. Six patients were steroid dependent. The median number of relapses was 6.5 (IQR 4.5-15.2) prior to rituximab. Thirteen patients had received at least ≥ 2 different immunosuppressive agents during their disease. Corticosteroid-related adverse events, including osteopenia, hypertension, cataract and diabetes mellitus were observed in 10 subjects. Rituximab was administered in a median time of 10.6 years (IQR 4.5-16.3) after diagnosis. All patients received 2 doses of 1g rituximab 2 weeks apart. The median age at rituximab administration was 31 years (IQR 18.7-49.0); all patients were in remission. Besides corticosteroids, concomitant immunosuppressive therapy included calcineurin inhibitors (n = 6) and mycophenolate mofetil analogues (n = 1). The median follow-up time after the first dose of rituximab was 44 months (IQR 9.5-67.2). Relapses occurred in 6/14 patients in a median time of 17.5 months (IQR 10.2-26.5). The number of relapses per year decreased to 0.27 from 0.87 (p < 0.001) after rituximab. Six patients received a repeat course of rituximab. One patient developed Pneumocystis jirovecii pneumonia, that was successfully treated with cotrimoxazole. At the last follow-up visit, corticosteroids were discontinued in 8 out of 14 patients and calcineurin inhibitors in 3 out of 7 patients.

**Conclusion:** Rituximab is a reasonable therapeutic approach for maintaining remission and avoiding steroid toxicity in adult minimal change disease. Randomized controlled studies are needed to further evaluate the safety and efficacy of rituximab in these patients.

**#5611**

**ASSOCIATION BETWEEN LOSS OF IMMUNE CHECKPOINT PROGRAMMED CELL DEATH PROTEIN 1 AND ACTIVE ANCA-ASSOCIATED RENAL VASCULITIS**

Björn Tampe

University Medical Center Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany

**Background and Aims:** Immune checkpoint inhibitors (ICIs) have made an important contribution on the survival of patients with certain cancers. ICIs interrupt co-inhibitory signalling pathways mediated by programmed cell death protein 1 (PD-1), programmed cell death protein-ligand 1 (PD-L1), and cytotoxic T lymphocyte-associated antigen (CTLA-4) that result in the elimination of cancer cells by stimulating the immune system. Immune-related adverse events have also been described and attributed to an enhanced immune system activation. Recent observations have suggested dysregulation of immune checkpoints in active antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Therefore, we here aimed to analyze abundance of immune checkpoint molecules PD-1/PD-L1 and its implications in ANCA-associated renal vasculitis.

**Method:** We here analyzed intrarenal PD-1 and PD-L1, and cytotoxic T lymphocyte-associated antigen (CTLA-4) that result in the elimination of cancer cells by stimulating the immune system. Immune-related adverse events have also been described and attributed to an enhanced immune system activation. Recent observations have suggested dysregulation of immune checkpoints in active antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Therefore, we here aimed to analyze abundance of immune checkpoint molecules PD-1/PD-L1 and its implications in ANCA-associated renal vasculitis.

**Results:** We here observed a predominant tubulointerstitial expression of PD-1 that is decreased in ANCA-associated renal vasculitis. Moreover, loss of tubulointerstitial PD-1 correlated with active ANCA-associated renal vasculitis. Consistent to the observed association with active glomerular and tubulointerstitial lesions. For independent validation, publicly available datasets were analyzed for PD-1 expression (encoded by PDCD1).
tubulointerstitial lesions. We identified that interstitial PD-1 correlated with tubular and/or glomerular PD-L1 positivity. Finally, PD-1 was associated with decreased local synthesis of complement factor B. Interestingly, we did not observe a correlation between PD-1 and complement C5 or its C5a receptor. Combined with our observations, this may implicate a link between im-paired PD-1/PD-L1 signalling, complement factor B, and active ANCA-associated renal vasculitis.

Conclusion: These findings could be of relevance because experimental data have already been described that PD-1 agonism can be used therapeutically to attenuate autoimmunity in multiple disease models. Furthermore, targeted therapy against complement C5/C5a receptor and factor B are both available and currently evolving in the treatment of AAV. Therefore, this pilot study expands our current knowledge and describes a potential interplay between immune checkpoints and the alternative complement pathway in active ANCA-associated renal vasculitis.

#5499
COULD MESANGIAL C3 DEPOSITION BE AN INDEPENDENT PROGNOSTIC MARKER IN IMMUNOGLOBULIN ANEPHROPATHY? Hakki Çetinkaya1, Meltem Gursu2, Halil Yazici3, Egemen Cebecli4, Necmi Eren5, Mehmet Riza Atilpamak6, Omer Faruk Akca7, Gültrar Manga Sahin8, Taner Basturk9, Kadır Gökhan Atilgan10, Nihal Aydemir11, Kenan Turgutalp12, Hamad Dheir13, MÜreyt Yilmaz13, Semahat Karahisar Sirali14, Erhan Tatlar15, Saïde Elif Gullulu Boz16, Nephrology, Istanbul University, Istanbul, Turkey, 4Haseki Training and Research Hospital, Nephrology, Istanbul, Turkey, 9Diskapi Training and Research Hospital, Nephrology, Istanbul, Turkey, 53Bakirkoy Sadi Konuk Training and Research Hospital, Nephrology, Istanbul, Turkey, 16Medical Faculty, Nephrology, Necmettin Erbakan University, Konya, Turkey, 21Medical Faculty, Ankara University, Nephrology, Ankara, Turkey, 22Medical Faculty, Nephrology, Trakya University, Edirne, Turkey and 23Haydarpaşa Numune Training and Research Hospital, Nephrology, Istanbul, Turkey

Background and Aims: Immunoglobulin A nephropathy (IgAN) is a common primary glomerulonephropathy and the role of complement activation in the pathogenesis has not been fully clarified. There is evidence that mesangial C3 deposition plays a role in the development of the disease. The aim of this study was to examine the effect of C3 deposition on the prognosis of IgAN patients.

Method: The study included 1135 patients with IgAN confirmed by biopsy using the database of the Turkish Nephrology Association Glomerular Diseases Working Group (TSN-GOLD). Patients were excluded from the study if they were aged <18 or >75 years, or if C3 staining had not been performed in the immunofluorescent analysis. C3 deposition was defined as immunofluorescent staining within the mesangium as 1+ positive and no staining, and 2+ and 3+ positive intensity staining (<2+ and ≥2+). Evaluation was also made according to the Oxford MEST-C classification. The primary endpoint was the development of end-stage renal failure (ESRF), and kidney transplantation, and an increase of 30% in glomerular filtration rate (GFR) compared to the basal value, or an elevation in proteinuria to a nephrotic level (3.5 g/day) were accepted as poor prognosis.

Table 2: Multivariable-adjusted logistic regression analysis for mesangial C3 deposition according to the Oxford classification.

<table>
<thead>
<tr>
<th>Oxford Classification</th>
<th>Odds Ratio (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>1.26 (0.89–1.80)</td>
<td>0.184</td>
</tr>
<tr>
<td>E1</td>
<td>1.24 (0.89–1.72)</td>
<td>0.196</td>
</tr>
<tr>
<td>S1</td>
<td>1.72 (1.27–2.32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T1-2</td>
<td>1.16 (0.89–1.51)</td>
<td>0.259</td>
</tr>
<tr>
<td>Crescent C1 -C2</td>
<td>1.11 (0.73–1.70)</td>
<td>0.611</td>
</tr>
</tbody>
</table>

Table 1: Baseline characteristics according to mesangial C3 deposition.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (n = 1135)</th>
<th>C3 negative (n = 532)</th>
<th>C3 positive (n = 603)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39.79 ± 12.68</td>
<td>39.08 ± 12.36</td>
<td>40.36 ± 12.93</td>
<td>0.720</td>
</tr>
<tr>
<td>Male (%)</td>
<td>699 (61.6%)</td>
<td>315</td>
<td>384</td>
<td>0.122</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.60 ± 15.54</td>
<td>28.70 ± 22.58</td>
<td>26.71 ± 5.00</td>
<td>0.325</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>396 (34.9%)</td>
<td>191</td>
<td>205</td>
<td>0.458</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>134.74 ± 20.05</td>
<td>134.66 ± 20.81</td>
<td>133.01 ± 19.43</td>
<td>0.523</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>82.40 ± 11.34</td>
<td>82.81 ± 11.34</td>
<td>82.06 ± 11.35</td>
<td>0.093</td>
</tr>
<tr>
<td>Microscopic hematuria (%)</td>
<td>808 (71.2%)</td>
<td>108 (46)</td>
<td>426</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T1 (%)</td>
<td>413 (36.4%)</td>
<td>122 (29.3%)</td>
<td>291 (48.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T2 (%)</td>
<td>47 (10.2%)</td>
<td>18 (38.3%)</td>
<td>29 (58.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>185.88 (175.67–196.09)</td>
<td>187.91 (173.46–202.37)</td>
<td>184.25 (169.88–198.61)</td>
<td>0.130</td>
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</table>

<table>
<thead>
<tr>
<th>Oxford classification (n = 896)</th>
<th>M1 (%)</th>
<th>E1 (%)</th>
<th>S1 (%)</th>
<th>T1 (%)</th>
<th>T2 (%)</th>
<th>Crescent C1 (%)</th>
<th>Crescent C2 (%)</th>
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<tbody>
<tr>
<td></td>
<td>675 (59.5%)</td>
<td>235 (20.7%)</td>
<td>479 (42.2%)</td>
<td>413 (36.4%)</td>
<td>72 (6.3%)</td>
<td>116 (10.2%)</td>
<td>14 (1.2%)</td>
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</tbody>
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<th>Hypertension (%)</th>
<th>Systolic blood pressure (mmHg)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>Microscopic hematuria (%)</th>
<th>T1 (%)</th>
<th>T2 (%)</th>
<th>Triglyceride (mg/dL)</th>
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<td>14 (1.2%)</td>
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</tbody>
</table>
Results: Mesangial C3 deposition was determined in 603 (53.1%) patients. In the evaluation of basal values between the groups with and without deposition, no statistically significant difference was determined in respect of age, gender, BMI, proteinuria level, or the presence of hypertension. In the follow-up period of mean 78 months survival, no significant difference was determined between the two groups in respect of the primary endpoint (C3+:53.1% vs. C3-:46.9%, p = 0.43). A significant correlation was determined between C3 deposition and segmental glomerulosclerosis (S1) according to the Oxford MEST-C classification (p = 0.001).

Conclusion: Although a correlation was seen between mesangial C3 deposition and the S1 MEST-C classification, the use of these alone or together as a prognostic factor in IgAN is not appropriate.

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**B3 - EPIDEMIOLOGY & OUTCOME**

#3057

OUTCOMES IN SRNS (FSGS) PATIENTS IN THE UK RADAR IDIOPATHIC NEPHROTIC SYNDROME REGISTRY AND THEIR RELATIONSHIP WITH TIME-AVERAGED PROTEINURIA

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Background and Aims: Idiopathic Steroid Resistant Nephrotic Syndrome, SRNS (incorporating FSGS) is an important cause of proteinuric renal disease leading to kidney failure. Here we describe the outcomes of SRNS using the UK National Registry of Rare Kidney Diseases Idiopathic Nephrotic Syndrome (RaDaR-INS) Cohort, including retrospective and prospective data from 4274 patients with nephrotic syndrome (NS) not attributable to glomerulonephritis or systemic disorders, recruited from 107 adult and paediatric kidney units across the UK since 2010. In patients with FSGS, severity of proteinuria at onset and during follow up is associated with renal failure. In this study, we tested for associations between defined proteinuria endpoints with both eGFR slope and renal survival, in children and adults.

Method: Participants included those with renal biopsy diagnosis of FSGS or minimal change disease (MCD), or monogenic NS. Patients with no proteinuria measurement ≥1.0 g/g >6 months after disease onset were excluded as likely fully steroid-sensitive. Patients with kidney failure (KF) (CKD stage 5 or on renal replacement therapy) at or prior to first proteinuria measurement after baseline were excluded. Disease onset was defined as time of renal biopsy; primary renal diagnosis (PRD) date if no biopsy date recorded, and first proteinuria ≥1 g/g if neither biopsy/PRD date was available. Baseline was defined as first proteinuria ≥1 g/g >6 months after disease onset. Kaplan-Meier methods were used to analyze renal survival, defined as absence of KF or death with survival time calculated from baseline to last follow up. eGFR slope was measured from 6 months after baseline for the duration of follow up.

Results: Of 612 MCD and FSGS patients meeting eligibility, median time from disease onset to baseline was 1.2 years (IQR 0.6-4.4). Median baseline age was 38 years (IQR 21–56) with paediatric patients representing 21% of the study population. Median proteinuria at baseline was 3.4 g/g (IQR 1.9-6.2), while mean eGFR was 89 mL/min/1.73 m² (SD 39). Mean rate of loss of eGFR over follow-up was 4.4mL/min/1.73 m²/year (SD 10.9). Complete proteinuria remission (CR) and FSGS partial remission (FPR) were defined as shown in Table 1 using values of time-averaged proteinuria (TA-PU) over months 6–24 from baseline. For patients achieving CR or FPR, the rate of loss of eGFR was slower (Table 1), with a higher probability of survival from KF/death (Table 1 & Figure 1), than patients failing to achieve CR or FPR.

Conclusion: This is a study of proteinuria and outcomes in a population of patients with FSGS or steroid-resistant MCD. We regard the latter group as likely also to have FSGS. In this population of patients with overt proteinuria, achieving partial or complete remission of proteinuria is associated with slower disease progression and reduced risk of KF/death.

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**Table 1: Achievement of proteinuria endpoints and association with survival from KF/death and rate of loss of eGFR in patients with MCD or FSGS.**

<table>
<thead>
<tr>
<th>Remission Category</th>
<th>Proteinuria endpoints: TA-PU during follow-up (6-24 months from baseline)</th>
<th>Patients achieving proteinuria endpoint n (%)</th>
<th>5-year KF/death survival (95% CI)</th>
<th>eGFR slope (ml/min/1.73 m²/year) Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>PU &lt;0.3 g/g</td>
<td>155 (25.3)</td>
<td>0.99 (0.94, 1.00)</td>
<td>−1.9 (7.9)</td>
</tr>
<tr>
<td></td>
<td>PU 0.3 to &lt;1.5 g/g AND 40% decrease in PU from baseline</td>
<td>146 (23.9)</td>
<td>0.96 (0.90, 0.99)</td>
<td>−2.3 (6.5)</td>
</tr>
<tr>
<td>FPR</td>
<td>No PU &lt;1.5 g/g associated with 40% decrease in PCR baseline</td>
<td>311 (50.8)</td>
<td>0.74 (0.68, 0.79)</td>
<td>−6.7 (13.2)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence intervals; CR, complete remission; eGFR, estimated glomerular filtration rate; KF, kidney failure; FPR, FSGS partial remission of proteinuria; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease; PU, proteinuria measured as protein-creatinine ratio; TA-PU, time-averaged PU.
Figure 1: Kaplan-Meier kidney failure/death survival curves (incl. 95% CI) for proteinuria endpoints in (A) all patients, (B) paediatric patients and (C) adult patients with MCD or FSGS.

**Abbreviations**: CI, confidence intervals; CR, complete remission; KF, kidney failure; FPR, FSGS partial remission of proteinuria; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease.
OFATUMUMAB AS A RESCUE THERAPY FOR PATIENTS WITH MEMBRANOUS NEPHROPATHY
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Background and Aims: Rituximab is the first-line treatment for patients with primary membranous nephropathy (MN) and nephrotic syndrome (NS) at high risk of progression to end-stage kidney disease. However, this drug is effective only in approximately two thirds of treated patients, and repeated rituximab infusions may be complicated by hypersensitivity reactions, which contraindicate retreatment. Ofatumumab, a fully human anti-CD20 antibody, could overcome these limitations.

Method: We retrospectively evaluated the response to a single 50–300 mg dose of intravenous ofatumumab in 17 MN patients referred to our institution who either experienced hypersensitivity reactions (rituximab-intolerant, n = 5) or failed to achieve NS remission after rituximab infusion (rituximab-resistant, n = 12).

Results: Over a median [IQR] follow-up of 5.0 [3.0-9.8] months, ten (58.8%) patients—five rituximab-resistant (41.7%) and all five rituximab-intolerant—achieved complete or partial NS remission, defined as proteinuria <0.3 g/day or proteinuria <3.5 g/day with ≥50% reduction from baseline, respectively. Ofatumumab infusion induced a progressive reduction in 24-hour urinary protein and IgG excretion, and a sharp increase in serum albumin and IgG levels. Peripheral B cells were depleted in all patients and started reconstituting by 3 months from baseline. Seven of the 12 subjects with PLA2R-related disease (i.e. with baseline anti-PLA2R antibody levels >2.7 RU/mL by ELISA) achieved antibody depletion during the follow-up (half of rituximab-resistant and all rituximab-intolerant). There were 14 non-serious infusion-related adverse events in nine patients, all of which completely resolved with temporary interruption of ofatumumab infusion.

Conclusion: Ofatumumab may be an effective and safe treatment option for all rituximab-intolerant and a substantial proportion of rituximab-resistant MN patients.

Table 1: Baseline characteristics. *Measured GFR by the Iohexol plasma clearance technique. Data are mean±SD, median [IQR] or number (percentage).

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 17)</th>
<th>Rituximab-Resistant (n = 12)</th>
<th>Rituximab-Intolerant (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.0±13.6</td>
<td>53.3±14.5</td>
<td>45.6±10.3</td>
</tr>
<tr>
<td>mGFR (mL/min/1.73m²)*</td>
<td>52.1 [38.6; 73.4]</td>
<td>41.9 [37.8; 72.8]</td>
<td>67.4 [55.8; 83.4]</td>
</tr>
<tr>
<td>Serum Albumin (g/dL)</td>
<td>2.5±0.5</td>
<td>2.5±0.5</td>
<td>2.6±0.6</td>
</tr>
<tr>
<td>Urinary Protein (g/24h)</td>
<td>9.0±4.3</td>
<td>10.3±4.3</td>
<td>6.2±2.8</td>
</tr>
<tr>
<td>Serum Anti-PLA2R (RU/mL)</td>
<td>66 [14; 117]</td>
<td>66 [11; 146]</td>
<td>53 [18; 89]</td>
</tr>
<tr>
<td>Ofatumumab Dose (mg)</td>
<td>300 [100; 300]</td>
<td>300 [63; 300]</td>
<td>300 [100; 300]</td>
</tr>
<tr>
<td>MN Onset (years)</td>
<td>9.9±5.1</td>
<td>8.5±5.3</td>
<td>13.2±2.4</td>
</tr>
<tr>
<td>Previous IS (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>12 (70.6)</td>
<td>7 (58.3)</td>
<td>5 (100.0)</td>
</tr>
<tr>
<td>Alkylating Agents</td>
<td>11 (64.7)</td>
<td>7 (58.3)</td>
<td>4 (80.0)</td>
</tr>
<tr>
<td>Calcineurin Inhibitors</td>
<td>7 (41.2)</td>
<td>4 (33.3)</td>
<td>3 (60.0)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>3 (11.8)</td>
<td>3 (25.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
THE ROLE OF CALCINEURIN INHIBITORS IN MONOGENIC PEDIATRIC STEROID RESISTANT NEPHROTIC SYNDROME: A RETROSPECTIVE, MULTICENTER STUDY


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Background and Aims: Response to calcineurin inhibitors (CNI) is associated with a significant improvement in long-term kidney survival of children with non-genetic steroid resistant nephrotic syndrome (SRNS). On the contrary, these agents are considered non-efficacious in monogenic SRNS and are contraindicated according to the latest International Pediatric Nephrology Association (IPNA) Clinical Practice Recommendations for SRNS. However, there is evidence suggesting that remission with CNI therapy in this subgroup of children with SRNS is possible, but no studies to date have assessed this question in a systematic way. We aimed to study the incidence of response to CNI in children with monogenic SRNS, factors predictive of remission and the effect of treatment on kidney survival.

Method: Retrospective cohort study of children 0–18 years with genetically confirmed SRNS treated with a CNI for at least 3 months. Demographic, clinical, genetic, biochemical, histopathologic and treatment data were collected at various time points: at clinical diagnosis, 6, 12, 24 months from CNI onset, and last available follow-up. Pathogenicity of all reported variants was assessed by a dedicated geneticist according to the American College of Medical Genetics guidelines and only patients with a pathogenic genotype were included in the analysis[1]. Patients were classified according to their response to CNI as complete, partial or non-responders based on the IPNA Clinical Practice Recommendations for SRNS[2].

Figure 1: (A) Cumulative incidence of complete and partial remission in rituximab-intolerant and rituximab-resistant patients, (B) % change in proteinuria and serum albumin, (C) B cell kinetics and (D) % change in anti-PLA2R levels after ofatumumab infusion.
#4286 ACCUMULATION OF MALADAPTIVE TUBULAR EPITHELIAL CELLS (TECs) IS UBIQUITOUS IN CKD AND REPRESENTS A COMMON INITIATING MECHANISM OF DISEASE PROGRESSION

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**Background and Aims:** Intestinal fibrosis, tubular atrophy and inflammation are common final pathways to end-stage kidney disease (ESKD), contributing to progressive nephron loss and functional decline in most chronic kidney diseases (CKD), including those considered to be glomerular in origin. Disease-associated maladaptive TECs have been described in rodent models and are characterized by a failed repair phenotype that contributes to tubulointerstitial fibrosis and inflammation. The contribution of equivalent maladaptive cell states to human CKD progression remains poorly described. The aim of this study was to characterize maladaptive TECs in the NURIteRe CKD cohort to assess their abundance and potential role in initiating inflammation and fibrosis in a large and heterogeneous patient population.

**Method:** Human maladaptive TECs were identified in an scRNA-Seq dataset (GSE171314) from IgA nephropathy patients by scoring cells with a TNF activation and a mouse proximal tubule failed repair (FR) gene signature[1]. The results were validated in a scRNA-Seq dataset (GSE171488) from patients with membranous nephropathy. Marker genes for these human maladaptive TEC clusters were derived using the Seurat R package and the top 50 candidates were combined into cell state-specific signatures. Single-sample signature scores were calculated for 310 kidney biopsy transcriptomes from various CKD etiologies in the NURIteRe cohort. Signature scores were correlated with eGFR and used in a time-to-event analysis (40% decline in eGFR or occurrence of ESRD) to predict renal event-free survival.

**Results:** Analysis of independent human scRNA-Seq datasets and scoring with TNF activation and mouse proximal tubule FR gene signatures revealed two distinct maladaptive TEC states associated with different tubular segments. A cluster of cells (FR-PT) with increased TNF activation and mouse FR signature expression were identified that clustered adjacent to proximal TECs, suggesting a lineage relationship. A second cluster of cells (DT2) with increased TNF activation was clustered adjacent to thick ascending limb (TAL) cells, suggesting distal tubule lineage. Maladaptive TEC clusters were detected at low levels in healthy controls but increased in CKD. FR-PT and DT2 cells are characterized by a pro-fibrotic and pro-inflammatory gene expression and likely represent a source of signalling molecules mediating stromal crosstalk in the kidney fibrotic microenvironment. To investigate their abundance in CKD, signature expression in NURIteRe kidney biopsy transcriptomes was summarized into a sample-level score. Signature scores for FR-PT and DT2 cells were generally elevated in all CKD etiologies with substantial variation within disease groups. Inverse correlation of eGFR with the scores suggested an accumulation of maladaptive TECs with kidney function decline, largely independent of primary diagnosis (Fig. 1). Pseudotime analysis revealed that this accumulation accompanied or preceded increases in myofibroblast and immune cell gene expression, suggesting a mechanism that may be driving disease initiation and progression. Importantly, high expression of the FR and DT2 signatures was associated with a decrease in renal event-free survival (Fig. 2), further supporting their relevance to human disease progression.

#C1 - BASIC SCIENCES & EXPERIMENTAL

##5399 VONAFEXOR AS A NOVEL THERAPY FOR CHRONIC KIDNEY DISEASE

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1Institute Necker Enfants Malades–Inserm University Paris City, Paris, France and 2ENYO Pharma, Lyon, France

**Background and Aims:** Chronic kidney diseases (CKD) are characterized by the progressive loss of renal function. The molecular mechanisms underlying this progression are still poorly characterized and probably multifactorial. Therefore, there is a real need to expand the very limited number of therapies able to slow down the rate of CKD progression. Recent findings indicate that NR1H4, a druggable nuclear receptor, might play an important role in CKD. The aim of this study was to investigate the benefit of Vonafexor, a novel small molecule and specific NR1H4 agonist in acquired and genetic models of CKD.

**Method:** Two complementary experimental models of CKD (the 75% excision of total renal mass (Subtotal Nephrectomy; Nx) and the Col4a3−/− mice, a model of Alport disease) were studied. NR1H4 and the expression of some of its downstream targets were evaluated by quantitative RT-PCR, western blot and immunohistochemistry. In the Nx model, mice were treated with Vonafexor by daily oral gavage from 5 to 8 weeks after the surgery. The possible beneficial effect was compared to that of Losartan and other NR1H4 agonists.

In the Alport model, mice were treated by Vonafexor from 5 to 8 weeks after birth. In both models, group of mice were sacrificed at 5 weeks to evaluate the extent of renal lesions at baseline. Renal lesions were quantified using imaging J. Renal inflammation, myofibroblast activation and podocyte number were quantified after specific staining. Human biopsies were also studied. RNAseq was performed using Illumina NovaSeq6000.

**Results:** We observed that NR1H4 expression and OSTa and OSTb, two downstream targets of NR1H4, were significantly reduced in remnant kidneys of Nx FVB/N mice compared to sham-operated animals 8 weeks after surgery. Co-localization staining revealed that NR1H4 is mainly expressed in proximal tubules and, to a minor extent, in Henle loops. Renal lesions were already present at 5 weeks in both experimental models. Remarkably, Vonafexor showed beneficial effects in terms of glomerulosclerosis and tubular dilatations and, more importantly, induced a reduction of interstitial fibrosis 8 weeks after nephrectomy as compared to the 5-week baseline. Lymphocytes and macrophage infiltration, as well as activated myofibroblasts, were also significantly reduced. Similarly, podocyte loss was stopped by Vonafexor treatment. Of note, the beneficial effect of Vonafexor was unique compared to other classes of NR1H4 agonists and also higher than that of Losartan. The same beneficial effect was found in Col4a3−/− mice. RT-PCR confirmed the activation of several NR1H4 downstream targets in mice treated with Vonafexor, while RNAseq analysis revealed that Vonafexor impacted the pathological activation of pathways involved in cell cycle, cell signaling and metabolism. These results may be relevant to humans, since NR1H4 expression was significantly reduced in biopsies from patients with CKD of different etiologies as compared to control kidneys.

**Conclusion:** Altogether our results identified Vonafexor a novel key drug to control CKD. This is consistent with recent results obtained in LIVIFY phase 2 clinical trial in which Vonafexor has already demonstrated beneficial effects on eGFR in NASH patients with mild to moderate CKD.

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Conclusion: This study suggests an important role for an accumulation of maladaptive TECs in CKD progression. These cells are observed in every CKD etiology that was included in this study, suggesting that targeting these cells could be an effective strategy to preserve kidney function broadly in CKD. Identification of surrogate blood or urine biomarker would allow for the identification of patients with increased levels of these cells regardless of disease etiology.

REFERENCE

#5592
THE SODIUM PHOSPHATE COTRANSPORTER NAPI-IIB IS UPREGULATED AND EXPRESSED DE NOVO IN KIDNEYS OF PATIENTS WITH CHRONIC KIDNEYS DISEASE
Rupert Busch1, Christoph Daniel2, Kerstin Amann3, Maja Lindenmeyer3, Nati Hernando1, Pedro Henrique Imenez Silva1 and Carsten Wagner1

1Institute of Physiology, University of Zurich, Zurich, Switzerland, 2Institute of Pathology, Friedrich-Alexander-University (FAU) Erlangen-Nürnberg, 3Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background and Aims: Renal reabsorption of phosphate is mediated by 3 main transporters located in the luminal brush border membrane of the proximal tubule, namely NaPi-IIa (SLC34A1), NaPi-IIc (SLC34A3), and Pit2 (SLC20A2). The expression of all three proteins has been shown to be reduced in animal models of kidney disease [1]. Recently, we demonstrated that NaPi-Iib, a paralogue of the SLC34 subfamily that is mostly expressed in small intestine and lungs, is also expressed in the loop of Henle. Its mRNA expression is enhanced in rodent models of kidney injury. However, the expression of NaPi-Iib has not been characterized in humans and it is unknown whether NaPi-Iib is also upregulated in chronic kidney disease (CKD).

Method: In this study, we examined the localization of NaPi-IIa, IIb, and IIc in kidneys of control healthy individuals (kidney donors) (eGFR: 111.6 ± 22.9 ml/min/1.73m²) and patients with diabetic nephropathy (eGFR: 31.9 ± 7.7 ml/min/1.73m²), anti-glomerular basement membrane nephritis (anti-GMB) (eGFR: 27.2 ± 22.6 ml/min/1.73m²), and hypertensive nephropathy (eGFR: 31.5 ± 5.3 ml/min/1.73m²) by immunofluorescence. Moreover, we analyzed data from various transcriptome data bases from healthy individuals and patients with CKD.

Results: In kidneys from healthy donors, NaPi-IIb staining was restricted to thin and thick limbs of the loop of Henle, while AQP1 was observed in proximal tubules and descending thin limbs. NaPi-IIc was abundantly found in proximal tubules and descending thin limbs. NaPi-Iic was abundantly found in...
proximal tubule cells. In biopsies from patients, NaPi-IIb signal was also found in addition to thin and thick limbs in cells of the collecting duct and in many proximal tubules. In contrast, the staining of NaPi-IIc was reduced in all groups of patients with CKD.

RNA expression data from the European Renal cDNA Bank (ERCB) confirmed our immunofluorescence findings. SLC34A2 (NaPi-IIb) mRNA was progressively more expressed in kidneys of patients with kidney disease of tubulointerstitial origin from CKD stages 1 to 5, while it was strongly upregulated from stage 4 onwards in CKD of glomerular origin. Single cell RNA sequencing data of patients with acute kidney injury and CKD [2] showed elevation of SLC34A2 expression in injured thick ascending limb, degenerative proximal tubule cells (14× higher, adj. p<0.0001) (de novo expression), and descending thin limb (3.7× higher, adj. p<0.0001). SLC34A1 (NaPi-IIa) expression levels were reduced in whole kidneys (ERCB data) and SLC34A1 and SLC34A3 expression also decreased in proximal tubule cells of patients with CKD.

Conclusion: The phosphate transporter NaPi-IIb is highly upregulated in kidneys from patients with various etiologies of CKD and its expression spreads to proximal tubule and collecting duct. In contrast, the expression of the main physiological phosphate transporters NaPi-IIa and NaPi-IIc is reduced in CKD. These findings may have implications for the development and maintenance of hyperphosphatemia in CKD patients and limit the use of specific NaPi-IIa and/or NaPi-IIc inhibitors in patients with CKD.

REFERENCES

#3819
THE PROTECTIVE EFFECT OF INTERLEUKIN-1 RECEPTOR ANTAGONIST ON KIDNEY FUNCTION: A MENDELIAN RANDOMIZATION STUDY
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Background and Aims: Interleukins (ILs), key cytokine family of inflammatory response, are closely associated with kidney function. However, the causal effect of various ILs on kidney function needs further investigation.

Method: We performed two-sample summary-level mendelian randomization (MR) analysis (Fig. 1). Genetic variants with strong association with serum IL levels were obtained from a previous genome-wide association study meta-analysis. Summary-level data for eGFR were obtained from CKDGen database. A replication analysis was performed in the independent UK Biobank data. As a main MR analysis, multiplicative random-effect inverse-variance weighted method was performed. Pleiotropy-robust MR analysis, including MR-Egger with bootstrapped error and weighed-median methods, were also implemented.

Results: We tested the causal estimates from nine ILs on eGFR traits. Among ILs, we found that genetically predicted serum IL-1ra level showed consistently significant association (P < 0.05) with eGFR, also supported by significant (P < 0.05) pleiotropy-robust MR results. Using 20 SNPs (18 of pQTL and 2 of eQTL SNPs), genetically predicted higher serum IL-1ra level was significantly associated (<0.05) with higher eGFR in multiplicative random effect IVW analysis (Fig. 2). In addition, the result was consistent towards eGFR decline phenotype of the outcome database. Otherwise, nonsignificant association was identified between other genetically predicted ILs and eGFR outcome (Fig. 3).

Conclusion: These findings support the clinical importance of IL-1 associated pathway in relation to kidney function in the general individuals, particularly highlighting the importance of IL-1ra.
Summary-level Mendelian randomization

GWAS meta-analysis for inflammatory cytokines of European ancestry individuals (N = 38,424)

376 cis-instrumental SNPs

SNPs of cytokines except for interleukins

80 cis-instrumental SNPs for 9 interleukins

UKB + CKDGen GWAS meta-analysis for log-eGFRcr of European ancestry individuals (N = 765,348)

CKDGen GWAS meta-analysis for log-eGFRcr of European ancestry individuals (N = 436,581)

UKB + CKDGen GWAS meta-analysis for log-eGFRcys of European ancestry individuals (N = 343,339)

UKB + CKDGen GWAS meta-analysis for degree of annual eGFR decline of European ancestry individuals (N = 343,339)

Figure 1:

(A) Scatter plot

(B) Leave-one-out analysis

Figure 2:
Figure 3:
**Using a Deep Learning Model to Evaluate Pathological Injury of Diabetic Kidney Disease**

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**Background and Aims:** Early diagnosis and evaluation play an important role in preventing the progression of diabetic kidney disease (DKD). Renal biopsy is the gold standard of DKD diagnosis. In 2010, the Renal Pathology Society (RPS) developed a consensus classification for DKD, which classifies DKD glomerular lesions and scores for tubulointerstitial lesion. However, as the pathologic heterogeneity of DKD patients and unparallel relationship between pathology features and clinical symptoms, it remains controversial whether is reliable to use RPS classification for renal outcomes prediction. Besides, the inconsistence between pathologists might magnify the gap between prediction and outcome. More reliable methods for DKD pathology assessment are needed. The development of machine learning (ML) algorithms especially convolutional neural networks (CNNs) enables it possible, which can provide automatic and precise analysis for complicated images. Thus, this study aimed to construct a ML-based model to assist and provide automatic decision supports to clinical doctors.

**Method:** We examined 204 DKD renal biopsied whole-slide images (WSIs) of Periodic Acid Schiff staining from Southeast University Institute of Nephrology whose database came from more than 30 hospital centers. All the WSIs were randomly annotated by three pathologists. We established a consecutive CNNs framework: DKD pathology evaluation system (DPES). It consists of three parts: 1. Based on classic UNet architecture, we developed a segmentation model whose backbone is replaced by ResNet 50 architecture for detecting glomeruli. 2. According to RPS classification, a CNN added with channel attention mechanism is built to discriminate sclerotic glomeruli, glomeruli with K-W node, and glomeruli with mesangial expansion. Through this method, the entire WSIs were divided into RPS grades 1-IV. 3. For the analysis of tubulointerstitial lesion, we constructed a segmentation model as previous description to calculate the area of the atrophic tubule and its percentage of the total tubules.

**Results:** For glomerular assessment, compared with other ML networks, DPES achieved better performance in segmentation for glomeruli (Intersection over Union (IOU): 0.82, Precision: 0.89, Accuracy: 0.91) and tubulointerstitial (atrophy (TA): IOU: 0.9; Precision: 0.94; Accuracy: 0.95; non-tubular atrophy (NT): IOU: 0.84; Precision: 0.90; Accuracy: 0.93). Interstitial fibrosis and tubular atrophy (IFTA) from network compared with three pathologists didn’t show statistically difference.

**Conclusion:** Our findings demonstrated that the DPES achieved similar performance with three pathologists. It suggests that machine learning algorithms can generate reliable results and provide more supports for clinical decision.

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**Effectiveness and Safety of Apixaban, Rivaroxaban and Warfarin in Patients with Advanced CKD and Atrial Fibrillation: A Nationwide US Cohort Study**

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**Background and Aims:** Head-to-head data comparing the effectiveness and safety of oral anticoagulants in patients with atrial fibrillation (AF) and advanced CKD or on dialysis are lacking. We compared the effectiveness and safety of apixaban, rivaroxaban and warfarin in patients with AF and CKD stages 3 to 5, including those on dialysis.

**Method:** We conducted a new-user, active-comparator, cohort study using data from two nationwide U.S. claims databases, Medicare and Optum Clinformatics. We included patients with nonvalvular AF and CKD who newly initiated warfarin vs. apixaban (N = 169,702), or rivaroxaban vs. apixaban (N = 129,396), CKD stages were determined based on a validated claims-based algorithm. The primary outcome was a composite of ischemic stroke or major bleeding to represent the net benefit of treatment. Secondary outcomes included the individual components of the primary outcome and all-cause death. We used 1:1 propensity score matching to adjust for 80 confounders. Adjusted hazard ratios (aHRs) were estimated with Cox regression analyses and absolute rate differences per 1000 person years (aRDs) with generalized linear regression in the propensity score matched sample.

**Results:** Compared with apixaban, warfarin and rivaroxaban were associated with a higher risk of the composite endpoint, regardless of CKD stage. Comparing warfarin vs. apixaban, the aHRs were 1.5 (1.3–1.6), 1.4 (1.0–1.9) and 1.3 (1.2–1.5) for CKD stages 3, 4, and dialysis, respectively (p-value for heterogeneity 0.16). Comparing rivaroxaban vs. apixaban, the aHRs were 1.5 (1.4–1.7), 1.7 (1.4–2.2) and 1.3 (0.9–1.8) (p-value for heterogeneity 0.38) for CKD stages 3, 4, and 5/dialysis, respectively; corresponding aRDs were 27.1 (12.3, 41.8), 32.9 (13.9, 40.5) and 20.7 (−28.9, 70.2) (p-value for heterogeneity 0.16). The higher rate of the primary endpoint for warfarin and rivaroxaban was driven by a higher risk of bleeding, with similar rates of ischemic stroke.

**Conclusion:** In patients with AF and CKD, apixaban was associated with a net benefit compared with rivaroxaban or warfarin, which was primarily driven by lower rates of bleeding. Benefits were consistent across severity of CKD.
Figure 1: Comparative effectiveness and safety of warfarin vs. apixaban or rivaroxaban vs. apixaban in patients with atrial fibrillation and CKD after 1:1 propensity score matching.
NON-ADHERENCE TO CARDIOMETABOLIC DRUGS AS ASSESSED BY LS-MS/MS IN URINE AND ITS ASSOCIATION WITH RENAL AND CARDIOVASCULAR OUTCOMES IN T2DM

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Background and Aims: Cardiovascular and renal complications have a detrimental impact on the prognosis and quality of life of patients with type 2 diabetes mellitus (T2DM). Guidelines recommend combination drug therapy to prevent or delay these complications[1]. However, non-adherence to medication is common and a barrier to successful disease management[2]. Most previous studies on adherence and outcome used indirect methods to assess adherence[3]. In this study we used liquid chromatography-tandem mass spectrometry (LC-MS/MS), a direct and objective adherence measure, to assess adherence to cardiometabolic drugs in a large real-world cohort of individuals with T2DM and analyzed non-adherence in the context of cardiovascular and renal outcomes.

Method: 1125 eligible PROVALID participants were included. PROVALID is a prospective observational cohort study of patients with T2DM followed annually at the primary health care level. Urine samples from the PROVALID biobank were screened for 79 cardiometabolic drugs and metabolites thereof by LC-MS/MS. An individual was classified as fully adherent when markers for all prescribed drugs were detected, partially non-adherent when at least a marker for one drug was detected and totally non-adherent when no marker for any prescribed drug was detectable. In order to assess outcome by adherence we defined a cardiovascular (myocardial infarction, stroke, and cardiovascular death) and a renal (ESKD, renal death, sustained 40% reduction in eGFR to < 60 ml/min per 1.73 m², sustained progression of albuminuria) composite endpoint.

Results: The mean age was 64.2 (±8.9) years and 46.1% were female. The mean duration of T2DM was 11.4 (±7.9) years. The mean HbA1c was 7.1 (±1.1)%, the mean eGFR was 77.6 (±23.6) ml/min/1.73 m² and mean albuminuria 67.3 (±287.9) mg/g creatinine. Participants were prescribed 5.4 (±2.0) cardiometabolic drugs on average. Based on the results of LC-MS/MS measurements, 56.3% were totally adherent, 42.0% were partially adherent, and 1.7% were totally non-adherent to screened cardiometabolic drugs. Adherence was highest to antplatelet and glucose lowering drugs and lowest to lipid lowering drugs (totally adherent individuals 90.1%, 89.2% and...
70.7%, respectively). Non-adherent patients had a longer history of T2DM (12.3 ± 8.5 vs. 10.7 ± 7.5, p = 0.003) and a higher number of prescribed drugs (5.8 ± 2.1 vs. 5.1 ± 1.9, p < 0.001). Age per se had no influence on adherence, however the number of prescribed medications had more impact on adherence in younger patients (Fig. 1). Ex-smokers were more likely to be adherent than current or never-smokers (odds ratio 1.4, p-value = 0.014). Patients who were adherent to lipid lowering drugs had significantly lower LDL (82.4 ± 29.8 vs. 111.4 ± 39.7 mg/dl, p < 0.001). A trend for lower HbA1c with adherence to glucose-lowering drugs and lower systolic blood pressure with adherence to antihypertensive drugs could be observed, however these differences were not statistically significant. In the longitudinal analysis, worse cardiovascular prognosis was especially seen with non-adherence to antplatelet drugs and worse renal outcome especially with non-adherence to antihypertensive drugs (Fig. 2).

**Conclusion:** Our analysis confirms that non-adherence, especially partial non-adherence, to cardiometabolic drugs is common in T2DM. A higher incidence of cardiovascular events was observed with non-adherence to antplatelet drugs, whereas non-adherence to antihypertensive drugs was associated with a higher renal event rate.

**REFERENCES**

#4404
KIDNEY FUNCTION TRAJECTORY BEFORE AND AFTER ARTERIOVENOUS ACCESS CREATION IN PATIENTS WITH PREDIALYSIS CKD

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Background and Aims: Timely arteriovenous (AV) access creation in view of starting hemodialysis is challenged by non-linear kidney function decline and the prospect of competing mortality. In addition, some studies have shown slower CKD progression following AV access creation in patients not on dialysis. While pathophysiological mechanisms, such as ischemic preconditioning and improved kidney perfusion, have been put forward to explain the apparent influence of AV access creation on estimated glomerular filtration rate (eGFR) trajectory, it cannot be ruled out that this finding resulted from an artefact induced by the use of models assuming linear (eGFR) decline before and after AV access creation. Our aim was to describe the kinetics of eGFR decline around the period of AV access creation and to identify different trajectory profiles using models relaxing this hypothesis.

Method: From 2013 through 2016, the CKD-REIN cohort included 3033 patients with CKD stages 3 to 5 from 40 nationally representative outpatient nephrology clinics in France. Participants were followed for 5 years or until initiation of kidney replacement therapy (KRT), death, or loss to follow-up, whichever came first. This study focused on patients who underwent their first AV access creation during follow-up. Linear mixed models with restricted cubic spline functions (two internal knots, one at AV access creation date, the other, one year before) were used to model a potential non-linear eGFR trajectory over time, based on routine labs. Random effects for the intercept and the spline function components allowed us to deal with individual variations in eGFR trajectory. Instantaneous rates of eGFR decline around AV access creation were then extracted. In addition, we performed latent class mixed models (LCMM) to identify distinct eGFR trajectories.

Results: During a median follow-up of 5.0 years (interquartile range [IQR], 4.6 to 5.2), 415 (14% of the total population) patients underwent a first AV access creation (32% women, 51% with diabetes). The median age at AV access creation was 69 years (IQR, 61 to 76), and the median eGFR, 13 ml/min/1.73 m² (IQR, 11 to 16). The median numbers of eGFR measurements before and after creation were 12 (IQR, 8 to 19) and 3 (IQR, 2 to 6) respectively. The average eGFR decline in the year before and after AV access creation, assuming constant slopes in each period, was 5.2 ml/min/1.73m² (95% confidence interval [CI], 4.8 to 5.5) and 3.4 ml/min/1.73 m² (95% CI, 3.1 to 3.7), respectively, with a mean difference of −1.8 ml/min/1.73m² (95% CI, −1.4 to −2.1). Analysis of instantaneous rates showed that the slowdown of eGFR decline began 8.3 months on average (95% CI, 7.8 to 8.6) before AV access creation.

Figure 1: Profiles of eGFR decline around the period of AV access creation in ml/min/1.73 m²/year.
creation. The LCMM identified two profiles of eGFR trajectories which mostly differed in the rate of eGFR decline (Figure). In both trajectories, the mean time to the slowdown of eGFR decline preceded time of AV access creation, by 9.1 and 7.2 months in the fastest and slowest eGFR decline trajectories, respectively.

Conclusion: In nondialysis patients, slowdown of kidney function decline appears to occur several months before AV access creation. Our findings do not support a causal biological effect of AV access creation on CKD progression, but favor alternative hypotheses including optimal management before AV access creation, greater uncertainty in eGFR estimation in advanced CKD due to muscle mass loss, or simply regression to the mean.

#5596
MODERATE AND SEVERE KIDNEY DYSFUNCTION ASSOCIATED WITH LEFT VENTRICLE DIASTOLIC DYSFUNCTION: A COHORT WITH DATA FROM ELECTRONIC HEALTHCARE RECORDS
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1UMC Utrecht, Department of Nephrology and Hypertension, Utrecht, Netherlands and 2UMC Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands

Background and Aims: Left ventricular diastolic dysfunction is observed in patients with chronic kidney disease (CKD) and may lead to heart failure with preserved ejection fraction (HFpEF). In this study, we investigate the association between kidney dysfunction and left ventricular diastolic dysfunction (LVDD) in a cohort using data from electronic healthcare records.

Method: We utilized electronic healthcare data from the Utrecht Patient Oriented Database (UPOD), including all patients treated at University Medical Center Utrecht (UMCU), a university teaching hospital. We extracted demographic patient data, admission data, medication orders, and laboratory results. All performed echocardiography from baseline (i.e., first visit to the hospital) to end of follow-up (i.e., death or censoring) were included. The estimated glomerular filtration rate (eGFR) was calculated using the creatinine formula without ethnicity. Participants were divided into four groups depending on their eGFR (mL/min/1.73 m²) as follows: normal kidney function (eGFR ≥ 90), mild kidney dysfunction (eGFR ≥ 60–89), moderate kidney dysfunction (eGFR ≥ 30–59), and severe kidney dysfunction (eGFR < 30). The association of eGFR with E/A and E/e’ ratio was tested by multivariable adjusted cox proportional hazards survival analysis, reporting hazard ratios (HR) and 95% confidence intervals (CI).

Results: We identified 6,216 participants who received echocardiography as part of their routine care between 2012 and 2022. The mean age was 66.9 years (SD: 12.04 years), and 41.7% of individuals were females. In total, 90.4% and 24.5% of the patients had, respectively, hypertension and diabetes. Twenty-six percent of participants had normal kidney function, 48.2% had mild kidney dysfunction, and 21.3% and 4% had moderate and severe kidney dysfunction, respectively. In total, 16,935 echocardiography were performed. The median time from the first to the final echocardiography was 7.08 (IQR: 2.89 years).

Adjusted multivariable analysis showed that patients with moderate (HR: 1.19; 95% CI: 1.09, 1.31) and severe kidney dysfunction (HR: 1.14, 95% CI: 1.14, 1.62) had higher probabilities of having E/A ratio < 0.75 or > 1.8 compared with those with normal kidney function. Similarly, for an E/e’ ratio > 14, participants with moderate and severe kidney dysfunction had higher probabilities, HR: 1.62 (95% CI: 1.49, 1.77) and 2.10 (95% CI: 1.83, 2.42), respectively, compared with participants with normal kidney function.

Conclusion: Moderate and severe kidney dysfunction are independently associated with LVDD. This association is independent of sex, age, hypertension, and diabetes status and is stronger for severe kidney dysfunction. Early recognition of LVDD in kidney dysfunction might help identify those at highest risk of developing HFpEF.

Table 1: Baseline characteristics. SD: standard deviation; eGFR: estimated glomerular filtration rate; SBP: systolic blood pressure; DBP: diastolic blood pressure.

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>N</th>
<th>Sex, females (%)</th>
<th>Age, mean (SD)</th>
<th>Deceased, (%)</th>
<th>Hypertension (%)</th>
<th>SBP (mean (SD))</th>
<th>DBP (mean (SD))</th>
<th>Diabetes (%)</th>
<th>HbA1c (mean (SD))</th>
<th>eGFR mL/min/1.73m²</th>
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<tr>
<td></td>
<td>6216</td>
<td>2594 (41.7)</td>
<td>66.9 (12.04)</td>
<td>1527 (24.5)</td>
<td>90.4%</td>
<td>130.8 (20.1)</td>
<td>74.21 (11.1)</td>
<td>23.8</td>
<td>44.58 (12.7)</td>
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<tr>
<td>Normal function eGFR &gt;90</td>
<td>(%)</td>
<td>26.4</td>
<td>60–89 (%)</td>
<td></td>
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<td>Mild dysfunction eGFR ≥60–89</td>
<td>(%)</td>
<td>48.3</td>
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<tr>
<td>Moderate dysfunction eGFR ≥30–59</td>
<td>(%)</td>
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<tr>
<td>Severe dysfunction eGFR &lt;30</td>
<td>(%)</td>
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</tbody>
</table>

Table 2: Hazard ratios from cox proportional hazard models. HR: hazard ratio; CI: 95% confidence interval; eGFR: estimated glomerular filtration rate; *multivariable analyses were adjusted for age, diabetes, and hypertension.

<table>
<thead>
<tr>
<th>Hazard ratios from Cox proportional hazard model</th>
<th>E/A &lt;0.75 or &gt;1.8</th>
<th>E/e’ &gt;14</th>
</tr>
</thead>
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<tr>
<td>E/A &lt;0.75 or &gt;1.8</td>
<td>Univariable analysis</td>
<td>Multivariable analysis*</td>
</tr>
<tr>
<td>E/e’ &gt;14</td>
<td>Univariable analysis</td>
<td>Multivariable analysis*</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Normal ≥ 90</td>
<td>1.16</td>
<td>1.08, 1.25</td>
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<tr>
<td>Mild ≥60–89</td>
<td>1.42</td>
<td>1.30, 1.56</td>
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<tr>
<td>Moderate ≥30–59</td>
<td>1.52</td>
<td>1.27, 1.81</td>
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<tr>
<td>Severe &lt;30</td>
<td>1.72</td>
<td>1.49, 2.00</td>
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ALBUMINURIA AND THE RISK OF CANCER: THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

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Background and Aims: Studies investigating the association of chronic kidney disease and cancer have focused on estimated glomerular filtration (eGFR) rather than on albuminuria. The few studies focusing on albuminuria provide results that vary considerably, probably due to a lack of consideration of eGFR, their limited sample sizes, and that different albuminuria measurement techniques were used. This study therefore aimed to investigate the eGFR independent risk of cancer incidence associated with albuminuria measured as ACR as well as by dipstick in a large Swedish population.

Method: We included subjects of the Stockholm Creatinine Measurements (SCREAM) project without a history of cancer, 250,768 subjects with at least 1 urine albumin-creatinine ratio (ACR) test (primary cohort), and 433,850 subjects with at least 1 dipstick albuminuria test (secondary cohort). Albuminuria was quantified as KDIGO albuminuria stages. The primary outcome was overall cancer incidence. Secondary outcomes were site-specific cancer incidence rates. Multivariable Cox proportional hazards regression models were used to calculate hazard ratios (HRs, 95% CIs) crude, and additionally adjusted for confounders including baseline eGFR.

Results: During a median follow-up of 4.3 (IQR, 2.0-8.2) years, 21,901 subjects of the ACR cohort developed de novo cancer. In multivariable analyses, adjusting among others for eGFR, subjects with an ACR of 30–299 mg/g or ≥300 mg/g had a 23% (HR, 1.23; 95% CI, 1.19-1.28) and 40% (HR, 1.40; 95% CI, 1.31-1.50) higher risk of developing cancer, respectively, when compared to subjects with an ACR < 30 mg/g. This graded, independent association was also observed for urinary tract, gastrointestinal tract, lung, and hematological cancer incidence (all P < 0.05). No significant associations of albuminuria with the incidence of melanoma, breast, and prostate cancers were found. Results were similar in the dipstick albuminuria cohort, and were robust in several sensitivity analyses.

Conclusion: Albuminuria was associated with the risk of cancer independent of eGFR. This association was primarily driven by a higher risk of urinary tract, gastrointestinal tract, lung, and hematological cancers.
Method: We compared the performances of the CKD-EPI21 equation and the original creatinine-based eGFR equation assuming non-Black race (CKD-EPI09-NB) in patients >18 years of age with measured GFR ascertained by chromium-51-EDTA plasma clearance at Aarhus University Hospital in Denmark during 2010–2018. We examined bias, accuracy, precision (defined as the interquartile range of the absolute bias), and correct classification of chronic kidney disease (CKD) stages (GFR ≥ 60, 30–59, and <30 ml/min/1.73 m²) using the chromium-51-EDTA clearance as the reference standard. Furthermore, we assessed the performance of the equations in the total cohort while stratifying by CKD stage. We assessed the performance in the total cohort and in cohorts of cancer patients and potential living kidney donors.

Results: In this predominantly White population, the CKD-EPI21 equation performed slightly better than the CKD-EPI09-NB equation, both when examining the total cohort (N = 4,668) and when examining cohorts of cancer patients (N = 3,313) and living kidney donors (N = 239). In the total cohort, the CKD-EPI21 equation demonstrated lower median absolute bias (−0.2 versus −4.4 ml/min/1.73 m²), higher accuracy (72% versus 70%) as well as equal precision (25 versus 25 ml/min/1.73 m²) and correct classification of CKD stages (86% versus 85%) when compared with the CKD-EPI09-NB equation. When we stratified by CKD stage, the CKD-EPI09-NB equation performed slightly better than the CKD-EPI21 equation among patients with a GFR < 60 ml/min/1.73 m².

Conclusion: In a selected cohort of Danish patients with measured GFR, the CKD-EPI21 equation performed slightly better than the CKD-EPI09-NB equation except for patients with a GFR < 60 ml/min/1.73 m².
Conclusion: BP control in the NUTuRE-CKD cohort at baseline was suboptimal when compared to all three major guidelines. Subgroups at highest risk of adverse outcomes demonstrated poorer BP control. Given the importance of BP control in people with CKD, further research into BP management approaches and barriers to achieving optimal control is required. Priority should be given to developing a patient-centred approach to reduce BP more effectively.

#5661
EARLY COMPENSATORY INCREASE IN SINGLE-KIDNEY eGFR AFTER UNILATERAL NEPHRECTOMY IS ASSOCIATED WITH A LOWER LONG-TERM RISK OF eGFR DECLINE
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Background and Aims: The healthy kidney has reserve capacity, allowing for an increase in single-kidney GFR (Δsk-GFR) in the remaining kidney after nephrectomy. We evaluated whether higher Δsk-GFR, as a reflection of renal resilience, is associated with a lower long-term risk of eGFR decline in individuals undergoing unilateral nephrectomy.

Method: We included 1777 participants from the observational SREAM project who underwent radical unilateral nephrectomy in Stockholm during 2006–2021. We calculated the Δsk-GFR using the eGFR (CKD-EPI 2009) at 3 months post-nephrectomy eGFR minus 50% of the pre-nephrectomy eGFR and evaluated its pre-nephrectomy determinants (age, sex, eGFR, comorbidities) with multivariable linear regression. Follow-up started at 3-months post-nephrectomy, and Cox regression was used to explore the association between Δsk-GFR and the subsequent risk of CKD progression (defined as composite of a decline >30% relative to three months post-nephrectomy eGFR or initiation of kidney replacement therapy), adjusting for age, sex and pre-nephrectomy eGFR.

Results: Mean (SD) age was 68 ± 11 years, 40% of patients were female. 92% had a kidney cancer diagnosis and mean (SD) pre-nephrectomy eGFR was 75 ± 19 mL/min/1.73m². Median (IQR) Δsk-GFR was 11 (7–20) mL/min/1.73m². Pre-nephrectomy determinants of Δsk-GFR were age (StB = −0.20, P<0.001) and pre-nephrectomy eGFR (St.B = 0.14, P<0.001). During a median follow-up of 4 years (maximum 15 years), 178 participants developed CKD progression. The group with a Δsk-GFR above the median value (11 mL/min/1.73m²) had a 42% lower risk of CKD progression (adjusted HR: 0.58, 95% CI: 0.42 – 0.80), compared to those with a lower Δsk-GFR (Figure).

Conclusion: A larger compensatory increase in single-kidney eGFR early after unilateral nephrectomy, suggesting better renal resilience, was associated with a lower risk of CKD progression during long-term follow-up. Evaluation of Δsk-GFR could help identify patients at higher risk of progressive kidney function decline.

#6279
ESKD TREATMENTS: A DIFFICULT CHOICE TO ELDERLY PATIENTS?
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Centro Hospitalar de Setúbal, Nefrologia, Setúbal, Portugal

Background and Aims: End stage kidney disease (ESKD) treatment choice may be very difficult mainly for elderly patients. Dialysis can be burdensome for the frail patients, offering more aggressive procedures and less quality of life. Conservative Care (CC) may shorten life in a fit patient. This study aimed to describe our elderly patients’ choices when it comes to CKD treatment options and reflect about them.

Method: We designed a single center retrospective observational, cross-sectional study regarding patients (pts) over 80 years old (yo) who attend the appointment of ESKD treatment modalities between July 2015 and and December 2021, since a Conservative Care Program is available in our hospital.

Results: During these 6,5 years, 113 pts over 80 yo were attended. Mean age was 85 yo (range 80–103). 66% were male and mean charlson comorbidity index (CMI) was 7 (sd ± 1,2). Mean seric creatinine was 3,69 mg/dl (sd 0,99; range 1,8-7,0). Mean estimated glomerular filtration rate was 17,41 (sd ±4,12) and 14,64 (sd ± 7,6) ml/min per 1.73 m² when calculated with BIS1 and CKD-EPI equation, respectively. Two patients were already on a regular program of dialysis. Regarding CKD etiology, 31,9% was from multifactorial origin, 27,4% was from undetermined origin, 10,6% was hypertensive, 8% was diabetic, 6,2% was from chronic pyelonephritis and 9,7% was in the context of cardiorenal syndrome. Regarding treatment options, 54% chose hemodialysis, 38,9% chose conservative care (CC), 2,7% chose peritoneal dialysis and 2,7% refused any treatment. We also observed a significant increase in the CC during these 6.5 years of study. Of those who chose hemodialysis, 22,95% (n = 14) died before starting on a regular program of dialysis, 62,3% (n = 38) actually started on a regular program and 14,75% (n = 9) still maintain follow-up in nephrology appointment. Regarding those who died before starting on dialysis treatment,
the mean time between choosing dialysis and death was 1.36 years (range 115 days to 3.46 years, median 1.36 years), and between starting on a regular program and death was 1.38 years (range 115 days to 4.9 years). The main cause of death was unknown (66%) (by lack of data), followed by infectious cause (26.6%). Considering those who chose CC, 31.8% (n = 14) died before starting the regular follow up, 54.5% (n = 24) are on a regular program of follow up, and 4.5% (n = 2) lately decided for dialysis. Regarding those who died before CC, the mean time between choosing it and death was approximately 1 year (range 29 days to 3.4 years), and between starting on a regular follow up and death was 0.68 years (range 14 days to 1.7 years). We didn’t find any statistical significance between CMI and the ESRD modality chosen (p = 0.709) or the occurrence of death (p = 0.496).

Conclusion: Even considering the poor prognosis and the high mortality rate, the majority of patients over 80 years old still chose dialysis over conservative kidney treatment. In our cohort, there was no survival benefit from those who choose dialysis instead of CC. CC should be offered as an alternative treatment to all the patients who may not benefit from dialysis. It is important to find tools who help us to guide patients in the best suitable choice in regard to ESKD treatments.

C4 - CO-MORBIDITIES (ANAEMIA, CARDIOVASCULAR, CKD-MBD, ETC.)

#6485
UNI-494 LOWERS URINARY B2-MICROGLOBULIN LEVELS IN RATS
Guru Reddy, Pramod Gupta, Atul Khare and Shalabh Gupta

Unicycive Therapeutics, Inc., Los Altos, United States of America

Background and Aims: Mitochondrial dysfunction in renal cells play a critical role in the pathophysiology of acute kidney injury (AKI) and chronic kidney disease (CKD). The proximal tubule is the primary sensor and effector in CKD progression and AKI. The measurement of urine B2-microglobulin (B2M) is a sensitive assay for proximal tubule injury. Nicorandil, a selective mitochondrial ATP-sensitive potassium channel activator, may be a promising AKI treatment, but its clinical use is limited by serious gastrointestinal side effects and rapid absorption and elimination. UNI-494, a novel nicorandil prodrug designed to improve its pharmacologic properties, may increase the short half-life and improve the safety profile of nicorandil. This study presents the efficacy data on the effects of UNI-494 in a rat ischemia-reperfusion (I/R) model, evaluating biomarkers of renal injury.

Method: 49 male Sprague-Dawley rats were randomly assigned to 4 groups to evaluate the in vivo efficacy of UNI-494 in a bilateral renal (I/R) model. Group 1, the Sham group, consisted of 10 subjects while groups 2–4 each had 13. Group 1 received no treatment, Group 2 a vehicle, Group 3 10mg/kg of UNI-494, and Group 4 20mg/kg of UNI-494. Treatments were administered as a single dose on Day 0, 1 hour prior to modeling. Body weights were measured on Days -1, 0, and 1. Urine B2M levels and urinary albumin-to-creatinine ratio (UACR) samples were collected within 24 hours after the surgery using the metabolic cages. Serum blood urea nitrogen (BUN) and creatinine samples were collected on Day -1 (pre-modeling) and 24 hours after modeling. T-tests were used to evaluate statistical differences between groups.

Results: B2M levels were significantly lower for the 20 mg/kg UNI-494 dose group compared to the vehicle group, and B2M content in both UNI-494 dose groups (10 and 20 mg/kg) was significantly lower compared to the vehicle group (Fig. 1). B2M levels and content were lower for the 20 mg/kg UNI-494 dose group than for the 10 mg/kg dose group (Fig. 1). There was no difference in body weight changes between the UNI-494 dose groups and the vehicle group. There were no statistically significant differences among all groups for serum creatinine and BUN pre-modeling and in UACR.

Conclusion: Lower levels of urine B2M levels in the higher UNI-494 dose group compared to the other groups indicate that UNI-494 may have a renoprotective effect. Additionally, the lower levels of B2M in the higher dose group compared to the lower dose group indicate a dose-response trend. Our study results are consistent with previously published data with nicorandil in a similar rat model of I/R. This potential renoprotective effect should be further investigated.
#3325
EXTRARENAL CYP27B1 ACTIVITY CONTRIBUTES TO THE CIRCULATING POOL OF 1,25(OH)2D

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Background and Aims: Alterations of vitamin D metabolism are ubiquitous in patients with chronic kidney disease (CKD) and a key feature of the syndrome of CKD-mineral and bone disorder. A central paradigm in vitamin D metabolism is that the kidneys are the only relevant source of activation of vitamin D for systemic effects. However, various cells and tissues exhibit CYP27B1 activity and are capable of producing 1,25(OH)2D, which could contribute to the circulating pool [1]. This longitudinal, observational study challenges the dogma of the kidneys as the only source of 1,25(OH)2D, by investigating vitamin D metabolites in anephric patients free of active vitamin D therapy.

Method: Anephric patients free of active vitamin D therapy were included at time of kidney transplantation. A subset had a second study visit at 12 months post-transplant. Liquid chromatography–tandem mass spectrometry was used to measure 25(OH)D2/3, 1,25(OH)2D3 and 24,25(OH)2D3. Metabolic ratios of vitamin D metabolites over precursors were used as measures of CYP24A1 (24,25(OH)2D3/25(OH)D3) and CYP27B1 (1,25(OH)2D/25(OH)D3) activity. Biointact PTH (1-84) was measured by an in-house immunoradiometric assay [2] and FGF23 was measured by ELISA (Kainos Laboratories, Tokyo, Japan). Interleukin 6 (IL6), tumor necrosis factor-A (TNF- A) and interferon-γ (IFN-γ) were measured using an electrochemiluminescence multiplex immunoassay (Human Proinflammatory 1 V-plex, MSD, Maryland, US). Two independent laboratories performed confirmatory analyses of 1,25(OH)2D.

Results: All anephric patients (n = 38) had detectable (>2.5 pg/mL) levels of 1,25(OH)2D, with a median value of 13.5 pg/mL (range 3.9 to 35.7 pg/mL). There was a significant correlation between levels of 25(OH)D and 1,25(OH)2D (r = 0.583, p < 0.001), with 25(OH)D levels explaining 34% of the variation in 1,25(OH)2D (Fig. 1). 1,25(OH)2D levels were not significantly correlated to PTH (r = 0.279, p = 0.09) or FGF23 (r = 0.280, p = 0.09), nor to any of the inflammatory markers; IL6 (r = 0.068, p = 0.69), TNF- A (r = −0.264, p = 0.11), IFN-γ (r = −0.001, p = 0.99). To validate our findings, anonymized samples of 17 anephric patients and 17 CKD stage 5D with residual renal function were sent to two independent laboratories. The presence of 1,25(OH)2D was confirmed in all anephric patients. Twenty-five anephric patients underwent a successful kidney transplantation and were free of active vitamin D therapy at a study visit 12 months post-transplant. After kidney transplantation, 25(OH)D-level decreased, while levels of 1,25(OH)2D and 24,25(OH)2D substantially increased. The metabolic ratios expressing CYP24A1 and CYP27B1 activity both increased (Fig. 2). At 12 months post-transplant, 1,25(OH)2D-levels correlated with levels of biointact PTH (r = 0.603, p = 0.002), but not with levels of FGF23 (r = −0.262, p = 0.21).

Conclusion: Extrarenal CYP27B1 activity contributes to the circulating active vitamin D pool and may sustain low-normal levels of active vitamin D, even in anephric individuals. While renal CYP27B1 activity is hormonally regulated, extrarenal CYP27B1 activity seems to be mainly substrate dependent.

REFERENCES

Figure 1: 25-hydroxy vitamin D (25OHD) and 1,25 dihydroxy vitamin D (1,25(OH)2D) levels in 38 anephric patients free of active vitamin D therapy, β = linear regression coefficient.
SAFETY OUTCOMES OF ORAL ANTICOAGULANT THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION AND CHRONIC KIDNEY DISEASE

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Background and Aims: The comorbid conditions of atrial fibrillation (AF) and chronic kidney disease (CKD) leads to an increased risk of thromboembolic complications in AF. But with the deterioration of kidney function, the risk of hemorrhagic complications increases dramatically. This problem makes it difficult to choose an effective and safe oral anticoagulant therapy. Clinical data on the use of new oral anticoagulants (NOACs) in patients with AF and advanced CKD are limited, which determines the relevance of conducting studies in comparison with vitamin K antagonists. The aim of study was evaluation of safety parameters for the using of rivaroxaban in patients with stage 4 CKD with AF.

Method: The study included 109 patients over the age of 18 with a diagnosis of stage 4 CKD (eGFR < 15–29 ml/min/1.72 m²) and non-valvular AF. They were randomized in a 2:1 ratio to either rivaroxaban 15 mg (n = 73) or warfarin (n = 36). The mean follow-up period was 18 months. In the warfarin group, time in therapeutic range (TTR) >70% was achieved in 34 (94%) patients. Exclusion criteria were a history of bleeding that required hospitalization; decrease in hemoglobin level below 80 g/l, platelet count below 100 × 10⁹/l; indications for taking antiplatelet therapy; chronic use of drugs that increase the risk of bleeding. The analysis of the observed hemorrhagic events was carried out using the BARC and ISTH scales. Classification of anemia was carried out according to the recommendations of the World Health Organization.

Results: Patients taking warfarin were significantly more likely to develop minor bleeding according to the BARC scales and ISTH and all clinically significant bleeding on the ISTH scale. In patients with AF and CKD receiving warfarin therapy, minor bleeding (MB) according to the BARC scale was observed in 72.2% (n = 26), minor clinically significant bleeding (MCSB) in 8.33% (n = 3), major bleeding in 8.33% (n = 3) of cases; and in the group of patients treated with rivaroxaban, MB was observed in 42.4% (n = 31, p < 0.01), MCSB in 2.74% (n = 2, p = 0.32), major bleeding in 2.74% (n = 2, p = 0.32) of cases. When assessing bleeding on the ISTH scale during therapy with VKA, MB – 61.1% (n = 22), MCSB – 19.4% (n = 7), major bleeding – 8.33% (n = 3); against the background of NOACs therapy, MB – 36.9% (n = 27, p = 0.01), MCSB in 8.2% (n = 6, p = 0.06), major bleeding in 2.74% (n = 2, p = 0.32). All clinically significant hemorrhagic events according to the BARC scale in the warfarin group occurred more than 16.6% (n = 6) compared with the rivaroxaban group 5.4% (n = 4, p = 0.06); when analyzed according to the ISTH scale, the number of patients receiving VKA anticoagulant therapy 27.7% (n = 10) significantly prevailed over patients on the background of NOACs therapy, MB – 10.9% (n = 8, p = 0.03). Analysis of hemoglobin level did not reveal significant dynamics and significant differences between the groups: the median hemoglobin level at inclusion was 129 g/l in the rivaroxaban group and 123 g/l in the warfarin group (p = 0.3), after 18 months - 130 g/l and 121 g/l, respectively (p = 0.7).

Conclusion: Data suggesting a favorable safety profile for NOACs (rivaroxaban) compared with VKAs (warfarin) in patients with AF and advanced CKD was obtained in this study. Taking rivaroxaban was accompanied by a significantly lower number of hemorrhagic events, which may indicate a safe effect of the drug. No significant changes in hemoglobin levels were found in both groups. Confirmation of these data may be key in choosing an anticoagulant in patients with AF and advanced CKD.

#3896

CYSTATIN C-BASED ESTIMATED GLOMERULAR FILTRATION RATE AND RISK OF STROKE IN THE GENERAL POPULATION

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Background and Aims: Previous results on the association between estimated glomerular filtration rate (eGFR) and strokes are mixed. Most studies derived the eGFR from serum creatinine, which is affected by non-kidney determinants and possibly has biased the association with stroke risks. We hypothesized that eGFR was independently associated with the risk of stroke in the general population.

Method: We performed a population-based prospective cohort study of adults aged 40 years or older in a community-based setting. Participants were recruited from the community health service centers and the community medical centers. The primary outcome was incident stroke, defined as a first-ever non-fatal stroke or fatal stroke. Participants were followed for up to 10 years. The primary exposure was the eGFR, estimated using the Modification of Diet in Renal Disease (MDRD) formula. We used age, sex, smoking status, diabetes, hypertension, and systolic blood pressure in the initial model to adjust for potential confounding variables. We used a multivariable regression model to estimate the association between the eGFR and the risk of stroke.

Results: Among 20,000 participants, there were 1,000 incident strokes. The median eGFR was 90 ml/min/1.73 m². The eGFR was inversely associated with the risk of stroke (p < 0.01). The risk of stroke was 40% lower in the group with the highest eGFR compared with the group with the lowest eGFR (p < 0.01). In the multivariable regression model, the eGFR remained inversely associated with the risk of stroke (p < 0.01).

Conclusion: The eGFR was independently associated with the risk of stroke in the general population. These findings provide further evidence that renal function is a risk factor for stroke.
population. Herein, we investigated the linear and nonlinear associations of the cystatin C-based eGFR (eGFR$_{cys}$) with the risk of total stroke and its subtypes in the UK Biobank participants.

**Method:** In this cohort study, we included 462,307 UK Biobank participants (94.5% Whites, 54% women, aged 56±8 years) free of stroke at enrollment. The eGFR$_{cys}$ and eGFR$_{cr}$ were calculated with serum cystatin C and creatinine, respectively. Outcomes of interest were the incidences of total stroke and subtypes. We investigated the linear and nonlinear associations using Cox proportional hazards models and restricted cubic splines, corrected for regression dilution bias.

**Results:** During averaged follow-up of 10.11 years, 4,427 incident strokes occurred, among which 3,447 were ischemic and 1,163 were hemorrhagic. After adjustment of confounders, the regression dilution-corrected hazard ratios (95% confidence intervals) for every 10 ml/min/1.73 m$^2$ decrement in eGFR$_{cys}$ were 1.10 (1.06-1.12) for total stroke and 1.11 (1.08-1.15) for ischemic stroke. A similar pattern was observed with eGFR$_{cr}$ although the association was weaker. When either eGFR was below 75 ml/min/1.73 m$^2$, the risks of total and ischemic stroke increased exponentially as eGFR decreased. However, when eGFR$_{cys}$ was above 75 ml/min/1.73 m$^2$, the risks did not significantly differ but seemingly decreased as eGFR$_{cys}$ exceeded 105 ml/min/1.73 m$^2$. A U-shape relationship was witnessed if eGFR$_{cr}$ was used instead. There was null association between eGFR and hemorrhagic stroke.

**Conclusion:** The risks of total stroke and ischemic stroke increased exponentially when the eGFR fell below 75 ml/min/1.73 m$^2$. 


Figure 1:
#2528

**APOL1 GENOTYPING AND PROTEINURIC KIDNEY DISEASE IN EUROPE**

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**Background and Aims:** Apolipoprotein L1 (APOL1) toxic gain-of-function variants (G1 or G2) are genetic factors driving a broad spectrum of progressive, proteinuric nephropathies referred to as APOL1-mediated kidney disease (AMKD). APOL1 genotyping is not routinely performed in kidney disease care, and prevalence of APOL1 variants among persons with chronic kidney disease (CKD) in Europe is not well known. These variants are common in persons of recent African ancestry. We report interim data of a global study estimating the prevalence of APOL1 genotypes in participants of recent African ancestry and proteinuric CKD, with a focus on data from Europe.

**Method:** Enrollment in this ongoing study will include up to 2,500 participants across different geographies who are of recent African ancestry and have focal segmental glomerulosclerosis (FSGS) or other proteinuric nondiabetic kidney disease (NDKD). The study includes a single visit during which blood samples are collected from participants to determine their APOL1 genotype using a validated polymerase chain reaction (PCR)-based assay. The percent of participants with two APOL1 variants and percent of participants in each genotype category (e.g., G1/G1, G1/G2, G2/G2) are assessed; genetic counseling services are available to participants, if desired.

**Results:** This interim analysis included 1,256 participants of whom 174 (13.9%) were from Europe. As shown in the table, among the 88 participants with FSGS and 86 participants with proteinuric NDKD, 54 (61.4%) and 32 (37.2%) have two APOL1 variants, respectively.

**Conclusion:** Our study will generate one of the largest global APOL1 genotyping data sets in participants with proteinuric kidney disease. These data begin to address a critical knowledge gap and highlight the importance of APOL1 genotyping in kidney disease care to identify AMKD, potentially optimize disease management, and enable referral for interventional clinical trials evaluating targeted therapies for AMKD.
Baseline Demographics and \textit{APOL1} Genotyping Results

<table>
<thead>
<tr>
<th></th>
<th>\textbf{FSGS} N = 341</th>
<th>\textbf{NDKD} N = 915</th>
<th>\textbf{Total} N = 1256</th>
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<tr>
<td><strong>Age, years, mean (SD)</strong></td>
<td>42.9 (13.3)</td>
<td>51.8 (13.7)</td>
<td>49.4 (14.2)</td>
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<td><strong>Region or country, n (%)</strong></td>
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<td><strong>North America</strong></td>
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<tr>
<td>United States</td>
<td>253 (74.2)</td>
<td>829 (90.6)</td>
<td>1082 (86.1)</td>
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<tr>
<td><strong>Europe</strong></td>
<td></td>
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</tr>
<tr>
<td>United Kingdom</td>
<td>88 (25.8)</td>
<td>86 (9.4)</td>
<td>174 (13.9)</td>
</tr>
<tr>
<td>France</td>
<td>52 (15.2)</td>
<td>51 (5.6)</td>
<td>103 (8.2)</td>
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<td>30 (8.8)</td>
<td>28 (3.1)</td>
<td>58 (4.6)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>6 (1.8)</td>
<td>6 (0.7)</td>
<td>12 (1.0)</td>
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<td><strong>G1/G1, G1/G2, or G2/G2</strong></td>
<td>164 (48.1)</td>
<td>210 (23.0)</td>
<td>374 (29.8)</td>
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<td>\textit{APOL1} genotype, n (%)</td>
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<tr>
<td>G1/G1</td>
<td>82 (24.0)</td>
<td>99 (10.8)</td>
<td>181 (14.4)</td>
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<td>66 (19.4)</td>
<td>91 (9.9)</td>
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<td>G2/G2</td>
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<td>20 (2.2)</td>
<td>36 (2.9)</td>
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<td>\textit{APOL1} genotype by region or country, n (%)$^a$</td>
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<td>178/829 (21.5)</td>
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<td>1/12 (8.3)</td>
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\textit{APOL1:} Apolipoprotein L1; \textit{FSGS:} focal segmental glomerulosclerosis; \textit{IA:} interim analysis; \textit{NDKD:} nondiabetic kidney disease; \textit{SD:} standard deviation

Notes: Eligible participants are at least 12 years of age and of African ancestry or geographic origin (Black, Caribbean, African American, Sub-Saharan African, Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture/origin). For more information about the study, please see https://apol1program.com/. This table includes participants in the Full IA Set with a genotyping result as of 01 Dec 2022. Percentages were calculated based on the number of participants in the Full IA set, unless otherwise specified.

$^a$ Percentages were calculated based on the total number of participants in each region/country per disease state.
(CKD) and cardiovascular (CV) complications based on estimated glomerular filtration rate (eGFR) and urinary albumin:creatinine ratio (UACR). GLP-1-like peptide-1 receptor agonists (GLP-1RAs) are recommended by the KDIGO 2022 Clinical Practice Guidelines for Diabetes and CKD in patients with type 2 diabetes (T2D) and CKD who need better glycemic control or CV risk reduction. In patients with T2D, once-weekly (OW) semaglutide, a GLP-1RA, reduces albuminuria and may preserve eGFR compared with placebo, irrespective of baseline eGFR or UACR. The aim of this analysis was to assess the treatment effects on kidney outcomes of OW semaglutide by KDIGO risk category at baseline compared with placebo.

**Method:** In a post hoc analysis from the SUSTAIN 6 trial (NCT01720446), randomised patients with T2D (N = 3,297) treated with OW semaglutide (0.5 mg and 1.0 mg) or placebo were stratified by baseline KDIGO risk category (low, moderate, high, and very high). The median follow-up time was 2.1 years. The treatment effect on the adjudicated endpoint of time to first new or worsening nephropathy (a composite of macroalbuminuria onset, doubling of serum creatinine and eGFR <45 mL/min/1.73 m², need for kidney replacement therapy, or death due to kidney disease) across KDIGO categories was analysed using Cox regression. Analyses of treatment for eGFR slope and change in UACR (log-transformed) across KDIGO categories were performed using random slope modelling and mixed models adjusted for baseline UACR and UACR (log-transformed) across KDIGO categories were performed using Cox regression. Analyses of treatment for eGFR slope and change in UACR (log-transformed) across KDIGO categories were performed using random slope modelling and mixed models adjusted for baseline UACR and UACR (log-transformed) across KDIGO categories were performed using Cox regression. Analyses of treatment for eGFR slope and change in UACR (log-transformed) across KDIGO categories were performed using random slope modelling and mixed models adjusted for baseline UACR and UACR (log-transformed) across KDIGO categories were performed using Cox regression.

**Results:** Participants with baseline eGFR and UACR values (N = 3,238) were stratified in the low (n = 1,596 [49%]; 60% male; mean 64 years), moderate (n = 831 [26%]; 62% male; mean 65 years), high (n = 445 [14%]; 62% male; mean 66 years) and very high (n = 366 [11%]; 59% male; mean 67 years) KDIGO risk categories. Regardless of treatment group, participants in the moderate-, high- and very high-risk groups were more likely to experience new or worsening nephropathy endpoint vs participants in the low-risk group, as predicted by KDIGO risk category classification. The treatment effect of OW semaglutide vs placebo on risk of new or worsening nephropathy, eGFR slope and change in UACR was consistent across KDIGO risk categories. The ongoing FLOW kidney outcomes trial has a population with T2D and CKD that corresponds to the high- and very high-risk KDIGO categories, and it will provide primary outcome data on potential kidney-protective effects of OW semaglutide; results are anticipated in 2024.

#3664 EVALUATION OF THE INTRODUCTION OF NOVEL POTASSIUM BINDERS IN ROUTINE CARE: THE STOCKHOLM CREATININE MEASUREMENTS (SCREAM) PROJECT

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**Background and Aims:** The pharmacological management of hyperkalemia has traditionally considered sodium polystyrene sulfonate (SPS) and, since late 2018, the novel potassium (K+) binders Patiromer and Sodium Zirconium Cyclosilicate (SZC). This study evaluated their patterns of use, duration of treatment and relative effectiveness in reducing plasma K+ levels in Stockholm’s contemporary routine care.

**Method:** Observational study of all adults who newly-filled a prescription for SPS, Patiromer or SZC during 2019–2021 in Stockholm, Sweden. Sweden offers universal healthcare and covers the cost of prescribed medications. We described patient characteristics of new initiators, including their comorbidities, medication use, eGFR and pre-treatment plasma K+ levels. We then quantified treatment duration by evaluating all subsequent dispensations. Lastly, we
compared their relative efficacy by evaluating post-treatment K+ during the following 60 days through multivariable logistic regression. Because the frequency and pattern of K+ monitoring differed per patient, we considered the K+ test closest to the end of 15-day intervals. Then, we estimated odds ratios and 95% confidence intervals of maintaining normokalemia (K+ < 5.1 and < 5.5 mmol/L) for the novel binders vs SPS.

**Results:** During 2019–2021, 1879 adults started treatment with SPS, and 147 with novel binders (41 with Patiromer and 106 with SZC). The median K+ at initiation for all three treatments was 5.7 mmol/L. Median eGFR was higher among Patiromer initiators (58 mL/min/1.73 m²) than initiators of SZC (31 mL/min/1.73 m²) or SPS (37 mL/min/1.73 m²). Patients on SPS stayed mean 61 days on treatment, and 14% filled three or more consecutive prescriptions suggesting chronic use. Patients on novel binders stayed mean 109 days on treatment, and 49% filled three or more prescriptions (Panel A). After 15 days of treatment, mean plasma K+ similarly decreased to 4.6 (4.3-5.1) and 4.8 (4.5-5.2) mmol/L in patients with SPS and novel binders, respectively, and this level was maintained during the 60 days post-treatment (Panel B). 76% of SPS users reached a potassium value < 5.1 mmol/L at day 15 versus 67% of patients in the novel binder group (between group difference 9%; 95% CI 0.92-2.57; p-value 0.07; Panel C). Furthermore, the proportion of patients with K+ < 5.5 mmol/L at day 15 was 91% for SPS and 85% for novel binders (Panel D). In multivariable logistic regression, the odds ratio for novel binders (vs SPS) in reaching K+ targets (K+ < 5.1 mmol/L) after 15 days was 0.68 (95% CI 0.42-1.17) and 0.78 (95% CI 0.42-1.44) after 30 days.

**Conclusion:** We observe modest use of novel K+ binders in Stockholm's contemporary practice, with longer treatment lengths than SPS. Both SPS and novel binders showed similar efficacy in achieving normal potassium values during the first 15 days of treatment and subsequent 2 months.
The present study aimed to characterize the performance of this feedback controller. 

**Methods:** We conducted a single-arm, prospective, interventional pilot study in subjects on chronic HD at three Avantus Renal Therapy dialysis centers in New York City. Subjects were treated with Fresenius 2008T HD machines. RBV was measured with the CLiC® device. CLiC® and HD machine data were fed into a research laptop running the UFR Feedback Controller software. The UFR recommendations (generated every 10 minutes) were evaluated by dialysis nurses, who then either implemented or disregarded them as they deemed clinically appropriate. The nurses were instructed to only override Controller recommendations if medically indicated, but not in an attempt to manage the subjects’ RBV trajectories themselves. RBV target range attainment with the UFR Feedback Controller was compared to standard of care treatments (data obtained retrospectively) in the same subjects.

**Results:** Fifteen subjects (58.9 ± 15.3 years, dialysis vintage 4.1 ± 2.4 years, baseline interdialytic weight gain 2.6 ± 0.8 L, treatment time 222 ± 28 min) were studied prospectively with the UFR Feedback Controller (63 study visits, 4.2 ± 1.9 visits per subject). Nine subjects contributed at least two complete treatments to each study period (Controller and standard of care, respectively) and were included in this analysis. The probabilities of achieving an RBV within the desired target range for each timepoint, stratified by study period (standard of care versus UFR Feedback Controller), are shown in the Figure. Use of the Controller was associated with a higher rate of RBV target range attainment for every timepoint. We confirmed these results with generalized linear mixed-effects models: Across all RBV target timepoints, use of the Controller was a significant predictor of better RBV target range attainment (P < 0.0001). Use of the UFR Feedback Controller was a significant predictor of better RBV target range attainment for timepoints 60, 90, 120, and 150 minutes, and a borderline significant predictor for timepoints 30 and 180 minutes.

**Conclusion:** Use of this UFR Feedback Controller was associated with a significant and clinically meaningful increase in RBV target range attainment. This technology individualizes the UFR to the patient’s plasma refill kinetics during the HD treatment and may assist clinicians with optimizing fluid management in their patients.

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**#4080**

**NOVEL EXTRACORPOREAL TREATMENT FOR SEVERE NEONATAL JAUNDICE: A MATHEMATICAL MODELING STUDY WITH ALLO-HEMODIALYSIS**

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**Background and Aims:** Neonate hyperbilirubinemia usually resolves within 3–5 days without complications however, severe neonatal jaundice (SNJ) is associated with long-term neurocognitive impairment, cerebral palsy, auditory neuropathy, deafness, or death. Globally, at least 481,000 term/near-term neonates are affected by SNJ annually, with 114,000 neonates dying and an additional 63,000 neonates surviving with kernicterus [1,2]. Phototherapy and exchange transfusions prevent/treat SNJ, but these modalities are scarce in some low and lower-middle income countries, where SNJ prevalence is increased due to higher prevalence of glucose-6-phosphate dehydrogenase deficiency, blood group incompatibilities, late referrals, and delayed diagnosis. We aimed to explore a model for allo-hemodialysis (alloHD), a novel potential modality to treat SNJ rapidly and effectively in neonates, possibly avoiding exchange transfusions.

**Method:** With alloHD, the neonate’s blood flows through hollow fibers of a 0.075 m² miniature low flux hemodialyzer (pore size 1.2 to 2.2 nm), while the blood of a healthy adult (“buddy”) flows counter-currently through the dialyzer, thus serving as the “dialysate”. Our mathematical model simulates the bilirubin kinetics in alloHD, with neonate and buddy blood flow rates at 15 and 30 mL/min, respectively. In the neonate model, bilirubin conjugation was assumed to be zero, resulting in excess unconjugated bilirubin that binds to albumin and causes SNJ. Bilirubin production rate in neonate and buddy were set to 6 and 3 mg/kg/day, respectively [3]. Buddy bilirubin conjugation rate was calculated to obtain normal steady state bilirubin levels.
We only simulated unconjugated bilirubin because the conjugated form is easily excreted. Simulations are performed with neonate and buddy albumin levels of 31 g/L and 43 g/L, respectively.

**Results:** Model simulations suggest that 3- to 6-hour alloHD session can reduce neonatal bilirubin levels by >30% (Fig. 1, left panel). Due to the high bilirubin conjugation capacity of an adult’s healthy liver, the buddy’s bilirubin level increases only transiently during the alloHD session (Fig. 1, right panel).

**Conclusion:** Our modeling suggests that a single alloHD session can lower bilirubin levels to 31 g/L and 43 g/L, respectively. Simulations are performed with neonate and buddy albumin levels effectively. In principle, this bilirubin reduction should lower the risks associated with SNJ, especially kernicterus and possibly avoiding exchange transfusions. Future modeling scenarios will incorporate the improved neonatal liver function over time and additional alloHD schedules.

## REFERENCES


### #3367
**NON-INVASIVE OPTICAL ESTIMATION OF INTRADIALYTIC CONCENTRATIONS OF UREMIC TOXINS IN BLOOD OF HEMODIALYSIS PATIENTS**

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**Background and Aims:** Hemodialysis (HD) adequacy is generally estimated by the dialysis adequacy marker Kt/V urea that poorly describes removal of uremic toxins with different removal kinetics, such as protein bound or middle molecule uremic toxins, which have direct effect on morbidity and mortality of end stage kidney disease (ESKD) patients. We have recently shown the feasibility of estimating an alternative dialysis adequacy marker that can be applied to dialysis sessions with varying settings and different uremic toxins, intradialytic time average concentration (TAC) of uremic toxins, such as urea, uric acid (UA), indoxyl sulfate (IS) and beta-2-microglobulin in blood of ESKD patients, from spent dialysate concentrations determined by laboratory methods [1]. The aim of this retrospective observational study was to estimate intradialytic TAC of uremic toxins UA and IS non-invasively from spent dialysate concentrations determined by optical methods.

**Method:** Twenty-two ESKD patients on chronic HD were enrolled into the study. For each patient 4 midweek dialysis sessions with different treatment settings were included (1 HD: Qb = 200 mL/min, Qd = 300 mL/min, dialyzer 1.5 m²; 3 HDF: median (interquartile range) Qb = 298 (296–356) mL/min, Qd = 795 (500–800) mL/min, Vsubst. = 21.8 (15–24.5) L, dialyzers 1.8 m² and 2.2 m²). During each dialysis session, blood samples were taken at 0 min (start) and 240 min after the start from the arterial blood line and dialysate samples were taken at 7 min and 240 min after the start from the outlet of the dialysis machine. Concentrations of UA and IS in serum and spent dialysate samples were determined with HPLC. In addition, UV absorbance and fluorescence of the spent dialysate samples were measured with spectrophotometer UV-3600 and spectrofluorometer RF-6000 (both from Shimadzu Corp., Japan), after which concentrations of UA and IS in spent dialysate samples were determined based on the optical properties of samples. Stability of HD treatment settings were monitored online and dialysis sessions with unstable blood and dialysate flow rates were excluded. TAC of UA and IS were calculated from serum concentrations and evaluated from laboratory and optically estimated logarithmic mean concentrations (Mln D) of spent dialysate.

**Results:** Mean intradialytic serum TAC values of UA and IS were 198.4 ± 37.8 μmol/L and 69.5 ± 37.8 μmol/L and strongly correlated to those estimated from optically determined Mln D 198.0 ± 38.9 μmol/L (R² = 0.75) and 69.5 ± 37.8 μmol/L (R² = 0.81), respectively. Mln D of UA and IS in spent dialysate based on laboratory methods were 102.2 ± 22.8 μmol/L and 5.9 ± 3.5 μmol/L and strongly correlated with the optically determined concentrations of 102.7 ± 23.1 μmol/L (R² = 0.97) and 6.1 ± 3.4 μmol/L (R² = 0.97), respectively.

**Conclusion:** Intradialytic serum TAC of UA and IS can be estimated non-invasively with optical methods from their concentration in spent dialysate independent of treatment modality. Optical online monitoring of spent dialysate in real-time could therefore provide additional information about treatment adequacy regarding the removal of uremic toxins’ other than urea. In future, TAC estimation models should be optimized for each uremic toxin to establish higher accuracy, considering real-time treatment settings, recirculation etc.

## REFERENCE

TEMPORAL CHANGES IN PLASMA ENDOTHELIN-1 AND BLOOD PRESSURE DURING MAINTENANCE HAEMODIALYSIS

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Background and Aims: Endothelin-1 (ET-1) is a potent endothelium-derived vasoconstrictor that plays an important role in the regulation of arterial blood pressure (BP). Elevated levels of plasma ET-1 have been reported in patients with end-stage renal disease (compared with controls), patients on dialysis (compared with non-dialyzed uremic patients), and patients on haemodialysis (compared with peritoneal dialysis). It has been suggested that ET-1 plays a role in BP response to HD; however, the temporal association of changes in ET-1 with changes in BP during the course of an HD session has not been well defined. Moreover, conflicting results have been reported as to the patterns of intradialytic ET-1 changes, with different studies reporting either a decrease, an increase, or no change in ET-1 during HD. The aim of this study was to investigate temporal changes in ET-1 in patients with different intradialytic BP profiles.

Methods: Data was obtained from a prospective cohort study of 50 maintenance, thrice-weekly HD patients admitted to Brigham and Women’s Hospital in Boston, MA, USA. BP was measured before, after, and every 15 min during dialysis using a calibrated ambulatory BP cuff. Blood samples were drawn before dialysis, at 30, 60, and 120 min into HD, and at the end of treatment. Following the exclusion of cases with missing data, shorter dialysis sessions, or very low pre-dialysis BP (below 85/55 mmHg), 42 patients were included in the analysis (17 females, median age 62 years, over 90% diagnosed with hypertension). One HD session was studied in each patient (median ultrafiltration 2.05 L, median duration 232 min). The patients were divided into three subgroups with different patterns of intradialytic systolic blood pressure (SBP): 1) patients with intradialytic hypotension (IDH) defined as: a) drop of...
SBP to or below 90 mmHg; or b) drop in SBP by at least 30 mmHg associated with at least two hypotension-related symptoms; or c) drop in SBP associated with multiple symptoms requiring intervention; 2) normotensive patients (NT) defined as patients in whom SBP remained between 90 and 130 mmHg for most of the HD session; 3) hypertensive patients (HT) defined as patients in whom the median intradialytic SBP was above 140 mmHg.

Results: 9 hypertensive patients (HT), 24 IDH patients, and 9 normotensive patients (NT) were identified. In the IDH group, at the end of HD, the median drop in SBP (from the pre-HD level) was 28 mmHg (25th – 75th percentile 10–45 mmHg). In HT and NT patients, SBP did not change significantly during HD. IDH patients had lower baseline ET-1 (2.2 pg/mL) compared with HT patients (3.4 pg/mL, P = 0.006) but similar compared with NT patients (2.3 pg/mL). ET-1 decreased over the course of dialysis in HT patients (P = 0.02) and NT patients (P = 0.008), whereas no change was observed in IDH patients (P = 0.30). At the end of HD, IDH patients had a similar ET-1 level (2.4 pg/mL) compared with HT patients (2.6 pg/mL) but higher compared with NT patients (1.4 pg/mL, P = 0.004). A moderate negative correlation was found between the dialysis-associated changes in ET-1 and SBP (r = -0.43, P = 0.005) as well as between the baseline ET-1 and baseline SBP in IDH patients (r = -0.42, P = 0.04).

Conclusions: HD patients may present various patterns of ET-1 changes during HD, which seem to be associated with BP response to HD. In particular, the patterns of ET-1 response to HD may vary among patients categorized as ‘hypertensive’ (the vast majority of patients in our study), who previously were observed to have an intradialytic increase in ET-1. Our results provide a possible explanation as to why previous studies that did not consider intradialytic BP patterns have yielded conflicting results regarding the direction of ET-1 changes during HD.

Results: At two weeks, survival and graft patency were 100%. Explant cellularity and collagen content were not significantly different between sham and CKD rats and were not influenced by SDF-1α. Endothelial cell coverage (RECA +) and smooth muscle cell presence (αSMA +) were visually similar irrespective of disease or bio-functionalization. Elastin+ (p = 0.11), pan-(CD68+, p = 0.08) and anti-inflammatory macrophage (CD163+, p = 0.52) surface area, as well as (anti)-inflammatory gene expression were not significantly different between groups. The twelve-week CKD-group was taken out of experiment prematurely due to rapid disease progression. In addition, preliminary death due to vascular rupture occurred in four animals (n = 2 pristine and n = 2 SDF-1α) in the twelve-week sham animals. While patent, all remaining sham explants at twelve weeks (n = 9) showed severe vascular dilatation and calcifications (von Kossa+). No differences in inflammatory and neo-tissue markers were found between twelve-week sham pristine and SDF-1α grafts or between explants over time.

Conclusion: CKD did not significantly alter inflammation or tissue formation of in situ tissue engineered vascular grafts. Additionally, SDF-1α bio-functionalization did not significantly alter cell engraftment or tissue formation. Mechanical stability of the graft appears to be the primary driver of neo-tissue formation. Future emphasis on in vitro to in vivo translation should be on the fine balance between tissue formation on one hand and fiber resorption on the other hand.

#4216 FEASIBILITY ANALYSIS OF AN ULTRASOUND-GUIDED PLACEMENT OF TUNNELED HEMODIALYSIS CATHETERS

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Background and Aims: Radiographic fluoroscopy (RAD) is the current standard for placement of tunneled central venous catheters (CVC) for hemodialysis. RAD requires structural and personnel infrastructure and exposes the patient to ionizing radiation. Here, we investigate the feasibility of solely ultrasound-guided placement of tunneled central venous dialysis catheters.

Method: We evaluated prospectively collected single center data of 134 consecutive patients who underwent CVC implantation between 2020 and 2021 regarding feasibility, safety, and catheter function. We used the inset guidewire to visualize the position of the catheter tip. In the case of inadequate visibility by ultrasound, we additionally used intracardiac ECG recording or agitated saline. A total of 1844 catheter days were assessed. As a historical control, we analyzed the position of 50 CVCs placed by RAD. Optimal CVC position was defined to be in between the cavalatrial junction (CAJ) and the right atrium (RA), according to the guidelines.

Results: The catheters were placed on the right side in 117 (87%) cases. The primary success rate for optimal position and function was 97.7% (n = 131). Placement solely by ultrasound was possible in 130 (97%) cases. There were no immediate procedure-associated complications related to the new technique. Effective blood flow averaged 292 ± 39 ml/min. Of all ultrasound-placed catheters, 6% were in the vena cava superior (RAD 24%), 70% in the CAJ (RAD 60%), and 24% in the RA (RAD 16%), resulting in a rate of 94% with optimal position.

Conclusion: Placement of CVCs for hemodialysis solely by ultrasound is an effective and safe alternative to fluoroscopy-assisted placement.
A COHORT OF DIALYSIS PATIENTS WITH LOW PREVALENCE OF UPPER ARM FISTULAS
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Background and Aims: International guidelines encourage the use of distal native fistula (AVF) which is the best first-line vascular access (VA). But, despite these indications, all over the world, except for Japan, the prevalence of upper arm fistula (UAF) is dramatically increasing. Previous surveys in our department included about 50% of Haemodialysis patients (HP) and showed prevalence of UAFs less than 5%—very low, if compared with those of our country, reported by DOPPS 5 study. We decided to analyse 100% of HP in our department, in order to confirm or exclude the low prevalence of UAF.

Method: Puglia, southern east of Italy, has 1.4 millions inhabitants, of which 1365 need dialysis; 1295 on haemodialysis in 17 different centers and 70 on peritoneal dialysis. The department is organized on a Hub and Spoke model for VA management (Fig. 1). Hub performs simple and complex AVFs, Graft, PTA of non matured or stenotic fistulas, PTA of central stenosis, and surgical rescue of thrombosed or stenotic fistulas. Our four spokes perform mainly simple distal forearm fistula (DFF). In December 2021 we collected datas of VA prevalence of all 1295 HP. The AVFs were classified, according to their anatomical site, in DFF, mean-proximal forearm fistula (MPFF) and UAF.

Results: The average age of 1295 HP was 69 ± 14.65 yo (65% males and 21% diabetics) and 458 of them (35%) where more than 75 yo. The prevalence of DFF, MPFF, UAF, GRAFT and CVC was 63.5%, 10.1%, 3%, 0.7%, 22.5% respectively (fig. 2). Patients aged ≥75 years, women and diabetics showed a higher prevalence of CVC and a lower prevalence of DFF.

Conclusion: Data collected on all patients confirm the low prevalence of UAF detected in the previous surveys— which involved only a part of haemodialysis patients. Zero upper arm fistulas is an utopian goal, but it seems possible to reduce the prevalence of proximal fistulas to 5% or less as the Japanese experience has showed.
TAUROLIDINE HAVE A SIMILAR INFLAMMATORY PROFILE TO PATIENTS ON HD WITH CENTRAL CATHETERS LOCKED WITH TAUROLIDINE-CITRATE (CVC-Hep).

Table 1: Inflammatory profile of patients with AVF and CVC according to a heparin-containing catheter lock solution with (CVC-TCH) and without taurolidine-citrate (CVC-Hep).

<table>
<thead>
<tr>
<th></th>
<th>AVF (N = 24)</th>
<th>CVC-Hep (N = 29)</th>
<th>CVC-TCH (N = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-TNFa</td>
<td>2.9</td>
<td>2.1-3.9</td>
<td>6.5*</td>
</tr>
<tr>
<td></td>
<td>4.1-8.0</td>
<td>2.9**</td>
<td>1.9-6.8</td>
</tr>
<tr>
<td>S-IL6</td>
<td>2.7</td>
<td>2.2-3.0</td>
<td>7.4*</td>
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<tr>
<td></td>
<td>4.7-8.9</td>
<td>2.8**</td>
<td>2.1-4.0</td>
</tr>
<tr>
<td>S-CRP</td>
<td>2.4</td>
<td>1.8-3.8</td>
<td>5.0*</td>
</tr>
<tr>
<td></td>
<td>3.1-9.4</td>
<td>3.8**</td>
<td>2.7-5.1</td>
</tr>
<tr>
<td>ExpTNF</td>
<td>1.3</td>
<td>0.8-1.5</td>
<td>2.0*</td>
</tr>
<tr>
<td></td>
<td>1.7-2.8</td>
<td>1.5**</td>
<td>1.2-1.9</td>
</tr>
<tr>
<td>ExpIL6</td>
<td>1.5</td>
<td>0.9-1.8</td>
<td>2.2*</td>
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<tr>
<td></td>
<td>1.6-3.0</td>
<td>1.7**</td>
<td>1.3-2.0</td>
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</tbody>
</table>

- P < 0.01 vs AVF; **Not significant vs AVF.

Conclusion: In patients under HD with cuffed tunneled CVC, the use of TCH lock solution after each HD session is associated with a significant gene expression level of IL-6 and TNF-alpha. After 3 months, gene expression levels of subjects with AVF compared to baseline, whereas in subjects with CVC-lock solution after each HD session is associated with IL-6 and TNF-alpha in peripheral blood mononuclear cells (PBMC) were measured at inclusion and after three months follow-up.

Results: Altogether eighty-five subjects (42 males and 43 females; mean age 61 ± 9 yrs; 39% diabetics) were initially included in the study. In 25 subjects the vascular access was AVF, while the rest used tunneled CVC; of these 31 used standard CVC-Hep and 29 used CVC-TCH. Five patients dropped out the study and thus 80 patients completed the 3-month follow-up and were finally evaluated. Inclusion, patients with CVC had significantly higher serum and expression levels of inflammatory markers compared to subjects with AVF.

Conclusion: In patients under HD with cuffed tunneled CVC, the use of TCH lock solution after each HD session is associated with a significant improvement in the inflammatory serum and gene expression state. Thus, the inflammatory profile of patients with CVC using TCH does not differ from that of patients with native AVF after at least three months of CVC-TCH use.

Abstracts
SAFETY AND EFFICACY OF VIRTUAL OUTPATIENT NEPHROLOGY CONSULTATION IN THE NORTHERN ALBERTA RENAL PROGRAM

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Background and Aims: There is a growing awareness among Canadian health care providers of the need to incorporate virtual consultations safely and effectively post pandemic. With the onset of the Covid-19 pandemic in March 2020, outpatient consultation in Northern Alberta Renal Program (NARP) was rapidly transitioned to virtual delivery (telephone or videoconferencing) in place of face-to-face visits. To scale up and sustain virtual consultation in kidney care programs, its safety and effectiveness in improving processes of care (reduced wait time and access to care) and patient-related outcomes must be established. Data establishing safety and effectiveness of virtual consultation in kidney care has been limited. We therefore aimed to evaluate the safety and effectiveness of virtual consultation in patients with advanced CKD or peritoneal dialysis (PD) being cared for in NARP.

Method: The study was conducted in NARP (one of the largest kidney care programs in Canada). The study populations comprised two categories of patients with kidney disease: 1) CKD (non-dialytic) being followed in the ambulatory care clinics and 2) chronic PD patients being followed up in a dedicated home dialysis clinic at 3-monthly intervals. Data were collected over two-time points, pre and post implementation of virtual kidney following the COVID-19 pandemic: March 2019-February 2020 (pre-implementation), and March 2020-February 2021 (post implementation). We were only allowed to collate data on the processes of care outcomes for CKD (clinic cancellations/no-shows, wait times to see a nephrologist from the point of referral and number of visits), and adverse clinical outcomes (peritonitis rates, all-cause hospitalizations, technique failure, defined as PD failure with transition to hemodialysis) for the patients on PD. Summary statistics and tests of associations applied as appropriate. Interrupted time series analyses were used to evaluate trends. All analyses were conducted using (STATA 15 software (Stata Corporation, 2017). The study was approved by the University of Alberta Research Ethics Board.

Results: In patients on PD, the studied outcome measures were not significantly impacted (no changes in the trend) pre and post virtual care implementation (Figs 1a-c). The absolute number of clinic visits in patients on PD did not change (data not shown). In the patients with CKD, there were significant reductions in the rate of clinic cancellations/no-show rates (Fig. 2a), and a reduction in wait time (by a median of two weeks) following virtual care implementation (Fig. 2b). The rates of clinic visits pre and post implementation did not change (Fig. 2c).

Conclusion: The implementation of virtual consultation with the onset of COVID-19 pandemic (and the attendant reduction in face-to-face contacts with patients) did not negatively impact the care of patients on PD regarding risk for adverse clinical outcomes (peritonitis rates, all-cause hospitalizations, and technique failure). In patients with CKD, implementation of virtual care
Figure 1c: All-cause hospitalization rates in peritoneal dialysis pre-and post-implementation of virtual care. (p = 0.52).

Figure 2a: Cancellation/ no-show rates in the patients with CKD pre-and post-implementation of virtual care. (P < 0.001).

Figure 2b: Changes in wait time to see a nephrologist for patients with CKD pre-and post-virtual care implementation. (P < 0.001).

Figure 2c: Nephrology visits by patients with CKD pre-and-post implementation of virtual care.

has led to significant improvements in the processes of care (reduction in wait times and enhanced access to care). These findings have implications in the design of sustainable virtual care programs for delivery of specialized kidney care in both dialysis and non-dialytic CKD in Canada and beyond.
#3637
ROLE OF CONTINUOUS GLUCOSE MONITORING OF BLOOD GLUCOSE CONTROL IN PATIENTS WITH DIABETES UNDERGOING HEMODIALYSIS: A PILOT STUDY

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Background and Aims: End-stage kidney disease (ESKD) is a global health problem, with a steep increase in its prevalence. Diabetes is a major cause and common comorbidity in patients with ESKD. As already known, glycemic control is an important factor in preventing micro- and macrovascular complications in diabetes. Besides, glycemic variability has recently been considered an important factor in the treatment of diabetes. However, both hypoglycemia and hyperglycemia can frequently occur in patients with diabetes undergoing hemodialysis. This study aimed to determine the role of continuous glucose monitoring (CGM) for glycemic control and glycemic variability stabilization in patients with diabetes undergoing hemodialysis.

Method: Eighteen patients aged ≥18 years with type 1 or 2 diabetes and ≥3 months on hemodialysis at the Eulji Medical Center, Daejeon, Republic of Korea between November 2021 and May 2022 were included. Patients underwent 7-day CGM twice: the baseline study period (T0) and the follow-up study period (T1), at a 12-week interval. Physicians modified the treatment strategy according to the T0 results, and then patients conducted T1. iPro2 CGM (MMT-7745) and Enlite glucose sensors MMT-7008A (Medtronic Minimed, Northridge, CA, USA) were used to assess glycemic control. As indicators of glycemic control, the mean glucose levels and glycated hemoglobin A1c (HbA1c) were measured. As indicators of glycemic variability, standard deviation (SD) and % coefficient variation (%CV) were measured.

Results: Data from 18 patients were analyzed. The mean age was 62.0 ± 11.2 years, male/female ratio was 13 (72.2%) / 5 (27.8%). The mean dialysis duration was 5.2 ± 3.5 years. Among the 18 patients, only one had type 1 diabetes, and the mean diabetes duration was 22.9 ± 7.0 years. The mean glucose levels decreased from 179.1 ± 42.3 mg/dL during T0 to 153.2 ± 25.6 mg/dL during T1 (P = 0.001). HbA1c decreased from 7.4 ± 1.3% during T0 to 6.9 ± 1.2% during T1 (P = 0.023). SD improved from 55.7 ± 19.8 mg/dL during T0 to 42.6 ± 15.3 mg/dL during T1 (P = 0.001). %CV improved from 30.5 ± 7.3% during T0 to 25.5 ± 5.5% during T1 (P < 0.001). During T0, the mean glucose level was significantly lower on a day with hemodialysis than on a day without (P ≤ 0.05), and SD and %CV were significantly higher on a day with hemodialysis than on a day without (P ≤ 0.05). After the physicians modified the treatment according to the T0 results, the mean blood glucose levels decreased on both the hemodialysis-on and hemodialysis-off days, as compared to those values during T0 (from 174.7 ± 46.5 to 154.6 ± 29.7 mg/dL, and from 184.7 ± 50.5 to 156.3 ± 28.7 mg/dL, respectively), and consequently there were no statistically significant differences between the hemodialysis-on and hemodialysis-off days.

Figure 1: Changes in glycemic markers and continuous glucose monitoring (CGM) metrics.

Figure 2: Changes in continuous monitoring (CGM) metrics on days with or without hemodialysis session.
during T1 (P = 0.638). SD improved on both the hemodialysis-on and hemodialysis-off days compared to those values during T0 (from 46.9±21.5 to 33.2±14.6, and from 39.5±20.6 to 32.3±13.3, respectively), and consequently, there were no statistically significant differences between the hemodialysis-on and hemodialysis-off days during T1 (P = 0.384). %CV improved from 27.8±10.9 on the hemodialysis-on day during T0 to 21.4±9.2 on that during T1, and there was no statistically significant difference between the hemodialysis-on and hemodialysis-off days during T1 (P = 0.166).

Conclusion: CGM could be a promising tool for individualizing treatment strategies in patients with diabetes undergoing hemodialysis.

#2819

**BIOELECTRICAL IMPEDANCE PARAMETERS AS EARLIER PREDICTORS OF FRAILTY AND FUNCTIONAL IMPAIRMENT IN ECUADORIAN HEMODIALYSIS PATIENTS**

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1Clínica de los Riñones MENYDIAL, Medical, Quito, Ecuador, 2Clínica de los Riñones MENYDIAL, Nutrition, Quito, Ecuador and 3Clínica de los Riñones MENYDIAL, Statistic, Quito, Ecuador

**Background and Aims:** Functional impairment (FI) and frailty are highly prevalent in hemodialysis (HD) population and are associated with morbidity/mortality. Bioelectrical impedance analysis (BIA) is a non-invasive test to assess body composition and water distribution. Few is known about BIA parameters as predictors of frailty and FI. The aim of the study was to study BIA parameters associated with frailty and FI and to determine their prevalence among Ecuadorian adult patients on HD.

**Method:** Observational-prospective-cohort study performed between January/2021 and October/2022 in one HD center. Clinical Frailty Scale (CFS) score ≥4 determined frailty diagnosis, and FI was labeled with Barthel Index (BI) <70. ROC curves were performed to determine the best cut-off for Phase Angle (PA) and Extracellular/Intracellular water ratio (E/I ratio) to predict frailty and FI (Fig. A). Pearson’s correlation coefficient between PA and E/I ratio with CFS score and FI were calculated (Fig. B), and univariate logistic regression analysis was performed.

**Results:** A total of 115 patients were included. Baseline characteristics, findings and variables with statistical significance are resumed in Table 1. The AUC of PA to predict non-frailty patients and non-functional impaired patients was 0.87 (p<0.001) and 0.79 (p<0.001), which corresponds to PA values of ≥4.35° and ≥3.62°, respectively. The AUC for E/I ratio to predict frailty and FI was 0.83 (p<0.0001) and 0.74 (p<0.0001), which corresponds to E/I ratio values of ≥0.97 and ≥0.99 respectively. Moderate-to-strong-negative correlation was found between PA and CFS score (r = −0.61, p<0.0001) as well as moderate-positive correlation between PA and BI (r = 0.47, p<0.0001) was found. Moderate-positive correlation between E/I ratio and CFS score (r = −0.56, p<0.0001) and moderate-negative correlation between E/I ratio with BI (r = −0.45, p<0.0001) were found. Univariate logistic regression analysis revealed that factors independently associated with frailty were age (OR = 1.04, CI-95%:1.02-1.06) and PA (≥4.35°) (OR = 0.17, CI-95%:0.11-0.24).

**Conclusion:** PA and E/I ratio obtained in a single non-invasive BIA can be used as screening tool, with sensitivity >80%, for earlier prediction of FI and frailty in HD patients allowing premature identification and intervention in this group of patients.

Figure A: ROC curves of Phase Angle and E/I ratio for frailty and functional impairment diagnosis.

Figure B: Correlation between Phase Angle value and clinical frailty scale score.
Limited Pharmaceutical Literacy in Patients on Hemodialysis in the Netherlands as Assessed with the Ralph Interview Guide

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Background and Aims: Patients with advanced chronic kidney disease typically use 15 or more different drugs. Proper use of these drugs requires sufficient pharmaceutical literacy, which is defined as health literacy in the context of medication use. Until now, no data are available on the prevalence of limited pharmaceutical literacy in patients with CKD or on hemodialysis. Recently, the Ralph (Recognizing and Addressing Limited Pharmaceutical Literacy) interview guide was developed in the Netherlands to assess pharmaceutical literacy skills. The current study aims to provide data on the prevalence of limited pharmaceutical literacy, associated problems, and the domains in which these problems occur, in hemodialysis patients using phosphate-binding drugs in the Netherlands.

Method: This study was part of a prospective observational study in a teaching hospital in Rotterdam, investigating a complex adherence-improving intervention in hemodialysis patients using phosphate-binding drugs. One of the aims of the original study was to explore pharmaceutical literacy at baseline, using the RALPH interview guide. The RALPH consists of eleven multiple-choice questions and several open-ended questions in three health literacy domains. The functional domain assesses the basic skills of reading, writing, and calculating. The communicative domain assesses more advanced skills, namely finding and understanding information and applying this information to the own situation. The critical domain assesses the even more advanced skills of critically analyzing information and applying this information to different situations. Limited pharmaceutical literacy was defined as the presence of at least one problem in one or more of the domains of the RALPH. The primary outcome was the prevalence of limited pharmaceutical literacy. Secondary outcomes were the prevalence of one or more problems in the domains. Data were analyzed using descriptive statistics (SPSS version 28.0).

Results: A total of 63 patients were included in the study. Mean age was 66 years, 65% were male. The main primary renal diagnoses were hypertensive nephropathy (31%) and diabetic nephropathy (19.1%). Seventy-three percent of patients received their drugs in a weekly drug dispensing system. The prevalence of limited pharmaceutical literacy was 79%. Fifty-two percent of patients had at least one problem in the communicative domain, 46% in the functional domain, and 78% in the critical domain. Around 90% of patients could correctly reproduce user instructions for phosphate-binding drugs. The most prevalent problems were lack of knowledge about the indication (40%) in the functional domain and finding understandable information (51%) in the communicative domain. In the critical domain, the most frequently encountered problems were a lack of adequate judgment of both reliability and applicability of information (62% and 65%, respectively). Almost half of the patients did not search for information. Furthermore, 32% of patients did not engage in shared-decision making or found this difficult to do. Reasons for this were a profound trust in the nephrologist and the patient’s conviction that the nephrologist knew what was best.

Conclusion: Limited pharmaceutical literacy is frequent in patients on hemodialysis: the majority of patients have problems with finding understandable information and judging its applicability and reliability. Judging its applicability and reliability. The results of this study are in line with earlier findings studying pharmaceutical literacy in Dutch community pharmacies in the Netherlands. However, the current study found slightly higher percentages for problems with finding understandable information and judging the applicability of information. This was expected, as our population generally uses more drugs and has a more vulnerable health status. Recent data show that limited health literacy in general negatively affects certain aspects of self-management, such as adherence, communication, and knowledge. This is also apparent in our study. These data together underline the need for dialysis healthcare providers to individualize their communication and support to meet their patients’ needs.

#3648

Individualized Anemia Therapy Improves Hemoglobin Outcomes and Decreases Epoetin Beta Drug Exposure in Hemodialysis Patients

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1Fresenius Medical Care, Global Medical Office, Computational Medicine, Bad Homburg, Germany, 2Renal Research Institute, New York, United States of America and 3Icahn School of Medicine at Mount Sinai, New York, United States of America

Background and Aims: Anemia is a common complication in hemodialysis (HD) patients. Its treatment with erythropoiesis-stimulating agents (ESAs) is challenging due to a nonlinear dose-response relationship and time delays between ESA administration and hemoglobin (Hgb) response. Anemia treatment protocols are frequently used in clinical settings. However, high variability of patient-specific disease characteristics complicate attainment and maintenance of desired Hgb levels. We developed a novel fully personalized ESA dose recommendation tool and present clinical results of a multi-center, randomized controlled trial (RCT) using this software.

Method: We conducted an RCT in adult HD patients in six dialysis facilities in the US. Patients were randomized 1:1 and treated with our personalized ESA dose recommendation tool for twenty-six weeks (intervention group) or continued to be treated using an anemol protocol that was used as part of this study.
of standard of care in those clinics (control group). The recommendation tool utilized a physiology-based model of anemia to estimate patient-specific physiological key characteristics, such as red blood cell lifespan, to create a patient-individual model from recent routine clinical data (gender, height, weight, Hgb measurements, and ESA treatment). These key characteristics and model-based outcome predictions were used to generate patient-specific ESA dose recommendations to stabilize Hgb levels in a target window of 10–11 g/dL. Dose recommendations were disseminated to the anemia managers of patients enrolled in the study for evaluation and further decision-making (Figure 1). This procedure was repeated biweekly with updated clinical data.

**Results:** Ninety-six patients were enrolled in the RCT. Patients were included in the statistical analysis when they remained in the clinical study for at least 30 days (n = 45 control group, n = 46 intervention group). We evaluated outcome measures showing efficacy and efficiency of the treatment in achieving target Hgb levels. Hgb-related outcomes were significantly different between the two study groups, with an improved Hgb control in the intervention arm, manifesting in a reduction of the Hgb distance to target by more than 30%. Epoetin-beta utilization in the intervention group was decreased by over 20%, while iron-related parameters showed no difference between the two arms (Table 1). Acceptance rate of dose recommendations was high; roughly 95% of the recommendations were accepted and implemented by the clinical staff.

**Conclusion:** A therapy software for personalized anemia management was developed for use with epoetin beta. The model-based ESA dose recommendation tool was evaluated in a clinical RCT in HD patients. Hgb control improved significantly in the group using the novel software tool, while ESA usage decreased, thus providing more efficient anemia management for the individual patient while reducing epoetin-beta drug exposure.

**Figure 1:** Schematic of the framework to determine individualized dosing recommendations.

**Table 1:** Primary and secondary outcomes and iron related parameters. Clinical variables are reported as Median (Q1, Q3). Wilcoxon rank sum tests were performed to compare distributions between the two groups (*** p < 0.001, ** p < 0.01, * p < 0.05, n.s. p > 0.05).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention, n = 46</th>
<th>Control, n = 45</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary &amp; secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hgb distance to target, g/dL</td>
<td>0.28 (0.18, 0.41)</td>
<td>0.42 (0.29, 0.67)</td>
<td>0.0005 (***)</td>
</tr>
<tr>
<td>Hgb in target, %</td>
<td>47.3 (38.5, 57.6)</td>
<td>47.5 (38.6, 46.2)</td>
<td>0.008 (**)</td>
</tr>
<tr>
<td>Mean Hgb, g/dL</td>
<td>10.4 (10.2, 10.7)</td>
<td>10.7 (10.3, 11.1)</td>
<td>0.03 (*)</td>
</tr>
<tr>
<td>Epoetin beta dose, mcg/30 days/kg</td>
<td>1.11 (0.63, 1.5)</td>
<td>1.45 (0.89, 1.97)</td>
<td>0.03 (*)</td>
</tr>
<tr>
<td><strong>Iron related parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron dose, mg/30 days</td>
<td>165 (60, 231)</td>
<td>148 (82, 231)</td>
<td>0.9 (n.s.)</td>
</tr>
<tr>
<td>Ferritin concentration, ng/ml</td>
<td>850 (567, 1053)</td>
<td>765 (608, 1249)</td>
<td>0.5 (n.s.)</td>
</tr>
<tr>
<td>TSAT, %</td>
<td>29.3 (25, 39)</td>
<td>33 (27.7, 45.1)</td>
<td>0.1 (n.s.)</td>
</tr>
</tbody>
</table>
Figure 1: Changes in nutritional parameters from baseline (cohort 1).

\[^a\]P < 0.001 vs. non-PTX group at baseline; \[^b\]P < 0.001 vs. baseline value of the same group. P-value in the graph represents between group changes over the study period.

Figure 2: Comparisons of nutritional parameters at baseline and follow-up (Cohort 2).
EFFICACY OF SACUBITRIL/VALSARTAN IN MAINTENANCE HEMODIALYSIS PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Background and Aims: Growing evidences have confirmed the effect of Sacubitril/Valsartan (SV) on hypertension and heart failure espacially EFHF in general population. However, data on ARNI treatment in maintenance hemodialysis (MHD) patients with EFHF are lacking. The present study was conducted to assess the efficacy and safety of sacubitril-valsartan in patients with HFpEF undergoing MHD.

Method: End-stage kidney disease (ESKD) patients undergoing MHD for more than 3 months with New York Heart Association (NYHA) class II–IV heart failure ejection fraction of 50% or higher, and elevated levels of N-terminal pro–B-type natriuretic peptide (NT-proBNP) were assigned to receive sacubitril-valsartan. Patients were followed up regularly after medication treatment. The alterations in clinical and biochemical parameters before and after taking sacubitril-valsartan (generally 50–200mg b.i.d) were investigated, and safety was also assessed.

Results: 120 patients were recruited in this study. Compared with baseline levels, NT-proBNP levels [7540.5 (3575.7–18373.0) vs. 4649.0 (2259.0–8187.0), P<0.001], systolic blood pressure [(157.8 ± 20.5) vs. (141.5 ± 16.8), P<0.001], diastolic blood pressure [(85.2 ± 14.9) vs. (78.5 ± 10.2), P<0.001], heart rate[(78.1 ± 9.0) vs. (74.5 ± 6.9), P<0.001], total cholesterol [4.7 ± 1.1 vs. 3.9 ± 1.3, P = 0.01] and Low Density Lipoprotein [2.4 ± 0.9 vs. 2.2 ± 1.1, P = 0.04] were markedly decreased after treatment with sacubitril-valsartan. The results of KCCQ scores [53.4 ± 16.1vs. 61.4 ± 15.7, P<0.001] and NYHA classification [P=0.01] showed obviously improvement after a median follow-up of 13 months. None of the patients showed adverse drug reactions.

Conclusion: Sacubitril/valsartan treatment improves significantly quality of life, symptoms of heart failure, NT-ProBNP and NYHA functional class in patients with HFpEF undergoing hemodialysis. Sacubitril/valsartan was safe and well tolerated.
Figure 2: KCCQ score of MHD patients before and after initiating sacubitril-valsartan with a median observation period of 13 months.

Table 1: Comparisons of the characteristics of MHD patients before and after initiating sacubitril-valsartan with median observation period of 13 months.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before sacubitril-valsartan</th>
<th>After sacubitril-valsartan</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>57.4 ± 15.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Female sex</td>
<td>45(37.5%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Follow-up time, month</td>
<td>13(8-17)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>CLINICAL PARAMETERS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>157.8 ± 20.5</td>
<td>141.5 ± 16.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>85.2 ± 14.9</td>
<td>78.5 ± 10.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate, b.p.m</td>
<td>78.1 ± 9.0</td>
<td>74.5 ± 6.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>KCCQ Score</td>
<td>53.4 ± 16.1</td>
<td>61.4 ± 15.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>LABORATORY VALUES</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>BUN, mmol/L</td>
<td>25.1 ± 14.1</td>
<td>23.6 ± 9.1</td>
<td>0.409</td>
</tr>
<tr>
<td>Creatinine, Mmol/L</td>
<td>773.1 ± 259.2</td>
<td>802.9 ± 290.6</td>
<td>0.103</td>
</tr>
<tr>
<td>eGFR, ml/min/1.73 m2</td>
<td>5.7 ± 4.1</td>
<td>5.5 ± 4.9</td>
<td>0.430</td>
</tr>
<tr>
<td>iPTH, pg/ml</td>
<td>466.3 ± 544.9</td>
<td>463.2 ± 552.0</td>
<td>0.918</td>
</tr>
<tr>
<td>Calcium, mmol/L</td>
<td>2.2 ± 0.3</td>
<td>2.2 ± 0.2</td>
<td>0.021</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.6 ± 0.7</td>
<td>4.7 ± 0.7</td>
<td>0.482</td>
</tr>
<tr>
<td>NT-proBNP,pg/ml</td>
<td>7540.5 (3575.7–18,373.0)</td>
<td>4649.0 (2259.0–8187.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac troponin T, ng/ml</td>
<td>0.1 ± 0.2</td>
<td>0.1 ± 0.1</td>
<td>0.151</td>
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<tr>
<td>Hemoglobin, g/L</td>
<td>100.2 ± 23.6</td>
<td>108.2 ± 18.1</td>
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<td>Phosphorus, mmol/L</td>
<td>2.0 ± 0.6</td>
<td>1.9 ± 0.6</td>
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<td>ASTU/L</td>
<td>16.5 ± 8.3</td>
<td>17.6 ± 11.3</td>
<td>0.367</td>
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<tr>
<td>ALTU/L</td>
<td>14.7 ± 10.5</td>
<td>16.7 ± 20.8</td>
<td>0.499</td>
</tr>
<tr>
<td>total cholesterol, mmol/L</td>
<td>4.2 ± 1.1</td>
<td>3.9 ± 1.2</td>
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<tr>
<td>triglyceride, mmol/L</td>
<td>1.6 ± 1.0</td>
<td>1.7 ± 1.1</td>
<td>0.910</td>
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<tr>
<td>Low Density Lipoprotein, mmol/L</td>
<td>2.4 ± 0.9</td>
<td>2.2 ± 1.1</td>
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<td>UA, umol/L</td>
<td>408.3 ± 121.3</td>
<td>398.7 ± 119.0</td>
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<td><strong>CARDIAC STRUCTURE AND FUNCTION</strong></td>
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<td>NYHA functional class</td>
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<tr>
<td>I</td>
<td>0</td>
<td>3</td>
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</tr>
<tr>
<td>II</td>
<td>68</td>
<td>71</td>
<td></td>
</tr>
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<td>III</td>
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</tr>
<tr>
<td>IV</td>
<td>17</td>
<td>14</td>
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<tr>
<td>LVEF, %</td>
<td>57.0 ± 10.3</td>
<td>58.7 ± 8.1</td>
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</tr>
<tr>
<td>e, cm/s</td>
<td>4.3 ± 2.5</td>
<td>4.9 ± 3.2</td>
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</tr>
<tr>
<td>LVDDd, mm</td>
<td>46.0 ± 7.8</td>
<td>47.8 ± 6.2</td>
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</tr>
<tr>
<td>AOR, mm</td>
<td>24.2 ± 3.4</td>
<td>24.2 ± 2.7</td>
<td>0.917</td>
</tr>
<tr>
<td>AAO, mm</td>
<td>33.5 ± 4.3</td>
<td>33.3 ± 4.1</td>
<td>0.763</td>
</tr>
<tr>
<td>LA, mm 37.0</td>
<td>37.5 ± 5.7</td>
<td>38.7 ± 6.1</td>
<td>0.082</td>
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<tr>
<td>IVsD, mm</td>
<td>12.8 ± 1.9</td>
<td>12.9 ± 2.0</td>
<td>0.844</td>
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<td><strong>ADVERSE EFFECTS</strong></td>
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<tr>
<td>Hypotension</td>
<td>0</td>
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<tr>
<td>Angioedema</td>
<td>0</td>
<td>0</td>
<td>-</td>
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#4454

PERITONEAL DIALYSIS (PD) EFFLUENT DERIVED EXTACELLULAR VESICLES TO ESTABLISH PD-INDUCED PERITONEAL ALTERATIONS

Micky Karsten1,2, Dirk Pegetel3,4, Johan de Rooij4, Marc Vervloet2,5 and Lily Jakulj1,2,6

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Background and Aims: Peritoneal dialysis (PD) is a life-saving kidney replacement treatment in patients with end-stage kidney disease (ESKD). Yet, long-term exposure of the peritoneal membrane to glucose and its degradation products results in fibrosis and loss of membrane function. At present, detection of early and specific peritoneal injury is challenging. With evolving therapies, biomarkers to assess peritoneal vitality and response to interventions mitigating peritoneal injury in PD-treated patients is mandatory. Extracellular vesicles (EVs) are nano-sized structures containing proteins, micro-RNAs (miRNAs) and lipids reflecting their cells of origin and have a role in intercellular communication. EVs have been widely investigated as potential easy-accessible and stable biomarkers, particularly in inflammatory conditions. Here, we describe a clinically applicable and robust technique to isolate and analyze the molecular cargo of peritoneal dialysis effluent (PDE) derived EVs (PDE-EVs).

Method: PDE was collected from adult patients treated with PD, excluding those with a recent peritonitis (<6 weeks). First, cell-free PDE was obtained by centrifugation. As a filtration and concentration quality control step celmiRNA39 packed in EV-sized liposomes was added to the cell-free PDE. PDE-EVs were isolated by subsequent filtration and size-exclusion chromatography (SEC). We used Western blot with the EV-markers Flotillin 1, 70 kilodalton heat shock protein (HSP70), and Syntenin to confirm the presence of EVs in the SEC-fractions. We used Calnexin as a marker of other intercellular membranes as an indication of purity. To confirm robustness of the filtration and concentration steps, exogenous cel-miRNA39 was quantified by qPCR. Endogenous miRNA21 and -10b were used to check if the PDE-EVs contain adequate amounts of small RNA for future analyses.

Results: PDE was collected from 13 patients (mean age 64.7 years (standard deviation 20.1 years); 62% female; 46% treated with APD; median PD-vintage 18 months (range 7–33 months)). Presence of PDE-EVs was confirmed by Western blot (Fig. 1). A weak staining was observed in PDE from a 1-hour dwell time. There was no difference in staining between 4-hour dwells, 24-hour PDE collection or a 10-hour dwell. No Calnexin staining was seen. Ct-values for exogenous cel-miRNA39 and endogenous miRNA21 and -10b, obtained by qPCR, showed robust signals for all types of PDE (Fig. 2). No relevant differences were seen between samples from different dwell duration or with different glucose concentrations of the instilled PD-fluids.

Conclusion: We present a reproducible and clinically applicable method to isolate and molecularly characterize PDE-derived EVs. Further characterization of the molecular cargo of PDE-EVs may serve as a novel means to monitor peritoneal changes over time during PD and as a potential future biomarker for risk stratification in terms of systemic (cardiovascular) sequelae by PD-induced inflammatory responses. This would fill two important caveats in contemporary PD-management.

Figure 1: Western blot confirming presence of extracellular vesicles (EV) in the peritoneal dialysis effluent with the EV-markers Flotillin 1, 70 kilodalton heat shock protein (HSP70) and Syntenin. A1 and A2 are samples from the same patient. A1: physioneal 3.86% with a 1-hour dwell time; A2: physioneal 3.86% with a 4-hour dwell time; B: 24-hour PDE collection with a mean glucose concentration of 1.36%; C: Physioneal 3.86% with a 10-hour dwell time.
Figure 2: Histogram indicating the Ct-values obtained with qPCR for cel-miRNA39, miRNA10b and −21 of the extracellular vesicles isolated from different types of peritoneal dialysis effluent.

POLY(I:C) INDUCES MORPHOLOGICAL CHANGES AND TYPE I INTERFERON-MEDIATED INFLAMMATORY RESPONSE IN MESOTHELIAL CELLS FROM PERITONEUM

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Background and Aims: Peritonitis is a major cause of morbidity and discontinuation of the therapy in peritoneal dialysis (PD) patients. Most of peritonitis episodes during PD may be imputed to bacterial infection, although in about 20% of the cases a viral origin may be hypothesized. Toll-like receptors (TLRs) play a critical role in innate immune responses by specifically recognizing molecular patterns from different microorganisms, including bacteria, fungi, and viruses. Polyinosinic-polycytidylic acid (Poly(I:C)) is a synthetic analogue of double-stranded RNA (dsRNA) that mimics the antiviral immune response by activating TLR3. Upon activation, TLR3 signaling pathway leads to the induction of NF-kB pathway and the interferon response (IRF3 activation). The aim of this work is to study the ex vivo and in vivo effect of Poly(I:C) treatment in primary human mesothelial cells (MCs) and mice peritoneum.

Methods: MCs were collected from effluent fluids of 8 clinically stable PD patients and amplified for ex vivo experiments. MCs were treated with Poly(I:C) (2 ng/μl) or TGFβ1 (2 ng/ml). After 48 hours of stimulation, samples were collected for RNA subsequent analysis. Poly(I:C) was intraperitoneally delivered to mice daily for 10 days, using two different doses: 30 mg/kg (n = 6) and 90 mg/kg (n = 4) of weight. Non-treated mice were used as control (n = 6). Mice were euthanized and peritoneal tissue was collected for the subsequent mRNA, protein, and histological experiments. Gene expression analyses of TLRs, interferon-stimulated genes (ISGs), and other inflammatory markers were performed by qPCR. Protein analysis from cell lysates was performed by western blot and cytokine and chemokine levels from cell supernatants were detected by ELISA assay.

Results: MCs from PD patients expressed a specific subset of TLRs, which were modulated by stimulation with Poly(I:C), being TLR3 the most induced receptor. Additionally, Poly(I:C) induced a bona fide mesothelial to mesenchymal transition (MMT), characterized by the acquisition of a spindle-like morphology, increased expression of mesenchymal markers such as SNAIL, TGFB1, FN1, MMP9, and MMP14, and decreased expression of the epithelial markers ECAD and CALB2. Moreover, Poly(I:C) increased mRNA and protein levels of several cytokines and chemokines, such as TNFα, IL-6, IL-1β, IFNβ, CXCL8, and CXCL9; and ISGs, including CXCL10, MX1, IFIT1, and IFITM1. In vivo, Poly(I:C) administration in mice induced peritoneal inflammation, characterized by increased gene expression of proinflammatory response-related factors, including Ccl5, Arg1, and the ISGs Cxcl10 and Ifit1, in a dose-dependent manner.

Conclusion: Treatment with Poly(I:C) is sufficient to induce a profibrotic/proinflammatory response in MCs in ex vivo and in vivo settings. These discoveries highlight the role of viral infections in peritoneum damage and may provide insight for further studies aimed at specifically counteracting the effect of viral infections in peritonitis in PD patients.
Carnaxide, Portugal and 3 Nova Medical School, Lisboa, Portugal

Detection and treatment. It's important to identify sarcopenic or at-risk patients in order to promote early intervention. It's also important to preserve renal function in PD patients. It's also important to preserve renal function in PD patients. We corroborate the association between age and frailty in the sarcopenic or at-risk patient. In multivariate analysis, age, higher CFS score, and residual urine output were related to probable sarcopenia. In the multivariable analysis, age (HR 1.135; 95% CI 1.015-1.269), CFS score (HR 2.637; 95% CI 1.008-6.900), and residual urine output were related to probable sarcopenia. We performed an exome-wide association study comparing proteinuria recipients and collected DNAs from 40 recipients of an allogeneic kidney transplant who maintained good graft function. The results of the study showed that proteinuria is a key factor in immunosuppression. The underlying mechanisms are unknown. We hypothesized that tolerance might be driven by inherited protein coding genetic variants with large effect, at least in some patients. We performed an exome-wide association study comparing the distribution of moderate to high impact variants in 36 tolerant patients, selected for genetic homogeneity using principal component analysis, and 192 controls, using an optimal sequence-kernel association test adjusted for small samples. We identified rare variants (allele frequency < 1%) of HOMER2 (3/36, FDR 0.0387), ICHQ (5/36, FDR 0.0362), and LCN2 (3/36, FDR 0.102) in 10 tolerant patients vs 0 controls. One patient carried a variant in both HOMER2 and LCN2. Furthermore, the three genes showed an identical variant in two patients each. The three genes are expressed at the primary cilium (p = 0.01), a key structure in innate immune responses. Both LCN2 variants were located 9 base pairs apart, in the 20 amino-acid long signal peptide of the encoded NGAL protein, suggesting the possibility of a shared functional effect.

Conclusions: Rare protein coding variants in a small set of primary cilium genes are associated with operational tolerance in a sizable portion of patients. Our findings have important implications for a better understanding of immune tolerance in transplantation and other fields of medicine.
INNATE IMMUNE MEMORY DETERMINES LONG-TERM KIDNEY ALLOGRAFT SURVIVAL

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Background and Aims: Historically, transplant medicine has focused primarily on the adaptive immune system, while the role of innate immune cells in the complex graft-reactive immune response has been understudied. The recently emerging concept of “trained immunity” is of particular interest in this regard. Trained immunity is a phenomenon in which innate immune cells develop a long-lasting memory in response to an initial stimulus, thereby re-programming cells for a stronger inflammatory response to future stimuli. We hypothesized that damage-associated molecular patterns (DAMPs), released during ischemia-reperfusion injury, and immunosuppressive medication can affect trained immunity, and investigated in a cohort of kidney transplant patients if trained immunity is associated with long-term allograft survival.

Method: An established in vitro trained immunity assay was used in which human peripheral blood mononuclear cells (PBMCs) were stimulated. After five days of rest, cells were restimulated with lipopolysaccharide (LPS), and IL-6 and TNF were measured in the supernatant as a readout of the trained immunity response (Fig. 1A). We tested a library of DAMPs, and immunosuppressive drugs commonly used in kidney transplantation, to determine their effect on trained immunity. Of 96 kidney transplant recipients, with a follow-up for graft survival >8 years, serum was obtained before- and one week after transplantation. Patient sera were used to stimulate healthy PBMCs in the trained immunity assay. The relationship between serum induced trained immunity and long-term allograft survival was analyzed by Kaplan-Meier and Cox regression analysis.

Results: We found that DAMPs can affect trained immunity, causing either an enhanced (HMGB1, histones, IL-1β) or suppressed (vimentin, ATP, and C1q) cytokine response after LPS restimulation (Fig. 1B). Prednisone and tacrolimus potently suppressed trained immunity (Fig. 1C). In the kidney transplant patient cohort, cells stimulated with patients’ serum showed considerable heterogeneity in the IL-6 and TNF production after LPS restimulation. The IL-6 and TNF response of cells stimulated with serum obtained one week post-transplantation was lower compared to cells stimulated with serum obtained before transplantation (Difference of 463 ± 428 pg/mL, p < 0.001 for IL-6; 1215 ± 1078 pg/mL, p < 0.001 for TNF). The trained immunity response to post-transplant obtained serum was strongly associated with long-term death-censored graft survival (p = 0.005 for IL-6 tertials, and p = 0.037 for TNF tertials in a Kaplan-Meier analysis), and remained significant after adjusting for potential confounders.

Conclusion: Trained immunity can be affected by stimulation with DAMPs, which are released during ischemia-reperfusion injury during transplantation, and by immunosuppressive drugs used in kidney transplantation. The net effect of patients’ serum taken one week after transplantation, containing a mixture of DAMPs and immunosuppressive drugs, has a suppressive effect on trained immunity compared with patients’ pre-transplant serum. Interestingly, the trained immunity response to post-transplant serum is strongly associated with long-term allograft survival. Thereby we have identified trained immunity as a novel and relevant immunological mechanism in organ transplantation.
Figure 1: DAMPs, immunosuppressive drugs, human serum and the relation with trained immunity. A. Schematic representation of the trained immunity assay. B. IL-6 cytokine production in the supernatant measured by ELISA (n = 6) Data are expressed as log2 fold change compared to untrained (RPMI) PBMCs. p-values were calculated using an unpaired t-test. C. IL-6 cytokine production in the supernatant measured by ELISA (n = 6) Data are expressed as log2 fold change compared to PBMCs trained with HKCA. p-values were calculated using an unpaired t-test. D. Kaplan-Meier survival analysis of serum-induced trained immunity and death-censored graft survival (green = low serum-induced trained immunity, red = high serum-induced trained immunity). P-values were calculated using the log-rank test and Breslow test.
**#6300**

**CHANGES IN ECHOCARDIOGRAPHIC INDICES FOLLOWING KIDNEY TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS**

Achilleas Betsikos¹, Marieta Theodorakopoulou¹, Maria Korogiannou², Smaragdi Marinaki¹, Aikaterini Papagianni¹, John Boletis¹, Costas Tsioufis² and Pantelis Sarafidis³

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**Background and Aims:** Cardiovascular disease is the leading cause of death in ESKD and uremic cardiomyopathy contributes significantly to the increased cardiovascular risk in these patients. Kidney transplantation is associated with improved survival compared to dialysis. This systematic review and meta-analysis (CRD42022371202) aims to assess the changes in echocardiographic indices in patients before and following kidney transplantation.

**Method:** We included studies in adult subjects with echocardiographic assessments before (baseline) and following kidney transplantation (>1 month follow-up). The primary outcome measure was left-ventricular mass index (LVMI). Literature search involved PubMed, Web-of-Science and Scopus databases, manual search of article references and grey literature.

**Results:** From 6463 records initially retrieved, 35 studies with a total of 2692 patients receiving kidney from living kidney donors (WMD; -76.90 g/m², 95%CI (-22.79, -10.49), I² = 88%, P < 0.001) and those on hemodialysis before (WMD; -21.16 g/m², 95%CI (-27.21, -15.12), I² = 88%, P < 0.001). In subgroup analysis, higher differences were evident among 6 studies (N = 163) evaluating LVMI <6 months after kidney transplantation (WMD -41.54 g/m², 95%CI (-51.51, -16.00), I² = 92% P < 0.001). In sensitivity analyses, patients receiving living donors (WMD; -76.90 g/m², 95%CI (-122.13, -31.67), I² = 88%, P < 0.001) and those on hemodialysis before KTx (WMD; -33.76 g/m², 95%CI (-51.51, -16.00), I² = 92% P < 0.001) presented higher LVMI reductions following transplantation.

**Conclusion:** Kidney transplantation is associated with significant reductions in LVMI compared to the pre-transplantation levels. This could be another factor contributing to the lower cardiovascular risk observed in KTRs compared to dialysis patients.

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**#3743**

**MULTIDIMENSIONAL RISK ASSESSMENT OF KIDNEY ALLOGRAFT REJECTION USING DONOR DERIVED CELL-FREE DNA**

Cindy Ursule-Dufait¹, Olivier Aubert¹,², Romain Brousse¹, Juliette Gueguen¹, Maud Racapé¹, Christophe Legendre¹,², Dany Anglicheau¹,², Carmen Lefaucheur¹,² and Alexandre Loupy¹,²

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**Background and Aims:** Post-transplantation patient care requires development and validation of non-invasive biomarkers to improve allograft monitoring and prevention from unnecessary and costly biopsies. Reports have suggested the association of donor derived cell-free DNA (dd-cfDNA) with allograft rejection. However, there is no proof of its added value on standard of care in large, unsellected and deep phenotyped cohorts.

**Method:** We enrolled 1134 kidney transplant recipients having concomitant evaluation of allograft histology, anti-HLA DSA and functional parameters between April 2013 and June 2018 in the derivation cohort, representing 1415 biopsies. Dd-cfDNA was measured in plasma at the time of the biopsy. Diagnoses were performed using Banff 2019 criteria. 171 AMR, 34 TCMR and 17 mixed rejections occurred. Parameters associated with rejection were assessed using uni- and multivariable logistic regression. We then developed a risk model using the variables that were independently associated with kidney rejection. The validation cohort comprised 1929 evaluations including 499 evaluations in one Belgian center and 1430 evaluations in nine North American centers.

**Results:** Higher levels of dd-cfDNA were observed for AMR and TCMR or both compared to other diagnoses (Fig. 1A). Dd-cfDNA incrementally increased with Banff acute lesions without significant increase for chronic lesions. In multivariable analysis, the variables independently associated with rejection were anti-HLA DSA (P < 0.0001), dd-cfDNA (P < 0.0001), eGFR (P < 0.033), proteinuria (P = 0.016), and previous history of rejection (P < 0.0001). Dd-cfDNA remained independently associated with kidney allograft rejection in validation cohorts from Belgium (P = 0.0006) and North America (P < 0.0001). Discrimination of the model without dd-cfDNA was 0.777 and 0.821 with its inclusion, showing its added value (Fig. 1B). The good discrimination performances of the model with dd-cfDNA were also confirmed in the validation cohorts from Belgium (AUC: 0.815) and North America (AUC: 0.826).

**Conclusion:** We here demonstrate the independent and added value of dd-cfDNA in addition to conventional features to predict rejection. This first integrative system shows improved performance for patient monitoring and could help physicians in decision-making process.
Figure 1: dd-cfDNA results according to the diagnoses and ROC curve of the model with dd-cfDNA. 1A: Dd-cfDNA according to the diagnoses. 1B: ROC curves of the integrative model with dd-cfDNA and without dd-cfDNA.

#6858

GRAFT SURVIVAL IN MULTIPLE KIDNEY TRANSPLANT RECIPIENTS FROM CHILDHOOD TO ADULTHOOD: AN ERA STUDY FROM 1978 UNTIL 2019

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**Method:** Using ERA Registry data, we investigated all patients on kidney replacement therapy (KRT) who received their first kidney transplant (KT) before 20 years of age between 1978 and 2019. Graft survival after first, second and third KT were studied alongside their risk factors, using Kaplan-Meier survival analysis and multivariable Cox regression models.

**Results:** Among 10012 paediatric KT candidates, 8601, 1962 and 412 received at least one, two and three KT. Graft survival at 5 and 10 years was 80.6% and 65.7% for first KT, 71.3% and 53.7% for second KT and 67.1 and 49.5% for third KT. Factors associated with increased graft failure risk were having glomerulonephritis or a recurrent disease as cause of kidney failure for first KT recipients (aHR 1.24, 95%CI 1.12-1.37 and aHR 1.24, 95%CI 1.13-1.37, respectively). Patients whose first KT lifespan was between 0–30 days or more than 5 years presented lower graft failure risks regarding their second KT compared to patients whose KT survived between 1–5 years (aHR 0.79, 95%CI 0.64-0.98 and aHR 0.73, 95%CI 0.61-0.88, respectively). Similar results were found for third KT recipients whose second KT lived for more than 5 years (aHR 0.61, 95%CI 0.41-0.92).

Patients who were transplanted for the first and second time before 2000 presented a higher graft failure risk compared to patients who received their KT between 2000–2007 concerning the first KT; and aHR 1.69, 95%CI 1.15-2.65 and aHR 1.63 95%CI 1.29-2.06 for the transplantation era before 2000 and between 2000–2007 concerning the second KT). Pre-emptive KT presented less graft failure compared to patients who received dialysis > 1 year for first and second KT (aHR 0.89, 95%CI 0.81-0.98 and aHR 0.63, 95%CI 0.51-0.78, respectively). Patients having received a LD KT had less chances for graft failure for first and second KT (aHR 0.77, 95%CI 0.7-0.84 and aHR 0.71 (0.6-0.85, respectively). Having a second LD KT (no matter the donor type for first KT) was advantageous compared to having a second DD.

**Conclusion:** Graft outcomes after pediatric kidney (re)transplantation have improved significantly over time for all recipient subgroups, especially for patients with LD KT, longer previous KT lifespan and pre-emptive KT. Patients with GN and recurrent diseases as causes of their kidney failure showed the poorest outcomes, highlighting the need for continued progress in this field.
Table 1: General characteristics of the study population.

<table>
<thead>
<tr>
<th>Characteristics at baseline</th>
<th>Total study population</th>
<th>Troponin level ≥11ng/l at baseline</th>
<th>Troponin level &lt;11ng/l at baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTRs n (%)</td>
<td>N = 305</td>
<td>N = 143</td>
<td>N = 162</td>
<td></td>
</tr>
<tr>
<td>Sex M n (%)</td>
<td>185 (60.6)</td>
<td>101 (70.6)</td>
<td>84 (51.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age years (IQR)</td>
<td>53 (20)</td>
<td>59 (16)</td>
<td>47.5 (19)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Time after RTx months (IQR)</td>
<td>72 (110)</td>
<td>72 (116)</td>
<td>72 (108)</td>
<td>ns</td>
</tr>
<tr>
<td>Time of dialysis before RTx (months) (IQR)</td>
<td>45 (78)</td>
<td>60 (71)</td>
<td>20 (75)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26 ± 4.9</td>
<td>26 ± 4.9</td>
<td>25 ± 4.9</td>
<td>ns</td>
</tr>
<tr>
<td>Hypertension n (%)</td>
<td>263 (86.2)</td>
<td>127 (88.8)</td>
<td>136 (83.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes n (%)</td>
<td>58 (19.0)</td>
<td>32 (22.3)</td>
<td>26 (16.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CAD/POAD n (%)</td>
<td>62 (20.3)</td>
<td>51 (35.6)</td>
<td>11 (6.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hyperlipidemia n (%)</td>
<td>76 (24.9)</td>
<td>49 (34.2)</td>
<td>27 (16.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CNI inhibitors n (%)</td>
<td>87 (28.5)</td>
<td>54 (37.7)</td>
<td>33 (20.4)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CNI inhibitors n (%)</td>
<td>126 (41.2)</td>
<td>79 (55.2)</td>
<td>80 (49.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>2 ± 0.8</td>
<td>1.9 ± 0.9</td>
<td>1.3 ± 0.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>eGFR (CKD-EPI) (ml/min/1.73 m²)</td>
<td>51 ± 20</td>
<td>42 ± 18.6</td>
<td>59 ± 17.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>UPCR value (mg/g)</td>
<td>135 (32)</td>
<td>141 (391)</td>
<td>133 (277)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Troponin (ng/l)</td>
<td>11 (13)</td>
<td>20 (16)</td>
<td>6.5 (5)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NT-proBNP level (ng/l)</td>
<td>292 (557)</td>
<td>574 (894)</td>
<td>139 (231)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>cPWV (m/s)</td>
<td>8 ± 2.2</td>
<td>9 ± 2.6</td>
<td>7.5 ± 1.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pulse pressure right arm</td>
<td>54 ± 15.6</td>
<td>58.6 ± 15.4</td>
<td>50.0 ± 11.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pulse pressure left arm</td>
<td>53 ± 15.6</td>
<td>57.7 ± 17.8</td>
<td>49.8 ± 12.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Follow-up characteristics (34 months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>2 ± 1.3</td>
<td>2.4 ± 1.5</td>
<td>1.55 ± 0.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>eGFR (CKD-EPI) (ml/min/1.73m²)</td>
<td>46 ± 22.4</td>
<td>37 ± 21.9</td>
<td>53.4 ± 20.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>increase of creatinine ≥ 30% n(%)</td>
<td>68 (22.3)</td>
<td>47 (32.9)</td>
<td>21 (13.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>UPCR (mg/l)</td>
<td>164 (422)</td>
<td>239 (688)</td>
<td>133 (277)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>increase of UPCR ≥500mg n(%)</td>
<td>47 (15.4)</td>
<td>32 (22.4)</td>
<td>15 (9.2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Troponin ng/l</td>
<td>13 (17)</td>
<td>25.5 (24.5)</td>
<td>8 (5)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NT-pro BNP ng/l</td>
<td>312 (836)</td>
<td>825 (2454)</td>
<td>186 (273)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>increase of NT-pro BNP ≥30% n(%)</td>
<td>159 (52.1)</td>
<td>79 (55.2)</td>
<td>80 (49.4)</td>
<td>ns</td>
</tr>
<tr>
<td>doubling creatinine n (%)</td>
<td>21 (6.9)</td>
<td>16 (11.2)</td>
<td>5 (3.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>return to dialysis n (%)</td>
<td>26 (8.5)</td>
<td>23 (16.1)</td>
<td>3 (1.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>cardiovascular events n(%)</td>
<td>17 (5.6)</td>
<td>9 (6.3)</td>
<td>8 (4.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>death n(%)</td>
<td>19 (6.2)</td>
<td>19 (13.3)</td>
<td>0 (0)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Data are presented as median (IQR) or mean (SD) or number (%)

#6395

**Tubuloreticular Inclusions: A New Prognostic Biomarker in Kidney Transplantation**

Sarah Gleeson1,2, Jack Beadle1,2, Linda Moran3, Ted Fitzgerald1, Candice Roufous1,2 and Michelle Willicombe1,2

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**Background and Aims:** Tubuloreticular inclusions (TRIs) seen on electron microscopy (EM) are classically associated with lupus nephritis (LN) and systemic viral infections in native biopsies. Traditionally a marker for enhanced type I interferon expression, little is known about their significance post-transplant. We aimed to look at a large cohort of transplant biopsies showing TRIs to investigate associations and outcomes.

**Method:** A retrospective analysis was performed on two prospective databases; an in-centre transplant registry and a histopathology database holding data on all kidney biopsies performed at our centre. All patients biopsied since 2015, who had EM examination were included. Where patients had more than one biopsy showing a TRI the earliest one was included. Demographic, clinical and transplant data was collected from the laboratory records.

**Results:** 2283 kidney transplant biopsies were performed between January 2015 and November 2022; 1898 (83.1%) had EM performed. Of 1898 with EM, 176 (10.8%) had evidence of TRIs. Of 176 patients, 34% were female, the median age was 52.2 (38.9-59.4) years, 32% had underlying glomerulonephritis as their cause of ESKD, 65% were deceased donors and 75% were of non-white ethnicity. TRIs were associated with serological evidence of autoimmunity (16%), viral infections (26%) and donor specific antibodies (28%), with no association found in 41%. Rejection occurred in 49%, including 31% of patients with no recognised association with TRIs. Allograft outcomes were poor, with all-cause allograft survival and death-censored allograft survival of 66% and 60%, after a follow up of 1.9+/−1.8 years post index biopsy. A comparison with a matched control group is planned.

**Conclusion:** In extension to previous work, we show that TRIs appear to be associated with alloimmunity. In this regard they may be a useful biomarker especially in cases where the diagnosis is unclear or biopsy findings are 'subthreshold'. Irrespective of aetiology, TRIs are associated with poor outcomes and warrant further consideration.
Background and Aims: Chronic diarrhea in post-renal transplant recipients due to Cytomegalovirus (CMV) presents as Blood CMV PCR (polymerised chain reaction) positive chronic diarrhoea and Gut-invasive (rectal tissue PCR positive, blood PCR-negative) compartmentalised CMV. The available literature on compartmental gut CMV is scarce. The aim is to study the clinical presentation and outcome of patients with compartmentalized gut invasive CMV when compared with Blood CMV positive chronic diarrhoea in renal transplant recipients.

Method: This is a retrospective single-centre follow-up study of patients with CMV disease who were transplanted between 2000 and 2020. Diagnostic variables like blood CMV PCR (polymerised chain reaction) positivity with constitutional symptoms, presence or absence of chronic diarrhoea, tissue PCR positivity and site of tissue biopsy were given harmony codes and 6 syndromes were identified – CMV diarrhoea (Blood PCR positive, presence of diarrhoea), compartmentalized gut invasive CMV (Blood PCR negative, presence of diarrhoea, rectal tissue quantitative CMV PCR positive), Acute CMV syndrome, CMV Esophagitis, CMV nephropathy, CMV cystitis. Out of which patients presenting with diarrhoea (first two groups) were included for analysis. The baseline descriptive statistical measures were carried out using analysis of variance. The time to CMV disease from transplant was computed by identifying the pattern of distribution at 10%, 50% and 90% between groups using reliability models. The time to death from diagnosis was analyzed by identifying the pattern by parametric log-logistic distribution. Survival analysis was done by a parametric reliability model identifying location, scale and threshold parameters, from which month-wise prediction of probabilities was found for survival. The proportion of adverse outcomes (relapse, death and graft loss) between the two groups were analyzed by one-way ANOVA and Tukey pairwise comparison. All the patients were followed up till death or last follow-up.

Results: Out of 2208 renal transplants done between 2000 and 2020, 118 (5.3%), patients developed CMV disease. Chronic diarrhoea was the presentation in 88 (57%), of which 47 had manifestations of CMV diarrhoea, and 41 had compartmentalized gut CMV. Induction agents used (CMV diarrhoea Vs compartmentalized gut CMV) were basiliximab (51% Vs 56%), ATG (27% Vs 17%), Grafalon (0% Vs 2.4%) and no induction (21%, 24%). Only 31.9% and 26.8% received Valganciclovir prophylaxis for pre-specified indications respectively. The time to CMV diagnosis from transplant for 10%, 50% and 90% of patients (in months) was 12.63, 154 and 139 months for compartmentalized gut CMV. The mean duration (weeks) of diarrhoea was similar in both groups (7 Vs 7.3). Associated opportunistic infections causing diarrhoea were higher in compartmentalized gut CMV (28% Vs 46% p = 0.08); the commonest being cryptosporidium. Quantitative PCR in the blood ranged from 1245 to 2511345 copies/ml; whereas in gut tissue, it ranged from 1132 to 3517920/25 mg. The major histopathological finding in compartmentalized gut CMV was active inflammatory pathology in 34 (83%) patients. The probability of survival was significantly lower (72.6%; CI 60% to 83%) in CMV diarrhoea when compared with compartmentalized Gut CMV (87.2%; CI 76% to 94%) for initial 12 months (p<0.05); however at 5 years (56.2%, Vs 58.5%) and 10 years (48.5% Vs 42.7%) the survival was similar. Compartmentalized gut CMV was associated with a higher relapse rate (19.5%) when compared with CMV diarrhoea (6.4%) on follow-up (p = 0.06). The mortality (36% Vs 29%; p = 0.490) and graft loss (25% Vs 22%; p = 0.692) were similar between both the group.

Conclusion: Compartmentalized gut invasive CMV represents a larger proportion of chronic diarrheal illness with a higher relapse rate, which needs invasive gut tissue PCR analysis, despite negative blood PCR, for early diagnosis and management.

Background and Aims: Chronic kidney disease is a frequent complication of heart (HT) and lung transplant recipients and is associated with worse survival. Current literature shows that probably the best renal replacement therapy option for these patients is kidney transplantation (KT). The aim of our work is to assess the results of renal transplantation in HT recipients.

Method: Retrospective descriptive single-center study including all heart transplant recipients who received a kidney transplantation in our center between 1992 and 2022. Data on renal and overall vital survival as a well as the factors that could have influenced them and associated complications were analyzed.

Results: We included 14 patients, 66% men, with a mean age of 56 years at the time of the KT. A total of 30.8% received an anticipated KT. A total of 85.7% received a KT from a cadaveric donor. In 90% of the induction immunosuppression consisted of thymoglobulin, prednisone, mycophenolate, and differed tacrolimus. The mean time between heart and kidney transplantation was 15 years. Six months after KT the mean GFR was 40 ml/min/1.73 m², at 12 months 35 ml/min/1.73 m² and at 5 years 30 ml/min/1.73 m². Renal graft survival was 84% and patient survival was 93% at 10 years. Regarding complications, the most frequent were urological (38.5%) followed by infections (30.8%). The incidence of acute rejection was 18%. Conclusion: Our data confirms that kidney transplantation in heart transplant recipients has very positive results. It is necessary to promote collaboration between HT and KT units with the aim of identifying promptly those patients who are candidates for KT, being able to perform it in the best conditions (preemptive transplantation, possibility of living donor transplantation).
LONG-TERM VISIT TO VISIT VARIABILITY IN HBA1C AND KIDNEY RELATED OUTCOMES IN PERSONS WITH DIABETES

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Background and Aims: Glycated hemoglobin (HbA1c) is central to the routine monitoring of glycemic control in persons with diabetes, and poor glycemic control is an established contributor to the occurrence and progression of CKD, but whether long-term visit-to-visit variability in glycemic control predicts kidney outcomes is not well studied.

Method: We included all adults with type 1 or type 2 diabetes in Stockholm, Sweden, during 2006–2019, who had at least one annual outpatient HbA1c test in three consecutive years. We evaluated associations between baseline and time-varying HbA1c variability score (HVS, the percentage of total HbA1c measures that vary by >0.5% [5.5 mmol/mol] during a 3-year window), with the risk of CKD progression (composite of >30% eGFR decline and kidney failure), acute kidney injury (AKI, by clinical diagnosis or increase in creatinine ≥0.3 mg/dL over 48 h or 1.5 times creatinine over 7 days), and worsening of albuminuria.

Results: We included 93,598 adults with diabetes undergoing 891,536 routine HbA1c tests (median 8 tests per person) during a median follow-up of 5.2 years. Compared with persons showing low HbA1c variability (HVS 0–20%), any increase in variability was associated with a higher risk of adverse kidney outcomes. For example, for patients with a baseline HbA1c variability of 81–100%, the adjusted HR was 1.47 (95% CI, 1.38-1.56) for CKD progression, 1.27 [1.19-1.36] for AKI, and 1.28 [1.21-1.36] for worsening of albuminuria.

Results were robust across subgroups (diabetes subtypes, baseline eGFR or albuminuria categories) and in sensitivity analyses including time-weighted average HbA1c or alternative metrics of variability.

Conclusion: A higher long-term visit-to-visit HbA1c variability is robustly associated with the risks of CKD progression, AKI and worsening of albuminuria.
Figure 2: Associations between 3-year baseline HbA1c variability score with kidney-related outcomes. Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease.
COMPLEMENT GENES PROFILE OF PATIENTS WITH SEVERE HYPERTENSION AND RENAL THROMBOTIC MICROANGIOPATHY

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Background and Aims: Hereditary or acquired complement system dysregulation found to be driving cause of endothelial damage in atypical haemolytic uremic syndrome (aHUS) – ultrarare life-threatening disease, that always manifests with renal thrombotic microangiopathy (TMA), resulting in poor outcome in absence of appropriate treatment. Nevertheless, several studies show high incidence of rare genetic variants of complement system in other TMA’s, including hypertension-induced TMA. Here we report results of complement genes screening in patients (pts) with histologically identified renal TMA and severe hypertension in Russia, at first diagnosed as hypertension-induced TMA.

Method: A total of 28 Caucasian pts diagnosed with renal TMA (confirmed by kidney biopsy in all cases) and severe hypertension enrolled in the study. The main characteristic of the clinical picture was the absence of microangiopathic hemolysis and thrombocytopenia in prevailing of the pts, thus most of the primary and secondary causes of TMA clinically excluded. Examination of DNA samples was performed in all pts using next generation sequencing (NGS) technology. For statistical analysis continuous variables were presented as Mean (=Standart deviation) or Median (interquartile range) as appropriate.

Results: Baseline demographic and clinical characteristics of group are listed as Mean (±Standart deviation) or Median (interquartile range) as appropriate.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male, n (%)</th>
<th>Female, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y.o.</td>
<td>36 ± 8.9</td>
<td>35 (31–43)</td>
</tr>
<tr>
<td>Hb, g/L</td>
<td>114 ± 26.2</td>
<td>111 (91–133)</td>
</tr>
<tr>
<td>PLT, 10⁹/L</td>
<td>245 ± 60.9</td>
<td>244 (190–287)</td>
</tr>
<tr>
<td>LDH, U/L</td>
<td>374 ± 132</td>
<td>365 (253–467)</td>
</tr>
<tr>
<td>Scr, μmol/L</td>
<td>683 ± 531</td>
<td>608 (243–892)</td>
</tr>
</tbody>
</table>

LDH, lactate dehydrogenase; Hb, haemoglobin; PLT, platelet cell count, Scr – serum creatinine

Conclusion: A quarter of pts with TMA and severe hypertension may have genetic defects in the complement system. These results confirmed that complement-mediated HUS may be misdiagnosed as hypertension-induced TMA. Lack of convincing hematological signs of TMA is common in this group, making aHUS diagnosis more sophisticated.
Background and Aims: Tubular epithelial cells under certain microenvironmental conditions, such as injury, driving inflammation, proliferation, fibrosis and inducing death of renal of its function in kidney injury is required. TWEAK is involved in tissue diet, gut microbiota, and kidney disease. However, a detailed characterization (SCFAs) produced by the microbial fermentation of indigestible fibers. It Butyrate is a well-known short-chain fatty acid

Method: A dose-response curve evaluated cell viability in murine tubular cells (MCT) at different butyrate concentrations using MTT assay. For this, cells were pre-treated with butyrate 0.5, 1 or 5 mM for one hour. After that, they were treated either with TWEAK (tumor necrosis factor-like weak inducer of apoptosis), a member of the TNF superfamily or TTI (TWEAK 100 ng/mL, /Gamma1-activated receptor

Results: When MCT cells were pre-treated with butyrate and then injured either with TWEAK or TTI (TWEAK, TNF-α, IFN-γ), the expression of klotho, a nephroprotector and anti-aging gene, and peroxisome proliferator-activated receptor F coactivator-1α (PGC-1α), a transcription factor that promotes mitochondrial biogenesis, were preserved, as opposed to decreased by cytokines only. Moreover, cells pre-treated with butyrate had decreased expression of inflammatory markers such as MCP1 as compared to increased expression upon cytokine stimulation. In the kidney-on-a-chip, cell viability was reduced after exposure to TWEAK compared to the cells treated only with butyrate, while cells treated with butyrate and TWEAK had lower toxicity as assessed by LDH release. Furthermore, results for Klotho, PGC-1α and the inflammation markers MCP1 and IL-6 were aligned with those in MCT cells.

Conclusion: In summary, in-vitro, butyrate prevents injury caused by TWEAK, preserves protective factors such as the anti-aging factor Klotho and the master regulator of mitochondrial biogenesis PGC-1α and decreases inflammation. Furthermore, these results were validated in a kidney-on-a-chip microphysiological system. Characterization of the mechanism behind the protection of butyrate for kidney injury is ongoing.

Figure 1: Weighted cumulative incidence of major adverse kidney (MAKE), and cardiovascular (MACE) events, and all-cause mortality, by treatment group.
Figure 1: Single-cell atlas of mouse AKI to CKD.

and 28). These data indicated that multi-identity cluster was rapidly adopting a pro-inflammatory phenotype early after AKI, which present a profibrotic phenotype in late chronic stages. We retrieved two distinct trajectories of macrophage populations, tissue-resident and monocyte-recruited. Starting at monocyte, multi-identity cluster progressed along lineage 1 towards pro-inflammatory cluster, suggesting that the monocyte-derived infiltrating multi-identity macrophages significantly contributed to the formation of the pro-inflammatory M1 cells. On the other hand, proliferative and immature cluster branched off along lineage 2 towards an endpoint of pro-repair cells, indicating that tissue-resident macrophages contribute to repair of kidney by local proliferation. Furthermore, ligand-receptor analysis identified enhanced interaction between diverse macrophage clusters and neighboring cells in the failed repaired stages after AKI, supporting that intercellular communication drives kidney fibrosis. Importantly, we identified that the Igf1-Igf1r interaction was highly specific in multi-identity macrophage and fibroblast intercellular communication.

Conclusion: Our study demonstrated the spatiotemporal dynamics of macrophage heterogeneity and the transitionary functions of multi-identity macrophages in the process of AKI to CKD transition.

Figure 2: Spatiotemporal profiles of major cell types after UIR.
ADMINISTRATION OF ASTRAGALUS MEMBRANACEUS IMPROVES RENAL CONDITIONS AND SERUM CARNOSINE LEVELS IN AN ACUTE KIDNEY INJURY MODEL

Kagemasa Kajiwara¹, Makoto Arai² and Tatsuya Nogami²

¹Tokai University, School of Medicine, Molecular Life Sciences, Isehara, Japan and ²Tokai University, School of Medicine, Department of Kampo Medicine, Isehara, Japan

Background and Aims: Astragalus membranaceus (AM) exhibits various pharmacological effects against many diseases, including chronic kidney disease (CKD) (see http://nccih.nih.gov/health/astragalus). Acute kidney injury (AKI) is a sudden episode of kidney failure. AKI occurs frequently but is believed to heal completely and is likely an important factor causing CKD pathogenesis or progression. Previously, we demonstrated the lethal dose in old mice is 20 mg/kg cis-diamminedichloroplatinum (CDDP), and the dosage that will cause AKI in young mice is 14 mg/kg of CDDP. Low doses of CDDP caused AKI in old mice. However, the same dosage in young mice would manifest AKI that was subsequently completely reversible. On administration of AM, old mice (50 mg/kg) showed significantly improved AKI pathology, suggesting the therapeutic effect of AM is age-dependent with regard to AKI pathogenicity. Here, we further examined the possible effect of AM in preventing AKI and delaying CKD progression.

Method: Female C57BL/6 mice were separated into three groups based on age: young, 10 weeks; middle-aged, 35 weeks; and old, 52 weeks. The mice received oral administration of either AM powder mixed with sterilized 0.5% methylcellulose 400 (w/v) (AM group) or 0.5% methylcellulose 400 alone in the control group (CG). Four hours after most recent dose (twice a day at 20 mg/kg AM), 0.5 mg/ml CDDP (reduced dose: 14 mg/kg or 0.9% NaCl for the CG) was injected intraperitoneally. We measured blood serum urea nitrogen (BUN) and creatinine (CRE) levels, which are biomarkers of AKI. Additionally, we assessed histochemical changes in kidney sections stained with anti-CD3 and anti-CD68 antibodies after the mice were sacrificed on day x. Thereafter, serum carnosine levels in the samples collected 4 hours after AM administration (n = 6 per group) were determined using a carnosine ELISA kit (Novus, NBP2-75013). Data were analyzed statistically with PRISM software. Significance was considered P = 0.05.

Results: The 14 mg/kg CDDP dose in old mice significantly increased BUN and CRE levels and caused histological damage in renal tubule epithelial cells and glomeruli. However, these pathological changes were not observed in young and middle-aged mice receiving the same CDDP dose. Histochemical analysis of the old mice showed a significant increase in the number of CD3- and CD68-positive cells following AKI induction (Fig. 1). However, the increase of these inflammatory markers was clearly ameliorated by the AM pretreatment in the experimental group. Serum carnosine levels were markedly increased in young and middle-aged mice following AM administration (Fig. 2). Moreover, the serum carnosine concentration in old mice was upregulated at levels corresponding to those in young mice with AM administration. However, serum carnosine levels showed no additional increase after AM administration in old mice and remained stable. Our findings suggest that normal renal conditions show a simple upregulation of serum carnosine level after AM administration. Furthermore, AM administration improves renal conditions in old mice with high levels of CD3 positive cells in particular (Fig. 1, arrow). Figure 2 shows the increased and then subsequent stabilizing of the serum carnosine levels (Fig. 2, arrow).

Conclusion: AM administration can upregulate serum carnosine in younger mice and shows at least some effectiveness in older mice, where serum carnosine is downregulated but concentrated. Serum carnosine might not be necessary for reducing the pathogenesis of AKI in younger mice, but it becomes important to prevent AKI in old mice. This indicates the effect of AM is probably age-dependent because AKI sequelae manifested spontaneously in all mice but were specifically ameliorated when administered to old mice as opposed to younger mice who recovered completely irrespective of AM administration.

Figure 1: AM decreased infiltration of CD-3 and CD-68 positive cells during reduced dose of cisplatin-induced AKI in old mice.
Background and Aims: Acute kidney injury (AKI) is a life-threatening condition. The absence of oxygen during the acute ischemic phase would disturb energy metabolism and cause kidney tubular epithelial cell damage. Fatty Acid Oxidation (FAO) is the main source of energy production of renal proximal tubular epithelial cells. Timely promoting FAO, increasing supplies of energy, and promoting cell proliferation are essential to improve kidney injury, but there is no clinically recognized effective treatment for this. Cyclin D1 (CCND1), a member of the cell cycle family, plays a vital role in cell proliferation. Our previous study found that CCND1 improved AKI accompanied with increased fatty acid oxidation. Therefore, we investigated the role and molecular basis for CCND1 involvement in fatty acid oxidation of AKI.

Method: CCND1 was evaluated in AKI in human kidney proximal tubular epithelial cells (HK-2 cells) and male C57BL/6J mice (wild type). The protective role of CCND1 in AKI was investigated in a mouse model of ischemia-reperfusion AKI treated by ultrasound-microbubble-mediated kidney-specifically transferring CCND1-expressing plasmids in male C57BL/6J mice (wild type). Eight-week-old male C57BL/6J mice (wild type) were subjected to bilateral renal artery occlusion for 30 min followed by 24 h of reperfusion. We evaluated FAO, proliferation, and autophagy in vitro and in vivo. In addition, we evaluated the concentrations of blood urea nitrogen and creatinine, evaluated kidney ultrastructure and so on.

Results: In vivo studies had shown that activation of CCND1 can prevent AKI-induced lipid accumulation, kidney tubule injury and kidney function declined after ischemia-reperfusion injury. Compared to test control, the treatment significantly (p < 0.05) lowered the concentrations of blood urea nitrogen and creatinine. Kidney specific overexpression of CCND1 promoted FAO, promoted proliferation and reduced apoptosis. Mechanistically, CCND1 activated the AMPK pathway, which increased the expression of phosphorylation AMP activated protein kinase (p-AMPK) and upregulated FAO. On the contrary, inhibiting the expression of CCND1 exacerbated impairment of FAO and disturbed energy metabolism.

Conclusion: Thus, CCND1 improved FAO and reduced lipid accumulation via active AMPK pathway in kidney proximal tubular epithelial cells (PTECs). Hence, reconstruction of the expression of CCND1 may be a novel therapeutic strategy for treating AKI.
SINGLE-CELL SPATIAL TRANSCRIPTOMICS OF THE KIDNEY IN HEALTH AND DISEASE DEFINES INJURY-SPECIFIC DOMAINS AND IDENTIFIES NOVEL CELL-CELL INTERACTIONS

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Background and Aims: Single-cell sequencing has revealed an unexpected diversity of cell types throughout the body. However, the loss of spatial context in many single-cell sequencing techniques hampers our understanding of cell-cell interactions, which are central to almost all (patho-)physiological processes, particularly in highly complex organs such as the kidney. In this study, we aim to profile the spatial organization of, and cell-cell interactions within, the healthy and diseased mouse kidney with single-cell resolution. We focus on changes induced by acute kidney injury (AKI), since AKI is highly prevalent and can progress to chronic kidney disease (CKD), with no targeted treatment strategy to prevent this AKI-to-CKD transition existing to date.

Method: To model ischemic AKI in the mouse, we performed bilateral ischemia-reperfusion injury on C57BL/6J mice. Kidneys were collected in the transition phase from AKI to CKD at 4 weeks after AKI (n = 3). Kidneys from non-surgery mice were used as controls (n = 3). To characterize the spatial complexity of the kidney with single-cell resolution we used seqFISH+, a sequential fluorescence in situ hybridization approach that allows the multiplexing of thousands of genes by sequential hybridization and confocal imaging, thus enabling RNA-quantification at the single-transcript level.

Results: Quantifying and clustering 1300 genes in 230,422 cells identified all major cell types of the kidney and revealed changes in the kidneys’ cellular composition at 4 weeks post AKI. While the cortical vasculature and cells of the proximal tubule segment 3 were reduced, the abundance of injured proximal tubule cells (identified by Haver1 and Vcam1 expression), immune cells and fibroblasts increased. Clustering the identified cell types on their neighbors within a 30um radius revealed distinct spatial domains comprising different combinations of cell types. Certain domains were consistently present across samples and corresponded to the known regional organization of the kidney, thus providing an internal validation. Other domains developed de novo after AKI, illustrating the structural changes induced by AKI. One of these injury-specific domains was comprised of injured proximal tubule cells, macrophages and fibroblasts, while another mainly comprised macrophages, dendritic cells and T cells. Ligand-receptor analysis within domains revealed novel cell-cell interactions, for example highlighting a Crlf1-expressing fibroblast population in close proximity to injured proximal tubule cells, which express the interleukin-6 cytokine Clcf1, a usually co-secreted binding partner of Crlf1. Zooming in on one injury-specific domain, we found that the fraction of fibroblasts and macrophages in the vicinity of injured proximal tubule cells increases with the degree of injury-related gene expression in these cells, suggesting a causal role of injured proximal tubule cells in defining a “pathogenic niche” associated with kidney disease progression.

Conclusion: This study provides a spatial characterization of the kidney with unprecedented resolution, highlights AKI-induced structural changes in the kidney, defines injury-specific spatial domains and reveals cell-cell-interactions relevant to disease progression from AKI to CKD.
ANGIOTENSIN II TYPE 1A RECEPTOR IN KIDNEY PERICYTES MEDIATES TERTIARY LYMPHOID TISSUE FORMATION AFTER ACUTE KIDNEY INJURY

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Background and Aims: Tertiary lymphoid tissues (TLTs) have been demonstrated as a major cause of sustained inflammation after acute kidney injury (AKI), indicating a possible contribution of ensuing chronic kidney disease (CKD). And heterogeneous fibroblasts play the crucial role of induction of TLT by secretion of chemokines. Angiotensin II receptors also express on fibroblasts including pericytes. Our study aimed to investigate whether the blockade of angiotensin II receptor could attenuate TLT formation and ensuing CKD after AKI.

Method: Ischemia-reperfusion injury (IRI) was used as AKI model. In vivo, systemic angiotensin II receptor blockade was performed by administration of an angiotensin II receptor antagonists called losartan after the recovery of AKI. Cell-specific angiotensin II receptor blockade was performed using Gli1-CreERT2;AT1Rfl/fl mice to knockout angiotensin II type 1a receptor in pericytes. We also investigated the effect of angiotensin II receptor blockade using 3T3 fibroblasts cell line.

Results: During the 8-month follow-up period after IRI, the activity of intra-renal renin-angiotensin system (RAS) elevated without treatment of losartan. We also displayed that multiple TLTs developed in ensuing CKD after IRI both in a CD-1 and C57BL/6 mice model, which were confirmed by staining of CD3 and B220 representing T and B lymphocytes, respectively. Notably, losartan could not only reduce the size and number of TLT, but also downregulate proinflammatory cytokines such as CXCL13, CCL21 and CCL19 which trigger the initiation of TLT. In vitro, using 3T3 fibroblasts cell line and primary pericytes isolated from kidney after IRI, angiotensin II administration could induce the development of fibroblasts with distinct phenotypes and stimulate production of aforementioned proinflammatory cytokines, particularly CCL19. Additionally, we discovered that angiotensin II-stimulated fibroblasts induced migration of lymphocytes via CCL19 production. Using Gli1-CreERT2;AT1Rfl/fl mice, we found that TLT formation decreased after IRI compared to control groups.

Conclusion: Losartan can reduce ensuing CKD and TLT formation. Distinctive pericytes inhibition by losartan is the plausible mechanism of amelioration of TLT formation. As a result, losartan might be the promising therapeutic agent to prevent AKI-CKD continuum.

KINETICS OF THE DE NOVO NAD/NADH PATHWAY FROM AKI TO CKD

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Background and Aims: Mitochondrial dysfunction and energy metabolism deficiency are part of the acute kidney injury (AKI) pathophysiology. In particular, recent studies highlighted the role of nicotinamide adenine dinucleotide (NAD) production in the pathogenesis of AKI. NAD is an electron carrier for mitochondria and a cofactor for cytoplasmic redox reactions. Its production is decreased during AKI following a decreased of the expression of PGClα (Peroxisome proliferator activated receptor gamma co-activator-1-α). PGClα inactivation worsened its overexpression prevented renal injury in a mouse model of renal ischemia. It was also shown that the consequences of PGClα decreased expression included the alteration of the de novo NAD synthesis pathway. This was due to a reduction in the expression of the Quinolinate Phosphoribosyltransferase (QPRT), which led to an accumulation of quinolinate. Consequently, the quinolinate/tryptophane (uQ/T) ratio increased in the urine. The modulation of this de novo has been studied mainly in the acute phase immediately following the injury. However its evolution with degree of severity and during the transition from AKI to CKD has not been described yet. In order to answer these questions, we designed the following studies: (1) A “severity” study in which we provoked ischemic AKI of increasing intensity in mice and quantified kidney PGClα and QPRT mRNA expression. (2) An “AKI to CKD” study in which we followed kidney PGClα and QPRT mRNA expression and uQ/T.

Method: Renal ischemia-reperfusion was performed in C57Bl6/J male mice using the new vascular occluder we recently developed (RIRI clamp), after nephrectomy of the contralateral kidney. For the ‘severity’ study, a 5–30 minutes ischemia was performed. Renal function (measurement of plasma creatinine and urea) and structure (Periodic Acid Schiff staining) were assessed 24h after ischemia. For the ‘AKI to CKD’ study, renal ischemia was performed during 10 minutes. Mice were sacrificed 1, 2, 3, 6 and 28 days after ischemia. For both studies, PGClα and QPRT mRNA expression was quantified by qPCR in the kidneys. Urinary Q/T was determined by mass spectrometry.

Results: PGClα and QPRT mRNA expression is inversely corrected to the AKI severity

We induced AKI in mice by unilateral ischemia reperfusion injury of increasing time to induce several degrees of AKI severity. The measurement of plasma urea and creatinine concentration confirmed that the severity increased with

Figure 1: Losartan attenuated TLT formation after AKI. (A) Representative images showed PAS staining of the kidneys of each group at day 240 after AKI or Nx. Scale bar, 50 μm. Original magnification, × 200. (B) Dot charts showed the numbers and sizes of TLTs in the kidneys of each group at day 240 after AKI or Nx. n = 5 for each group. Data were expressed as the mean ± SEM. *P < 0.05, **P < 0.01, ***P < 0.001 by one-way ANOVA with post hoc Tukey’s correction.
thecdurationofischemia.PGC1α andQPRTmRNAexpressiondecreasedprogressivelywithischemiaseverityuntilreachingplateauat15minutesofischemiaforPGC1α(Fig.1A),likeplasmacreatinineandurea,whereasQPRT(Fig.1B)decreasedislinearuntil30minofischemia.PGC1αmRNAdecreaseisalsoinverselycorrelatedtokidneydysfunction(p < 0.001)(Fig.1C).

**PGC1α and QPRT expression recovery after AKI**

A 10-minute ischemia led to the development of Chronic Kidney Disease (CKD), as evidenced by an incomplete recuperation of the kidney function at 28 days. QPRT and PGC1α mRNA expression showed a progressive but incomplete recuperation during the transition from AKI to CKD compared to sham mice (Fig. 1D, E). uQ/T increases after ischemia and is restored during transition from AKI to CKD (Fig. 1F).

**Conclusion:** In addition to confirming the decrease of PGC1α and QPRT mRNA expression during AKI, we show that it is correlated to the severity of the ischemic AKI. Furthermore, we describe the recovery during renal repair and transition to CKD.

**#6078 MODULATION OF TRYPTOPHAN METABOLISM IN SEPSIS-INDUCED ACUTE KIDNEY INJURY (AKI): A NEW THERAPEUTIC APPROACH TO PREVENT NEUROCOGNITIVE IMPAIRMENT**

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**Background and Aims:** Partial recovery following AKI could lead to long-term consequences that predispose to chronic dysfunction and may also accelerate progression of neurocognitive impairment. In this scenario, a tight crosstalk between kidney and brain named “kidney-brain axis” seems to play a pivotal role leading to detrimental outcome for AKI patients. Notably, many studies suggest a high relationship between kidney damage and brain dysfunction (cognitive impairment, taste and olfactory dysfunction, peripheral nerve dysfunction) even after the resolution of AKI. Furthermore, patients who suffered AKI may afterward show a disturbance of arousal, also called “brain fog”. Although major advances have been made in our understanding of the pathophysiology of AKI and brain dysfunction, there are no available preventive and therapeutic strategies in this field. Recent findings have revealed remarkable link existing between dyslipidemia/low High-density lipoprotein (HDL) levels and Kynurenine pathway (KP) alterations that lead to the production of neuroactive metabolites such as kynurenine (KYN) and quinolinic acid (QA) in AKI setting.

**Method:** Sepsis-induced AKI (SI-AKI) was induced in a porcine model by intravenous infusion of a saline solution containing 300 μg/kg of LPS. After LPS injection, 12 animals were treated with different doses of recombinant HDL (rHDL) (20–40 mg/kg) (rHDL group), while 6 animals did not receive treatment (LPS group). Animals were sacrificed after 24h from the start of experimental procedure.

**Results:** Endotoxemic pigs developed oliguric AKI with increased tubular and glomerular damage and interstitial inflammatory infiltrate. We found that rHDL treatment significantly decreased the inflammatory process and tubular damage, preventing AKI, especially in the rHDL 40 mg/kg group. Then, we evaluated the Indolamine-2,3-dioxygenase 1 (IDO1) enzyme activation, which is the first and rate-limiting step of KP, upregulated during inflammation in both sera and brain tissue, and has been linked to cognitive dysfunction. In our model, LPS induced an increased activation of the IDO-1 gene expression at brain level in endotoxemic animals, meanwhile it appears to be reduced in both treated arms (p < 0.005). Furthermore, sera from the rHDL group showed a significant reduction in IDO1 activity (KYN/Tryptophan ratio) (p < 0.05) and QA levels (p < 0.005) compared with the LPS group. Moreover, a significant decrease of both systemic and brain IL-6 levels was observed after rHDL treatments.

**Conclusion:** Our preliminary data indicated that HDL-enhancing therapies may decrease the inflammatory response, the retention of waste products and neuroactive compounds, improving renal and cognitive function in SI-AKI.
Background and Aims: The "weekend effect" is the finding of worse outcomes in hospital admissions occurring over weekends. The reasons for this are still unclear but shorter staffing has been suggested to contribute. Little is known about the impact of the "weekend effect" on renal outcomes. We aim to analyze the impact of the weekend effect on patients admitted with acute kidney injury (AKI). We evaluated one-year renal outcome and mortality in patients admitted for AKI over weekends and weekdays.

Method: We conducted a retrospective analysis of all adult patients admitted in a tertiary medical center in Portugal over a period of 6 months with a diagnosis of AKI. Variables were retrieved using clinical and laboratory data. AKI was defined and severity was accessed according to Kidney Disease Improving Global Outcomes classification. Patients were categorized according to weekdays or weekend admission. Outcomes were in-hospital mortality, hemodialysis (HD) requirement and one-year mortality. Statistical significance was defined as a P-value <0.05.

Results: We included 163 patients with mean age of 69.8±16.2 years and 52.7% were male. The majority of patients were admitted on weekdays (74.2%, n = 121). Also, the majority had AKI stage 3 (65.6%, n = 107). Forty eight patients (29.4%) required HD during hospitalization and in-hospital mortality was 24.5%. There were no significant differences in HD requirement (31.4% vs 23.8%, p = 0.434), mortality (25.6% vs 21.4%, p = 0.680) nor HD requirement at discharge (25.6% vs 26.2%, p = 0.681) between weekday or weekend admissions. Of the 123 patients discharged, during the one-year follow-up 30.1% (n = 37) died and 7.3% (n = 9) required HD. There were no differences between weekdays or weekend admissions concerning mortality (32.2% vs 24.2%, p = 0.507) and HD requirement (7.8% vs 6.1%, p = 0.746).

Conclusion: In this cohort of patients with AKI there was no "weekend effect", which reflects the adequacy of care independently of the day of admission. The retrospective design with a limited number of patients may have influenced the results. Further studies focusing on renal outcomes are required to better understand the occurrence of the weekend effect and its long-term impact.
Table 1: Comparison of variables between patients with AKI and without AKI.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with AKI (n = 59)</th>
<th>Patients without AKI (n = 127)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of recipient (years)</td>
<td>51 (41 – 57)</td>
<td>52 (42.5 – 59)</td>
<td>0.503</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Male n (%)</td>
<td>56 (94.9%)</td>
<td>104 (81.9%)</td>
<td>0.017</td>
</tr>
<tr>
<td>• Female n (%)</td>
<td>104 (5.1%)</td>
<td>23 (18.1%)</td>
<td></td>
</tr>
<tr>
<td>Graft-recipient weight ratio</td>
<td>0.97 (0.86 – 1.10)</td>
<td>0.93 (0.84 – 1.08)</td>
<td>0.514</td>
</tr>
<tr>
<td>MELD score</td>
<td>18 (15 – 22)</td>
<td>15 (10 – 21)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes Mellitus n (%)</td>
<td>23 (39.0%)</td>
<td>36 (28.3%)</td>
<td>0.147</td>
</tr>
<tr>
<td>Hypertension n (%)</td>
<td>9 (15.2%)</td>
<td>15 (11.8%)</td>
<td>0.514</td>
</tr>
<tr>
<td>Preoperative serum creatinine (mg/dl)</td>
<td>0.9 (0.7 – 1.1)</td>
<td>0.7 (0.6 – 0.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preoperative e GFR (ml/min/1.73 m²)</td>
<td>94.4 (72.1 – 113.2)</td>
<td>107.7 (95.7 – 124.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of Spontaneous bacterial peritonitis n (%)</td>
<td>9 (15.3%)</td>
<td>16 (12.6%)</td>
<td>0.621</td>
</tr>
<tr>
<td>History of AKI/HRS n (%)</td>
<td>36 (61.0%)</td>
<td>26 (20.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline proteinuria (g/24 hrs)</td>
<td>0.7 (0.4 – 0.9)</td>
<td>0.2 (0.2 – 0.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood loss intraoperative (ml)</td>
<td>1800 (1500 – 2300)</td>
<td>1500 (1000 – 2000)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median p RBC transfusion intra op (units)</td>
<td>6 (4 – 8)</td>
<td>3 (1.5 – 6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median FFP transfusion intra op (units)</td>
<td>2 (0 – 4.5)</td>
<td>1 (0 – 3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Use of inotropes intraoperative n (%)</td>
<td>37 (62.7%)</td>
<td>24 (18.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biopsy proven rejection</td>
<td>4 (6.8%)</td>
<td>4 (3.1%)</td>
<td>0.256</td>
</tr>
<tr>
<td>Re exploration</td>
<td>6 (10.2%)</td>
<td>2 (1.6%)</td>
<td>0.007</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>6 (3 – 9)</td>
<td>5 (4 – 5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median days to normalization of graft function, median(IQR)</td>
<td>18(15-23)</td>
<td>10(8-12)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Hospital Stay median(IQR),days</td>
<td>20 (14.5 – 26)</td>
<td>14 (12 – 18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality (n,%)</td>
<td>16(27.1%)</td>
<td>11(18.6%)</td>
<td>0.009*</td>
</tr>
<tr>
<td>Further episodes of AKI (after 1month from surgery) n (%)</td>
<td>10 (16.9%)</td>
<td>2(0.4%)</td>
<td>0.01</td>
</tr>
<tr>
<td>eGFR at 90days (ml/min/1.73 m²) median(IQR)</td>
<td>91 (74 – 108.5)</td>
<td>106 (94.5 – 120)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR at last follow up (ml/min/1.73 m²) median(IQR)</td>
<td>88 (68 – 102)</td>
<td>100 (90 – 114)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Conversion to CKD at last follow up n (%)</td>
<td>6 (10.1%)</td>
<td>1 (0.78%)</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

Table 2: Score assigned to each significant variable of the best fit model.

<table>
<thead>
<tr>
<th>Variable present</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>17</td>
</tr>
<tr>
<td>MELD score &gt;14</td>
<td>12</td>
</tr>
<tr>
<td>History of AKI/HRS</td>
<td>14</td>
</tr>
<tr>
<td>Preoperative e GFR &lt;90 ml/min/1.73 m²</td>
<td>18</td>
</tr>
<tr>
<td>Preoperative proteinuria &gt;0.5 gram/day</td>
<td>25</td>
</tr>
<tr>
<td>Use of intraoperative inotropes</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>
Figure 1: ROC curve for the scoring model. AUC 0.925 (95% CI: 0.886 – 0.964, p < 0.001).
Background and Aims: Diabetic kidney disease (DKD) is a leading cause of end-stage kidney disease (ESKD), however therapies targeting causal pathways have been limited by disease heterogeneity. Integrating electronic health record (EHR) data and genomics may uncover hidden subphenotypes in DKD. In this study, we use deep learning to identify a novel genetic variant of ARHGEF18 associated with significantly higher risk of DKD and ESKD (Figure 1A). We further employed quantitative microscopy techniques and biochemical assays to elucidate the mechanistic role of ARHGEF18 and its variant in podocytes.

Method: DKD patients from the Mount Sinai BioMe Biobank were used in this study. Unsupervised clustering and accounting for population structure in a deep learning framework identified two clusters: Cluster M (mild) and S (severe). We then performed a genome wide association study (GWAS) of patients within each cluster compared with healthy controls. For mechanistic studies of the novel variant, cytoplasmic, focal adhesion, cytoskeletal morphometrics as well as live-cell motility, Rho GTPase activity, and protein degradation experiments were performed using confocal and total internal reflection fluorescence (TIRF) microscopy as well as cell-free biochemical assays using immortalized human podocytes expressing ARHGEF18 wild-type (WT) and mutant transcripts.

Results: We employed autoencoders and unsupervised clustering of EHR data on 1,372 DKD patients to establish two clusters with differential prevalence of ESKD. There was a greater prevalence of proteinuria in Cluster S compared to Cluster M (Figure 1B). Further exome sequencing study in these patients identified a novel variant in ARHGEF18, a Rho guanine exchange factor highly enriched in podocytes (Figure 1A). Nephroseq database showed an increased ARHGEF18 expression in chronic kidney disease (CKD) kidney biopsy samples compared to healthy controls (Figure 1C). Overexpression of ARHGEF18 mutant transcripts in human immortalized podocytes led to impairments in cell adhesion, focal adhesion architecture, and cell motility. Live TIRF microscopy experiments showed preferential subcellular localization of GEF18 mutant to the periphery of migrating podocytes whereas GEF18 WT localized at the perinuclear/cytoplasmic region (Figure 2A, B). GEF18 mutant cells also displayed an increased RhoA activation (Figure 2C). Upon inhibition of protein synthesis using cycloheximide (CHX), we observed a significantly slower degradation of GEF18 mutant protein over a 12h period indicating increased protein stability (Figure 2D). GEF18 mutant also showed resistance to ubiquitin mediated degradation leading to pathologically increased protein levels.

Conclusions: We report a novel gain of function variant of ARHGEF18 that drives podocyte dysfunction through impaired protein localization and degradation. Targeting this pathway could help regulate RhoA activation and cytoskeletal rearrangements preventing podocyte effacement in DKD.
Figure 1: (A) Manhattan plot for exome wide association study comparing cluster S with DKD controls. (B) Baseline urinary albumin to creatinine ratio (UACR) plotted for individuals in each cluster in BioMe. (C) ARHGEF18 mRNA expression in CKD and healthy renal biopsy specimens.
RENAL ORGANOID FROM URINE-DERIVED HUMAN ADULT RENAL PROGENITOR CELLS CAN SPONTANEOUSLY GENERATE LONG RENAL TUBULES
Fabio Sallustio¹, Francesca Giannuzzi², Angela Picerno², Francesca Montenegro², Silvia Maiullari², Antonella Cicirielli², Alessandra Stasi¹, Giovanni Pertosa¹ and Loreto Gesualdo¹
¹University of Bari Aldo Moro, Department of Precision and Regenerative Medicine and Ionian Area, Bari, Italy and ²University of Bari Aldo Moro, Department of Interdisciplinary Medicine, Bari, Italy

**Background and Aims:** Organoids are self-organizing 3D aggregations of cells that represent the structure and function of organs. Kidney organoids have the potential to advance the field of nephrology by providing a tool for the study of human kidney development and disease, by providing a tool for in vitro drug screening, and ultimately, for regenerative therapy. They can be derived from embryonic stem cells or induced pluripotent stem cells. We aimed to explore for the first time, the potentiality of human adult renal progenitor cells (ARPCs), isolated from urine of healthy subjects and patients, to generate spheroids and organoids for regenerative purpose.

**Method:** ARPCs were isolated from urine by immunolabeling. Optical microscopy, immunofluorescence experiments and cytotoxicometric analysis were used to characterize spheroids and organoids. CD133, NANOG, SSAG, OCT 3-4 and GATA-3, SOX2 stemness marker antibodies were used to study spheroids and CD13, Lotus tetragonolobus lectin, ZO-1, uromodulin, and aminopeptidase antibodies were used to investigate renal tubular markers. PKH26 was used to study cell migration from organoids to tubules. Real-time PCR was used to generate gene expression data of aquaporin profile in renal tubules. Chick embryo chorioallantoic membrane (CAM) assays were used as in vivo model for angiogenesis.

**Results:** We isolated ARPCs from urine of healthy subjects or CKD patients. Usually, organoids were generated using complex induction protocols with several chemical factors. However, for the first time we generated renal spheroids and organoids under 3D culture conditions without any stimulation, such as chemokines or growth factors, starting from ARPCs isolated from subject urine. We showed that the spheroids express high levels of stem cell markers as CD133 and NANOG, functional and constitutional marker of ARPCs, and high levels of stem cell markers that normally are low or not at all expressed in ARPCs and are typical of embryonic stem cells: GATA-3, SSEA4, and Sox2. Moreover, the spheroids were able to induce angiogenesis when implanted in chick embryo chorioallantoic membrane. The urine-derived CD133+ organoids can spontaneously generate long renal tubules in 6–12 days, as showed by PKH26 tagging. The renal tubules were positive for the proximal tubule cell markers CD13 (aminopeptidase N), Lotus tetragonalobus lectin and ZO-1. Moreover, renal tubules expressed the aminopeptidase A (CD249) that is normally present in proximal tubules and glomeruli of the kidneys and that catalyzed the conversion of the Angiotensin II in Angiotensin III which is important in the local regulation of blood pressure. Also uromodulin was expressed by tubules. It is normally present in epithelial cells of the thick ascending limb of Henle’s loop, and after proteolytical cleavage, is secreted into urine. In addition, the renal tubules express several genes typical of renal tubules as AQP1 channel protein that facilitates the flow of water molecules into the cells of the proximal tubule and descending limb of the loop of Henle; yGlut enzyme used for the transport of amino acids across cell membranes; Na/H exchanger 1 (SLC9A1), transporter involved in the regulation of pH homeostasis, cell migration and cell volume; Na/Gluc-1 co-transporter SGLUT1, which promotes the passage of glucose across the membrane in renal tubular cells. In some cases, tubule structures were similar to that found in nephrons, including proximal convoluted tubule, Loop of Henle, Distal Convolutetubule and collecting duct, as shown by optical microscopy.

**Conclusion:** For the first time we demonstrated that kidney organoids can be generated starting by urine-derived human adult renal progenitor cells from patients and for the first time we showed that these organoids can generate, spontaneously, without specific stimulation, long portions of renal tubules. These results open new perspectives in the field of the regenerative medicine.
as ARPCs can be isolated from urine of patients and used to generate spheroids for the study of human kidney development and disease, for in vitro drug screening, and ultimately, for regenerative therapy.

#4950
CARNITINE ACETYLTRANSFERASE (CRAT) MODULATES MESOTHELIAL CELL RESPONSE TO FIBROTIC STRESS
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Background and Aims: It has been shown that long-term exposure to the high glucose load of peritoneal dialysis (PD) fluids can induce peritoneal fibrosis causing loss of peritoneal ultrafiltration capacity. TGF-beta is a master regulator factor in the onset of peritoneal fibrosis and recent findings suggest that production of it is dependent on a hyper-glycolytic state caused by glucose-based PD solutions. Currently, a different class of bio-compatible PD solutions are under development; they are based on two synergistic strategies: reducing the amount of glucose, and using osmotic-metabolic agents that may provide metabolic benefits able to mitigate local and systemic glucose over-exposure [1, 2]. One such is L-carnitine [1]. The aim of the present study is to explore the role of L-carnitine and carnitine acetyltransferase (CrAT, a key enzyme in L-carnitine metabolism) on the modulation of TGF-beta pro-fibrotic effects.

Method: CrAT proved overexpressed in the human mesothelial cell line Met5A. Plasmid-coding CrAT ORF (Origene RG21296) was transfected by Lipofectamine 3000 and subsequently cells underwent antibiotic selection. Single clones were isolated, and CrAT expression was measured at the gene and protein level by real-time PCR and WB respectively. Metabolomic analyses were performed on WT and CrAT overexpressing mesothelial cells. WT and CrAT-overexpressing mesothelial cells were also treated with and without TGF-beta in the presence of physiological and supra-physiological L-carnitine concentrations (50 μM and 2 mM, respectively). The expression of fibrosis and inflammatory markers was analyzed.

Results: Gene and protein expression analyses confirmed CrAT overexpression in several clones and the two with the highest expression rate were used in subsequent analyses. WT and CrAT-overexpressing mesothelial cells displayed a different metabolic profile, as gleaned by unsupervised hierarchical clustering analysis of the top 50 significant metabolites employing ANOVA and partial least square-discriminant analysis (Figure 1). Most interestingly, they showed a different behavior in response to TGF-beta (Figure 2). In detail: treatment with TGF-beta significantly increased the expression of fibrotic markers alpha-smooth muscle actin (alpha-SMA) and vimentin (VIM) as well as that of pro-inflammatory markers interleukine-6 (IL-6) and interleukine-1β (IL-1β) at a physiological L-carnitine concentration (50 μM). Treatment with supra-physiological L-carnitine levels (2 mM) significantly reduced the up-regulation of the markers analyzed. Similarly, TGF-b was unable to modulate the expression of alpha-SMA, VIM, IL-6 and IL-1β in CrAT-overexpressing cells.

Conclusion: Studying CrAT-overexpressing mesothelial cells may prove to be a useful tool in elucidating how L-carnitine metabolism manages to keep in check the development of fibrosis and inflammation during PD. The use of L-carnitine as an osmo-metabolic agent in PD solutions could significantly slow down the progression of fibrosis in PD therapy.

REFERENCES

Figure 1: Metabolomic PCA analyses reveal a significant effect from CrAT-overexpression in mesothelial cells.

Figure 2: The TGF-beta effect on the expression of fibrotic and pro-inflammatory markers in mesothelial cells overexpressing CrAT.
ROLE OF ENDOTHELIAL CELLS IN VASCULAR CALCIFICATION
Luisa Artioli, Paola Ciceri and Mario Gennaro Cozzolino
University of Milan, Health of Sciences, Milan, Italy

Background and Aims: Vascular calcification (VC) represents a common pathological feature of cardiovascular disease and VC caused by hyperphosphatemia is one of the hallmarks of chronic kidney disease (CKD). Therefore, elucidating the pathogenesis of VC may have significant clinical benefits for CKD patients. Vascular smooth muscle cells challenged with high-phosphate (Pi) actively participate to VC by trans-differentiating into simill-osteoblastic cells that acquire the capability to deposit hydroxyapatite crystals in the extracellular matrix of tunica media in arteries. The role of endothelial cells (ECs) in high-Pi calcification has been poorly investigated until now. Nonetheless, following particular stimuli ECs can lose their endothelial characteristics and acquire several different phenotypes transdifferentiating with a process known as endothelial-to-mesenchymal transition (EndMT). Given the central role of VC for CKD patients wellbeing we decided to investigate whether ECs may have a role in VC process.

Method: We set up an \textit{in vitro} calcification model with human aortic ECs (HAECs) challenged with 2, 2.5, 3, 3.5 mM high-Pi for 7 days. Calcium deposition, cell viability and cell trans-differentiation were evaluated.

Results: In our model we observed deposition of calcium phosphate crystals induced by high-Pi that resulted significant from 3 up to 3.5 mM Pi (Ctr 0.43 ± 0.01; 3 mM Pi 6.72 ± 1.15; 3.5 mM Pi 17.31 ± 1.88; micromol Ca$^{++}$/mg protein; $P < .01$; Fig 1A-B). We found that calcification is mediated by Pi-influx, as demonstrated by the inhibition of calcium deposition by Phosphonomiform acid (PFA), an inhibitor of Na/Pi cotransporter Pit-1 (3.5 mM Pi 15.52 ± 1.97; 1 mM PFA 0.6 ± 0.05; micromol Ca$^{++}$/mg protein; $P < .0001$; Fig 1A, C). In addition, in our model high-Pi did not show any significant toxic effect at every concentration tested compared to control cells. In Pi-treated ECs we observed a clear change in cell-morphology from cobblestone to spindle shaped, a recognized sign of EndMT. Moreover, we observed a change in extracellular matrix composition more similar to osteoblastic matrix. In facts, ECs treated with Pi were Alcian Blue positive, a staining that binds glycosaminoglycans contained in bone matrix, with blue granules of calcium-phosphate in the cytoplasm of treated cells.

Starting from day 5 up to day 7 the transition was confirmed by an up-regulation of SNAIL and N-cadherin mRNA expressions, one of the master genes and one the markers of EndMT process, respectively. A modification of endothelial phenotype was also supported by a progressive decrease in protein expression of Von Willebrand factor and VE-Cadherin observed at day 9 of calcification ($-53.7\%$ and $-32.6\%$ respectively).

Moreover, from day 5 till day 7 we found some osteoblastic differentiation signs such as a progressive increase of RUNX2 and BMP2 mRNA expression and an increase of protective MGP mRNA levels.

Conclusion: Our data demonstrate that HAECs are able to calcify. High-Pi induces trans-differentiation in simill-osteoblastic cells and a progressive loss of endothelial characteristics through the EndMT process. More studies are needed to better elucidate the role for ECs in CKD VC process.

Figure 1: (A) Representative images HAECs challenged with 2, 2.5, 3 and 3.5 mM Pi and 1 mM PFA, stained with Alizarin Red. (B–C) Calcium deposition measured by de-staining and normalized by protein content expressed as #x03BC;mol Ca$^{++}$/protein.
Transcriptional coactivator with PDZ-binding motif

Background and Aims: Podocytes, highly-specialized renal epithelial cells, display the outer aspect of the glomerular filtration barrier. Changes of their complex 3D morphology with interdigitating foot processes are the leading cause for 80% of chronic kidney disease (CKD) cases. During injury development podocytes release increased amounts of extracellular vesicles like exosomes with disease-specific small RNA cargo composition. Exosomes are referred to as important means of cell-cell communication and display an interesting tool for understanding intercellular communication in CKD pathogenesis. It is not clear if exosomes could serve as delivery system for specific small RNAs to podocytes as potential therapeutic approach. To address this, we investigated if isolated exosomes, directly transfected with fluorescently labeled small RNAs, are suitable for exosomal cargo trafficking and for functional delivery of small RNAs in cultured podocytes.

Method: We isolated exosomes from cultured, murine podocytes and transfected them directly with Cy3-labeled siRNAs and miRNAs using ExoFect siRNA/miRNA transfection kit. The transfected exosomes were characterized by transmission electron microscopy and Western blot. The fluorescently labeled exosomes were incubated with cultured, murine podocytes and exosome cargo uptake was observed time- and localization dependently by confocal laser-scanning microscopy. Isolated exosomes were also transfected with filamin A (FlnA)-siRNAs and pre-miR-21 and were co-incubated with cultured, murine podocytes. Transfection- and knockdown efficiency were confirmed by RT-qPCR, Western blot and immunofluorescence microscopy, respectively.

Results: The isolated exosomes displayed a typical shape and size of 20 nm revealed by transmission electron microscopy. This was also consistent after transfection. They also exhibited exosomal marker proteins CD9 and TSG101 before and after transfection. We could show that cultured, murine podocytes take up fluorescently labeled exosomal RNAs. We could observe an increasing amount of fluorescently labeled RNA intracellularly compared to a decreasing amount of fluorescently labeled RNAs in the periphery over 1 week of treatment indicating a time-dependent exosome uptake by podocytes. Transfection of exosomes with FlnA-siRNAs led to a decrease of FlnA-expression in podocytes co-cultured with transfected exosomes as revealed by immunofluorescence microscopy and Western blot. Podocytes incubated with pre-miR-21-transfected exosomes exhibited a 338-fold upregulation of miR-21 in RT-qPCR.

Conclusion: Here we show that direct transfection of exosomes with fluorescently labeled small RNAs is a useful tool for exosome cargo trafficking in podocytes. Additionally, we proved that small RNAs transfected into exosomes can be functionally used for RNAi in cultured podocytes. This might be a novel strategy for regulating protein and miRNA expression in cultured podocytes.

A NOVEL STRATEGY TO TARGET V2R IN RENAL CARCINOMA

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Background and Aims: The vasopressin V2 receptor (V2R) is a G-protein Coupled Receptor (GPCR) selectively expressed in the kidney. V2R is located at basolateral membrane of principal cells of the distal nephron and thick ascending limb cells and in response to circulating levels of vasopressin (AVP), promotes sodium and water reabsorption. Ectopic expression of V2R plays a role in clear cell renal carcinoma (ccRCC). A recent study shows that tolvaptan, a V2R-antagonist, inhibits cancer growth in an experimental model of ccRCC. However, polyuria remains a serious side effect, limiting the repositioning of this drug in clinical practise. Recent evidences demonstrate that ccRCC have an up regulation of the transferrin receptor 1 (TfR1). Based on this, we developed Transferrin-conjugated liposomes (TF-LPs) encapsulating tolvaptan to allow a site-specific delivery to the tumor site, in the attempt to reduce drug side effects. We performed in vitro studies to evaluate the effect of TF-LPs on cell proliferation and the immunoblotting of cyclin A2, an essential regulator of the cell cycle that participates in the regulation of S phase as well as mitotic entry.

Method: Liposome formulation and characterization. Liposomes composed of DSPC/DSPPEPEG2000/DSPPEPEG-MAL were mixed with tolvaptan and prepared by hydration of a thin lipid film, followed by extrusion. Transferrin was conjugated to liposomes at room temperature, overnight. The resulting liposomes were then purified by ultra-centrifuge (80000 rpm, 40 min, 4°C). Liposomes were characterized in terms of colloidal dimensions, polydispersity index and surface charge by dynamic light scattering (DLS) and Zeta analyzer Nano Z, Malvern, UK. Liposome encapsulation efficiency of Tolvaptan was measured by spectrophotometry (Epoth, Biotek) at the wavelength of 266 nm. In vitro studies. Caki-1 cells were cultured until the exponentially growing phase. Cells were then incubated with TF-LPs with or without tolvaptan in growth medium with 0.2%FBS for 24h. Cell viability was assessed by measuring the mitochondrial activity by the 3(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay quantified by spectrophotometry at 570nm. Cell lysate were immunoblotted and Cyclin A2 primary antibody tested as a marker of cell proliferation.

Results: The liposomes we have generated have an average diameter of about 100 nm, a low polydispersity index (<0.2) and a 50% encapsulation efficiency. MTT assay showed that, compared with control, cells treated with TF-LPs encapsulating tolvaptan have a reduction in cell proliferation. Interestingly, this reduction starts at lower concentrations and timescales than in a previous study performed with free drug. To further confirm the previous result, we also performed immunoblotting of cyclin A2 which is usually linked to cell proliferation and as such is often found expressed at a high level in human cancers. The expression level of this protein is significantly reduced when cells are treated with TF-LPs+TOLV while it remains the same in the treatment with TOLV.

Conclusion: In this study we developed and tested TF-LPs encapsulating tolvaptan with cytotoxic activity on tumor cells. The preliminary results of this study will be confirmed by subsequent in vivo studies to demonstrate the advantages of this system: site-specific delivery to the tumor site and reduction of drug side effects.
**Results:** In this in silico electrophysiological model, the resting membrane potential is maintained at $-75$ mV, as this value is cited by various experimental studies. The ionic concentrations and biophysical parameters for all ion channels are varied in the physiological ranges. Under the voltage clamp protocol, the voltage steps are increased from a holding potential of $-80$ mV to $-10$ mV with a $10$ mV step voltage. In Figure 1, the red and blue solid lines represent recorded outward KA current from the isolated USM cell under both control and applied Tamsulosin dose conditions. Figure 1 reveals that the KA current is elevated after the application of the Tamsulosin drug regarding all step voltages. As a result, the total outward current is elevated and the USM action potential duration is shortened. It is also observed that the steady-state activation curve of the KA channel is shifted to more negative after applying Tamsulosin. The USM cell is electrically less excitable with the Tamsulosin.

**Conclusion:** This first in-silico study reveals the KA ionic current, which plays a major role in coordinating ureteral contractions, is altered due to Tamsulosin. It implies that the pharmacological maneuver of Tamsulosin is substantially beneficial to treat dysfunctional peristalsis by reducing the symptoms and installation complexities from the ureteral stents procedure.

**REFERENCES**


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*Figure 1: Tamsulosin Effects in USM cell electrophysiology.*
#3475

NOVEL OPTIMISED PROTOCOL FOR ISOLATION OF PTEC AND SYSTEMATIC CHARACTERISATION FROM HUMAN KIDNEY BIOPSY

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Background and Aims: Human kidneys have a role in water homeostasis, acid-base control, reabsorption of compounds, and secretion of xenobiotics and endogenous metabolites, exposing them to substances that could cause harm. This results in an alarming number of acute kidney injuries (AKI) worldwide, estimated at 13%. Furthermore, one-quarter of hospitalised cases are due to drug-induced AKI [1]. Current methods for nephrotoxicity assays are based on animal testing and/or the use of simple human cell lines. Meta-analyses show that we can correctly predict human drug responses in only 10–50% [2]. Our work aimed to develop a novel and optimised protocol for isolating proximal tubular epithelial cells (PTEC) from human kidney biopsy to aid future research regarding AKI and nephrotoxicity studies.

Method: Isolation and cultivation of primary human adult PTEC obtained with biopsy during the regular diagnostic procedure was performed. We used a protocol consisting of micro-dissection of a tissue sample to get ∼1 mm³ fragments, enzymatic dissociation with 0.2% collagenase type 1, and use of selective culture media (Advanced DMEM/F12 with added insulin, transferrin, and selenite (all three together termed ITS), epidermal growth factor (EGF), and hydrocortisone). Light microscopy was used for morphologic characterisation. Some cells were cultured on Transwell inserts, and the transepithelial electric resistance (TEER) was measured in mature cells that formed a confluent culture. For phenotypic characterisation, several markers characteristic of PTEC were chosen [3], and immunocytochemical staining was performed using a fluorescent microscope to evaluate the PTEC phenotype.

Results: Following the described protocol resulted in isolating cells that formed first colonies after 24 h. Using light microscopy, the cells exhibited a cobblestone appearance, reached confluence after eight days, and showed dome (hemicysts) formation after 13 days. The isolated cells were marked positive using immunocytochemistry for sodium-glucose cotransporter 2 (SGLT2), multidrug-resistant protein 4 (MRP4), organic anionic transporter 1 and 3 (OAT1 and OAT3), organic cationic transporter 2 (OCT2), p-glycoprotein (p-gp), multidrug and toxin extrusion protein 1 (MATE1), and N-cadherin.

Conclusion: In this study, we developed a protocol for isolating and cultivating primary human PTEC from biopsy samples. To the best of our knowledge, we have performed the most extensive systematic characterisation following the isolation of PTEC from kidney biopsy reported to date.

REFERENCES


Figure 1: Micrographs of the stained samples: (1) for cytoskeleton (phalloidin), (2) p-gp, (3) OCT2, (4) N-cadherin, (5) SGLT-2, (6) MRP4, (7) MATE1, (8) OAT1, and (9) OAT3. For all samples, a mounting medium with DAPI was used to stain the nuclei. The magnification of all shown images is 10× (according to the manufacturer’s microscope specifications).
#4085

POLY(ADP-RIbose) POLYMERASE 1 AFFECTS THE VASOPRESSIN-MEDIATED AQP2 EXPRESSION VIA AN INTERACTION WITH BETA-CATENIN

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Background and Aims: Poly(ADP-ribose)ylation (PARylation), which is mediated by poly(ADP-ribose) polymerases (PARPs), catalyzes the transfer of ADP-ribose from NAD+ molecules to acceptor proteins, regulates diverse cellular processes. Since PARP1 gene-deficient mice revealed an increase in urine volume, we aimed to examine the role of PARP1, the most abundant type of protein in the PARPs family, in the vasopressin-mediated AQP2 regulation.

Method: 1) Immunoblotting for PARP1 in mpkCCDc14 cells; 2) Pulldown assay of biotin-conjugated NAD+ and immunoprecipitation (IP) assay using poly(ADP-ribose) (PAR) antibody; 3) qRT-PCR and immunoblotting for AQP2; and 4) Bioinformatics for elucidating PARP1-interacting proteins in kidney collecting duct (CD) cells.

Results: Immunoblots showed that dDAVP treatment (10−9 M, 2 h, 6 h, 24 h, and 48 h) induced the cleavage of PARP1 (both 89 kDa and 25 kDa) in mpkCCDc14 cells. dDAVP treatment (10−9 M, 24 h) also increased the abundance of total PARylated proteins in biotin-NAD+ pulldown and IP assay of PAR in mpkCCDc14 cells. On the other hand, siRNA-mediated PARP1 knockdown significantly attenuated the dDAVP-induced mRNA and protein abundance, suggesting a role of PARP1 in AQP2 regulation. PARP1 cleavage induced by dDAVP was not changed under PARP1 knockdown, indicating that PARP1 cleavage is unlikely to be involved in AQP2 regulation. In contrast to PARP1 knockdown, PARP1 inhibitor (PI34) did not reduce the dDAVP-induced AQP2 abundance, despite the significant decrease in the PARylation. The results suggest that dDAVP-regulated AQP2 expression is associated with PARP1 protein per se, but not with PARP1-mediated PARylation. Bioinformatics study revealed that 408 proteins interact with PARP1 in the kidney CD cells. Among them, 49 proteins were mapped on the vasopressin V2 receptor (V2R) signaling pathway. In particular, β-catenin, which is phosphorylated (S552) by dDAVP, was identified as the PARP1-interacting protein mapped on the V2R signaling. Immunoblotting demonstrated that siRNA-mediated knockdown of PARP1 was associated with decreased dDAVP-induced phosphorylation of β-catenin at S552 in mpkCCDc14 cells.

Conclusion: PARP1 is likely to play a role in vasopressin-mediated AQP2 regulation via the protein interaction with β-catenin rather than PARylation of proteins and/or PARP1 cleavage in the kidney CD cells.

Figure 1: A co-expression Venn-diagram showing differentially expressed genes (DEG) count in renal sinus fat (RS) compared with omental (OAT) and subcutaneous adipose tissue (SAT) (RS vs OAT n = 26, RS vs SAT n = 22).

#4362

A DISTINCT TRANSCRIPTOME SIGNATURE IN HUMAN RENAL SINUS ADIPOSE TISSUE – A POTENTIAL IMPORTANCE FOR RENAL DYSFUNCTION?

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Background and Aims: Previous studies have suggested that the anatomical location and function of adipose tissue (AT) is of relevance for normal as well as impaired renal function. Renal sinus AT (RSAT) is a perivascular fat compartment located around the renal arteries. The aim of this study was to perform a transcriptomic characterization of RS in comparison with omental (OAT) and subcutaneous (SAT) AT in healthy individuals.

Method: 30 kidney donors (15 men (50%), age 50 ± 11 years, BMI 25.8 ± 2.9 kg/m², eGFR 83 ± 9 mL/min/1.73 m², HOMA-IR 2.5 ± 1.1) were included in the study. RS, OAT and SAT biopsies were performed during laparoscopic unilateral nephrectomy. RNA-sequencing analyses and untargeted transcriptomics were performed. Analysis of differentially expressed genes (DEG) was employed to discover quantitative changes in expression levels between two adipose depots (RSAT) vs OAT and SAT, respectively. Gene Ontology (GO) term enrichment was used to summarize the function of genes that were differentially expressed.

Results: Paired samples of renal sinus fat (RSAT) to be compared with omental (OAT) or subcutaneous adipose tissue (SAT) were available in 26 and 22 subjects, respectively. Out of 12210 genes characterised in these AT depots, 463 genes (3.7%) were uniquely expressed in RS when compared to both OAT and SAT (co-expression Venn-diagram in figure 1). In addition, DEG analyses showed that 1639 genes had higher, whereas 384 had lower, expression in RS than in OAT. For RSAT versus SAT the corresponding numbers were 3789 and 2534, respectively. Among the gene that were differentially regulated, the following pathways were most significantly enhanced in RSAT compared to OAT or SAT (figure 2): chemotaxis and cell migration (e.g. cell and leukocyte chemotaxis and leukocyte migration), and immune response (e.g. T-cell activation, immune response-activating signal transduction, adaptive immune response). Conversely, ATP synthesis (e.g. oxidative phosphorylation, cellular respiration, mitochondrial complex) and extracellular matrix pathways were significantly attenuated in RS compared to SAT and OAT, respectively (not shown). A targeted analysis of specific gene markers that have previously been reported to be associated with chronic kidney disease (CKD) showed that AT expression of pro-inflammatory factors such as visfatin, IL-6, IL-11, IL-1α and IL-18 were higher in RSAT vs SAT or OAT (not shown). In addition, the expression of some genes, differently regulated in RSAT, and known to associated with progression of CKD, e.g. Fc Gamma Receptor Ila (FCGRIIa), NF-kappa-B inhibitor beta (NFKBIB), Nuclear Factor, Erythroid 2 (NFE2) and Oncostatin M (OSM), were positively correlated with BMI (data not shown).

Conclusion: This study in healthy kidney donors indicates that the transcriptome signature of renal sinus AT seems to be distinct from subcutaneous and omental AT. Gene ontology analyses pointed towards an inflammatory environment and lower mitochondrial function in the renal sinus compared to other adipose tissue depots. These findings are likely to define depot-specific AT functions that may be of importance for renal function and disease.

Figure 2: Gene Ontology (GO) term enrichment of the differential expressed genes (DEG) that were most significantly upregulated in renal sinus fat (RS) versus omental (OAT) and subcutaneous adipose tissue (SAT) (RS vs OAT n = 26, RS vs SAT n = 22).
MOLECULAR AND FUNCTIONAL CHARACTERIZATION OF THE PERITONEAL MESOTHELIAL AND ENDOTHELIAL CELL BARRIER

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Background and Aims: Solute transport across cellular levels is mediated by paracellular and transcellular pores, channels and carriers. Knowledge on their cell specific expression, regulation and function in peritoneal dialysis (PD) is limited.

Method: Polarized primary (HPMC) and immortalized human peritoneal mesothelial (MeT-5A), microvascular (HCMEC) and umbilical vein endothelial (HUVEC) cells underwent RNA sequencing and gene enrichment analysis. Key findings were confirmed by western blotting (WB), confocal and single molecule localization microscopy (SMLM). Arteriolar transcriptome and proteome datasets of non-CKD, CKD5 and PD children (n = 6/group) underwent targeted transport pathways analysis. Key transporter proteins were quantified in parietal peritoneum (n = 20–30/group) and related to peritoneal transport rates available in 23 children. Barrier function was studied in vitro (transepithelial electrical resistance, TER, and molecular weight dependent flux), ex vivo and in vivo.

Results: Junction, transmembrane and transcytotic transporter expression was highly cell type specific on RNA and protein level. Sealing Claudin (CLDN5) was only expressed in mesothelial cells, sealing CLDN5 in endothelial cells. TER which reflects functional junction status, was 50% lower in HCMEC compared to HUVEC and the two mesothelial cell lines; 4- and 10-kDa dextran permeability was higher in HCMEC. At nanoscale, SMLM yielded highest distance of junction molecules in HCMEC and different spatial organisation, reflecting the low TER. In sheep peritoneum, removal of the mesothelium abolished tissue TER. In mice, short-term LPS exposure to modify mesothelial permeability resulted in faster transperitoneal 4- and 70-kDa dextran transport, suggesting a specific barrier function of the mesothelium. In human parietal peritoneum, total endothelial surface area per section was age dependently 1.5- to 2-fold higher than the respective mesothelial surface area, and further increased with double-chamber PD fluid, due to major hypervascularisation. Tight junction proteins CLDN-1 to -5, and -15, ZO-1, occludin and tricellulin, and transcellular transporter ENaC, PIT1, and SGLT1 were detected in mesothelial and arteriolar endothelial cells. In CKD mesothelial CLDN-1 and arteriolar CLDN-2 and -3 were more abundant than in non-CKD controls, and PD patients had highest mesothelial and arteriolar CLDN-1 and mesothelial CLDN-2, lower mesothelial and arteriolar claudin-3 and lower arteriolar ENaC. D/P creatinine and D/D0 glucose correlated with arteriolar CLDN-2 and with mesothelial CLDN-4 and -15, which are pore forming junctions, and for creatinine with mesothelial PIT-1, a sodium/phosphate co-transporter.

Conclusion: We provide the first in-depth analysis of peritoneal determinants of solute transport. The molecular expression pattern of the mesothelial and endothelial cell barrier and transporter proteins differs substantially. Disruption of the mesothelial layer increases peritoneal solute absorption rate. In the human peritoneum, peritoneal transporter status is modified by CKD and PD, and pore forming junction proteins are associated with dialytic solute transport function. These represent a promising target for therapeutic intervention.

REDUCTION OF SUBACUTE LEAD INDUCED PARATHORMONE LEVELS FOLLOWING ANTIOXIDANTS OR VITAMIN D/CALCIUM ADMINISTRATION IN RATS

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Background and Aims: Lead (Pb) is a toxic heavy metal; exposure is associated with many diseases. Accordingly, the World Health Organization considers Pb one of 10 chemicals of major public health concern. Experimental evidence suggests that Pb exposure induces both structural and functional kidney alterations. Epidemiological studies on lead exposed workers, show alteration on calcium metabolism (reduction in serum calcium, phosphorous and vitamin D and increase level of PTH) that increases with exposure length. Two of the suggested molecular mechanism of lead toxicity are: protein binding sites competition with endogenous cations such as calcium or zinc and the production of free radicals. The aim of this work is to analyze the effect of lead exposure, the therapeutic administration of antioxidants (melatonin or silymarin) or VitD +Ca and its potentially beneficial effect on calcium metabolism.

Method: Male Wistar rats (150–180 g body weight) of 6 weeks of age were housed in groups of three in standard cages with free access to water and food (Rodent Lab Standar Diet), under a 12/12 hour light/dark cycle, C, control: untreated rats not exposed to Pb or treatment; Pb, exposed to Pb for 1 month and assessed immediately; Pb 1NT, exposed to Pb for 1 month followed by 1 month without any treatment; Pb 1TM, exposed to Pb for 1 month followed by 1 month of melatonin treatment; Pb 1TS, exposed to Pb for 1 month followed by 1 month of silymarin treatment; Pb 1TVDca, exposed to Pb for 1 month followed by 1 month of VitDca treatment. M, melatonin (10 mg/kg/body weight/day dose), S, silymarin (200 mg/kg/body weight/day dose) or total amount of VitD (232 IU/Kg/day) and Calcium 299 mg/Kg/day received from diet and therapeutic regimen were equal to 1.8 fold the daily requirement of VitD 800 IU/Kg/day and Calcium 1000 mg/Kg/day. Chemicals: Lead acetate trihydrate, Pb(CH3CO2)2.3H2O purity 99.99% from Sigma 215902, Melatonin Sigma M5250 98% TLC, VitaminD3 ampoules (100 000IU/mL), vitamin D oral ampoules (100 000IU/2 mL) from TRB Lab. Rat parathyroid PT Elisa Kit CUSBIO, 25-hydroxy Vitamin D3 ELISA Kit (Colorimetric) Kit NOVUS

Results: Blood Lead Levels There were statistical differences between the control group and all other groups P<0.0001. The group exposed to Pb for 1 month without any subsequent treatment (Pb 1NT) show differences in BLL with rats exposed to Pb and subsequently treated with antioxidant or VitD therapy and with the group immediately assessed after lead exposure. BLL were all in µg/dL C 2.3, Pb 11, PbNT14.15, PbTM 10.28, PbTS 10.23 and Pb VDca 10.18 Vitamin D Blood Levels Interestingly the highest mean vitamin D blood level was found in rats exposed to Pb for 1 month followed by 1 month of VitDca therapy (Pb 1TVDca) and the lowest mean value was found in rats exposed to Pb for 1 month and assessed immediately (Pb). Pb Blood Levels Pb blood levels were increased in rats exposed to Pb without any other treatment, whether assessed immediately after exposure or after one month. All therapies reduced blood Pb under control levels. Conversely a negative moderate correlation was found between blood levels of PTH vs. VitD r = −0.533 and r² = 0.2843 P (two tailed) = 0.002.

Conclusion: All therapies using the antioxidants (melatonin or silymarin) or VitD+Ca supplementation reduced the lead induced increase in parathorome levels in rats.

Abstracts

#5837
#6057
In mechanistic studies, ISx upregulated mRNA levels of hairy and enhancer of markers were recovered by AHR antagonist and knockdown (KD) of antagonist CH223191, while downregulated gene expressions of osteogenic The ISx-induced mineralization defects of BMSCs were counteracted by AHR μM significantly downregulated mineralization of BMSCs, particularly in the early stage of osteogenesis. ISx-induced AHR upregulated Hes1, which inhibited expressions of not only Runx2, but also BMP2, which has not been published before. A study of the underline signal transduction pathways relevant to the AHR genomic control system may provide potential therapy for low bone formation in early CKD.

**Conclusion:** ISx under clinically relevant concentrations attenuated mineralization of BMSCs, particularly in the early stage of osteogenesis. ISx-induced AHR upregulated Hes1, which inhibited expressions of not only Runx2, but also BMP2, which has not been published before. A study of the underline signal transduction pathways relevant to the AHR genomic control system may provide potential therapy for low bone formation in early CKD.

**Method:** Mineralization of D1 cells (mouse BMSCs) was evaluated by alizarin red S staining (ARS). The mRNA expressions and protein levels of osteogenic markers including Runx2, BMP2, ALP, and osteocalcin were determined by quantitative real-time polymerase chain reaction (RT-PCR) and western blotting. AHR translocation into the nucleus was evaluated by an immunofluorescence confocal microscope. Reporter gene assays were adopted to study the transcriptional regulation of Runx2 and BMP2. Results: ISx at concentrations <50 μM significantly downregulated mineralization of BMSCs with the most influence in the early stage of osteogenesis. ISx decreased the mRNA expressions and protein levels of osteogenic markers Runx2, BMP2, ALP, and osteocalcin. ISx of 50 μM induced AHR translocation into the nucleus and upregulated AHR target genes CYP1a1 and CYP1b1. The ISx-induced mineralization defects of BMSCs were counteracted by AHR antagonist CH223191, while downregulated gene expressions of osteogenic markers were recovered by AHR antagonist and knockdown (KD) of AHR. In mechanistic studies, ISx upregulated mRNA levels of hairy and enhancer of split (HES1), which is a primary target of NOTCH signaling. Although there were no significant differences in expressions of Notch1~4, the upregulated Hes1 was attenuated by the antagonist and KD of AHR, which indicated that Hes1 was directly regulated by AHR. We identified putative binding sites of transcription repressor Hes1 in the promoter area of BMP2 and Runx2. Following experimental treatment of ISx, expression levels of BMP2 and Runx2 monitored by reporter assays were downregulated, which indicated that Hes1 plays as a transcription repressor to downregulated BMP2 and Runx2.

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**Method:** Mineralization of D1 cells (mouse BMSCs) was evaluated by alizarin red S staining (ARS). The mRNA expressions and protein levels of osteogenic markers including Runx2, BMP2, ALP, and osteocalcin were determined by quantitative real-time polymerase chain reaction (RT-PCR) and western blotting. AHR translocation into the nucleus was evaluated by an immunofluorescence confocal microscope. Reporter gene assays were adopted to study the transcriptional regulation of Runx2 and BMP2. Results: ISx at concentrations <50 μM significantly downregulated mineralization of BMSCs with the most influence in the early stage of osteogenesis. ISx decreased the mRNA expressions and protein levels of osteogenic markers Runx2, BMP2, ALP, and osteocalcin. ISx of 50 μM induced AHR translocation into the nucleus and upregulated AHR target genes CYP1a1 and CYP1b1. The ISx-induced mineralization defects of BMSCs were counteracted by AHR antagonist CH223191, while downregulated gene expressions of osteogenic markers were recovered by AHR antagonist and knockdown (KD) of AHR. In mechanistic studies, ISx upregulated mRNA levels of hairy and enhancer of split (HES1), which is a primary target of NOTCH signaling. Although there were no significant differences in expressions of Notch1~4, the upregulated Hes1 was attenuated by the antagonist and KD of AHR, which indicated that Hes1 was directly regulated by AHR. We identified putative binding sites of transcription repressor Hes1 in the promoter area of BMP2 and Runx2. Following experimental treatment of ISx, expression levels of BMP2 and Runx2 monitored by reporter assays were downregulated, which indicated that Hes1 plays as a transcription repressor to downregulated BMP2 and Runx2.

**Conclusion:** ISx under clinically relevant concentrations attenuated mineralization of BMSCs, particularly in the early stage of osteogenesis. ISx-induced AHR upregulated Hes1, which inhibited expressions of not only Runx2, but also BMP2, which has not been published before. A study of the underline signal transduction pathways relevant to the AHR genomic control system may provide potential therapy for low bone formation in early CKD.
dehydrated, with no other noticeable findings. Blood lab tests showed a serum creatinine \( (\text{Cr}) \) of 2.86 mg/dL (baseline 1.10 mg/dL, estimated glomerular filtration rate of 72 mL/min/1.73 m\(^2\)), a corrected serum total calcium (sCa) of 16.0 mg/dL and a normal serum phosphate of 4.0 mg/dL. The patient was admitted in the oncology ward with the collaboration of the nephrology department and was started on fluid therapy with 3000–4000cc NaCl 0.9%/day for a target urinary output of 75–200 mL/h. Hypercalcaemia work-up showed low PTH of 8.8 pg/dL (reference range: 12–69 pg/dL). Measurement of PTHrP and 1,25(OH)\(_2\)D were requested but took longer. After 3 days, despite the improvement of both sCr 2.23 mg/dL and sCa 13.6 mg/dL, zolodreric acid was started. Results revealed an increased 1,25(OH)\(_2\)D of 309 pg/dL (reference range: 10.9–79.3 pg/dL) and negative PTHrP. At the 6th day, a clear improvement of analytical (sCr 1.60 mg/dL; sCa 11.9 mg/dL) and clinical status, so the patient was discharged. The diagnosis was GIST 1,25(OH)\(_2\)D overproduction causing malignant hypercalcaemia and prednisolone on 20mg id was started. In June 2022, the patient had tumour progression, presenting lethargic, disoriented, and dehydrated; blood lab results showed AKI (sCr 197 mg/dL) and worsening hypercalcaemia (SCa 14.7 mg/dL). He was admitted for fluid therapy and bisphosphonates but, even though there was a recovery of the hypercalcaemia and renal function, the patient’s clinical status got worse and he had a fatal outcome in the following days.

Conclusion: Malignant hypercalcaemia caused by GIST 1,25(OH)\(_2\)D overproduction is a rare condition. The work-up of an oncological patient with ureteral obstruction is a rare condition. The work-up of an oncological patient with ureteral obstruction.

### LYMPHOCYTE SENESCENCE: A CROSS-SECTIONAL STUDY COMPARING SYSTEMIC LUPUS ERYTHEMATOSUS AND END STAGE RENAL DISEASE

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Background and Aims: Immunosenescence, as a consequence of ageing or chronic inflammation, encompasses a spectrum of lymphocyte characteristics, including the presence or absence of certain lymphocyte surface molecules. Aim of the present study was to evaluate the immunosenescent effect of two different forms of chronic inflammation, Systemic Lupus Erythematosus (SLE), a chronic autoimmune disease and end stage renal disease (ESRD), a chronic inflammatory disorder.

Method: Certain lymphocyte surface molecules, including CD31, CD45RA, CCR7, CD28, CD27, for T, and IgD, CD27 for B lymphocytes, were analyzed by flow cytometry, and distinct naïve, active and senescent lymphocyte subtypes were determined, in SLE and ESRD patients. Results were compared to healthy controls (HC) of similar age, sex and nationality.

Results: Lymphopenia was significant in both SLE and ESRD patients, compared to HC, affecting B cells 75.1(14.4–52.0)% of HC, 97(32–341) and 214(84–576) cells/\(\mu\)L, respectively, \(P < 0.0001\), and CD4+ cells 651.2(71.1–1478.2), 713(234–1509) and 986(344–1591) cells/\(\mu\)L, respectively, \(P < 0.0001\). The allocation of B cell subpopulations was remarkably different between SLE and ESRD patients, with the SLE showing a clear shift to senescent (IgD--CD27-) 11.75(2.3–74.2)% vs. 8.1 (1.7–35), and ESRD patients, to naive subpopulations, compared to HC: 69.9(1.1–92)% vs. 62 (4.3–86.9)%), \(P = 0.019\). Instead, senescent subtypes of CD4+ lymphocytes were reduced in SLE, compared to ESRD and HC, 3.2 (0.1–42.2)% 6.0 (0.4–56.4)% and 3.5 (0.3–19.5)% for CD4+CD28null cells and 1.2 (0.1–23.9)% 2.5 (0–51.9)% and 1.9 (0–17.9)% for CD4+CD28-CD57+ cells. CD8+ lymphocyte subtypes presented a complete redistribution, in favor of CD8+CD45RA-CCR7+ (central memory), CD8+CD45RA+CCR7+ (naïve), and 53.1(1.8–92.4)%, 52.2(0.1–91.5)% and 23.4(0.1–92)% respectively, and lowering the terminally differentiated populations (CD57+CD28null) 7.8 (0.2–54.4)% and 12.8(0–71.6), respectively. CD8+CD28null cells were significantly reduced in SLE, compared to ESRD and HC, 31.9(1.1–87.2)%, 44.4(14–89.7)% vs. 34.5(6.4–72.3)%, respectively, \(P = 0.04\).

Conclusion: Senescent phenotype of B lymphocytes predominated in SLE patients, while ESRD patients showed a completely different profile, with increased senescence involving mainly CD8+ lymphocytes.

### EFFECTS OF COMMON OSMOLYTES ON THE EXPRESSION OF FOXP3 SPLICE VARIANTS IN HUMAN PBMCs

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Background and Aims: Regulatory T cells modulate autoimmune and allogenic responses in glomerulonephritis and transplantation. The two most abundant fork-head box P3 (FOXP3) splice variants, full-length FOXP3 (FOXP3-FL) and FOXP3 lacking exon 2 (FOXP3-Δ2), confer suppressive ability to regulatory T cells. Some studies showed a weaker suppressive ability of FOXP3-Δ2. Renal organic osmolites, urea and Trimethylamine N-oxide (TMAO), play critical roles in the hyperosmotic renal environment with high concentrations of Na+ and glucose. However, the effects of these osmolites on FOXP3 splice variants in peripheral blood mononuclear cells (PBMCs) remain unclear. The aim of this study was to evaluate the effects of common osmolites on the expression of FOXP3 splice variants in human PBMCs.

Method: PBMCs were isolated from the blood of healthy donors using ficoll density gradients and cultured in RPMI-1640 with or without additional osmolites at 37°C. A part of PBMCs were activated with 25ng/ml Phorbol-12-myristate-13-acetate (PMA) and 1ug/ml ionomycin (PMA-IONO), FOXP3-FL and FOXP3-Δ2 mRNA were detected by qPCR after 4hrs’ incubation, using specific primers. The relative expression value was calculated by the formula of \((1+E^\beta Ct)/(1+E^\beta Ct))\) Ct (target gene). Values are given as the mean±S.E.M. Statistical significance was determined by One-Way ANOVA with Post Hoc Test, using Graphpad Prism 9. A P-value <0.05 was considered significant.

Results: The cell viabilities after 4 hours’ incubation were all above 90%. PMA-IONO significantly increased the relative expression of both FOXP3-Δ 2 (from 0.001051 to 0.001609, \(P = 0.0289\), \(n = 5\)) and FOXP3-FL (from 0.001024 to 0.001684, \(P = 0.0101\), \(n = 5\)) (Figure 1). However, increased concentrations of urea (from 5mM to 50mM) had no effect on either of the two FOXP3 splice variants (\(P > 0.05\), \(n = 5\), Figure 1). TMAO of 4mM significantly reduced FOXP3-FL in the PMA-IONO-activated PBMCs from 0.001605 to 0.0007208 (\(P = 0.0051\), Figure 2). However, TMAO didn’t affect FOXP3-FL expression in non-activated PBMCs and had little effect on FOXP3-Δ2 expression either (\(P > 0.05\), \(n = 4\)). On the other hand, compared with control group, the high concentration of glucose (25mM) significantly increased the expression of FOXP3-Δ 2 from 0.002815 to 0.003461 (\(P = 0.0375\), \(n = 3\)) in non-activated PBMCs (Figure 2). The high concentration of NaCl (147mM) had no significant effect on either of the FOXP3 splice variants (\(P > 0.05\), \(n = 3\), Figure 2). Furthermore, the equal osmolality of mannitol didn’t affect the mRNA expressions of FOXP3 splice variants, either (\(P > 0.05\), \(n = 3\), Figure 2). But compared with glucose group (0.003461), the expression of FOXP3-Δ 2 was significantly lower in mannitol group (0.002785) (\(P = 0.0479\), \(n = 3\), Figure 2). It suggested that the effect of high glucose in non-activated PBMCs was independent of the osmolality change.

Conclusion: In isolated human PBMCs, PMA-IONO increases both FOXP3-Δ 2 and FOXP3-FL expressions. PMA-IONO-induced FOXP3-FL increase can be inhibited by TMAO. Urea and NaCl had little effect on FOXP3 splice expressions. High concentration of glucose increases FOXP3-Δ 2 mRNA in non-activated PBMCs, which was independent of the osmolality change.

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Figure 1: Expressions of FOXP3-Δ 2 (Exon 2 deleted) mRNA (A) and FOXP3-FL (full length) mRNA (B) in human peripheral blood mononuclear cells (PBMCs) without (Control) or with the presence of PMA, ionomycin (IONO) and different concentrations of urea in RPMI-1640 at 37°C for 4 hours. Values are given as the mean±S.E.M. N=5. Statistical significance was determined by One-Way ANOVA with LSD Post Hoc Test. A P-value < .05 was shown.

Figure 2: Expressions of FOXP3-Δ 2 (Exon 2 deleted) mRNA (A) and FOXP3-FL (full length) mRNA (B) in non-activated human PBMCs without (Control, the concentration of glucose and NaCl is 11mM and 140mM respectively) or with addition of glucose (25mM in total), NaCl (147mM in total) or mannitol (14mM). Values are given as the mean±S.E.M. N=3. Statistical significance was determined by One-Way ANOVA with LSD Post Hoc Test. A P-value < .05 was shown.

#3500
CENTRAL DIABETES INSIPIDUS ASSOCIATED WITH ACUTE MYELOID LEUKEMIA
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Background and Aims: Central Diabetes Insipidus (CDI) is a rare condition in which there is decreased release of antidiuretic hormone (ADH) from the posterior lobe of the pituitary gland resulting in polyuria. CDI is most commonly idiopathic with other known causes being primary or secondary tumors, cranial nervous system (CNS) infiltrative diseases, head trauma or neurosurgical procedures. Acute Myeloid Leukemia (AML) is rarely associated with CDI. We report a case of elderly male patient with recently diagnosed AML who developed polyuria due to CDI.

Method: Review of medical literature and hospital patient case workup based on reviewed medical literature.

Results: A 78-year-old male patient diagnosed with acute myeloid leukemia was started on treatment with Decitabine and Venetoclax 4–6 weeks prior to his hospitalization with chief complaints of back pain and oropharyngeal mucositis. The patient was also noted to have significant polyuria with hypernatremia during his hospitalization. His urine output ranged around 6–7 liters per day and his serum sodium levels were noted to be elevated to 162 mmol/L. 24-hour urine osmolality was calculated at around 1700 milliosmoles/day. Though patient’s initial labs were suggestive of osmotic diuresis as a cause of his polyuria from ongoing hyperosmolar IV fluids input and significant increased oral dietary osmolar input, his polyuria persisted despite decreased total daily osmolar input. Further investigation with desmopressin suppression testing was notable for doubling of his urine osmolality with 10 mcg intranasal desmopressin administration with urine osmolality reaching to a peak of 447 mOsm/kg, indicating CDI as a reason for patient’s ongoing polyuria. Patient’s urine output as well as hypernatremia improved with initiating the patient on daily Desmopressin. MRI head with and without contrast ruled out any intracranial masses or infiltrative CNS diseases.

Conclusion: The pathogenic mechanism for association between CDI and AML is not completely clear, but it is thought to be secondary to infiltration of the central nervous system with leukemic cells, especially Sella Turcica, though this may not be evident on CNS imaging studies in all the cases, like in our patient. Polyuria can present in patients with AML either before or after the diagnosis of AML and sometimes it might be the only presentation in patients with AML which would lead to further workup and diagnosis of AML.
Early identification of CDI in these patients lead to prompt management and avoidance of any significant electrolyte imbalances which could be sometimes attributed to patient's chemotherapeutic agents rather than to the patient's disease process itself.

**#3508**

**FUROSEMIDE DECREASES KYNURENIC ACID SYNTHESIS IN RAT KIDNEY IN VITRO**

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**Background and Aims:** Loop diuretics are highly potent agents, particularly beneficial in patients with impaired kidney function or heart failure exacerbation. Furosemide, due to fast onset and short time of action, remains the most commonly used drug from this class of diuretics. Inhibition of sodium-potassium-chloride cotransporter (NKCC2) in the thick ascending limb of Henle's loop is the main mechanism of furosemide's action. Other effects of furosemide, like modulation of potassium channels activity or activation of prostaglandin synthesis, were previously described. It was postulated that furosemide may exacerbate kidney injury in a dose dependent manner. Kynurenine acid (KYNA) is a tryptophan derivative synthesized from L-kynurenine (L-KYN) by kynurenine aminotransferases (KATs). KAT I and KAT II are the main KAT isoenzymes. Non-selective antagonism towards ionotropic glutamatergic receptors, as well as activation of aryl hydrocarbon receptors and the α7 nicotinic acetylcholine receptors are known mechanisms of KYNA's action. KYNA was shown to regulate water and electrolyte balance through natriuretic effect. By some researchers KYNA, together with other tryptophan metabolites, is classified as uremic toxin. We aimed to analyze the influence of furosemide, widely used loop diuretic, on KYNA's synthesis and the activity of both KATs in rat kidney in vitro.

**Method:** The influence of furosemide on KYNA's production with KAT I and KAT II activity was tested in rat kidney homogenates in vitro after 2 hours incubation in the presence of KYNA precursor L-KYN and furosemide. Diuretic was examined at increasing concentrations: 1 μM, 10 μM, 50 μM, 100 μM, 500 μM and 1 mM. Enzymatic KYNA's production was measured by high performance liquid chromatography (HPLC) with fluorometric detector. All applicable international, national and institutional guidelines for the care and use of animals were followed.

**Results:** Furosemide at 500 μM and 1 mM lowered KYNA formation in kidney homogenates in vitro to 80% (p < 0.05) and 70% (p < 0.05) of control value, respectively. At 1 mM concentration furosemide inhibited kidney KAT I activity in vitro to 38% (p < 0.01) of control value. Similarly, furosemide at 500 μM and 1 mM concentration decreased kidney KAT II activity in vitro to 53% (p < 0.01) and 18% (p < 0.001) of control value, respectively.

**Conclusion:** Our study presents a novel mechanism of action of furosemide. Inhibition of KYNA synthesis in the kidney by furosemide may have influence on kidney function.

**#6679**

**ANALYSIS OF MACROPHAGE POPULATIONS IN THE KIDNEY WITH RENAL TUBULAR CELL-SPECIFIC SENESCENCE INDUCTION**

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**Background and Aims:** Ageing is a risk factor for multiple diseases, including kidney disease. To improve quality of life, pharmaceutical treatments are given to ageing patients, often with side-effects and cross-reactions. Research is needed into the effects and mechanisms of ageing in order to identify new druggable targets to improve quality of life. Cells can become senescent with age and are seen at sites of tissue injury. Senescent cells (SCs) undergo irreversible cell-cycle arrest, but remain metabolically active, producing a range of signalling molecules called the senescence associated secretory phenotype (SASP, made up of pro-inflammatory/fibrotic elements). Senescent cells within the kidney post-acute kidney injury (AKI) may be involved in ongoing damage, leading in some cases to chronic kidney disease (CKD), possibly due to interactions with macrophages. We hypothesise that the recruitment of monocytes/macrophages by senescent cells is due to the signalling components present in their SASP.

**Method:** Pax8 is renal tubule marker. We use Pax8-creERT2;mdm2 fl/fl mice to study kidney-specific senescence induction in absence of age/injury. Upon administration of tamoxifen, the mdm2 alleles are floxed out by cre recombinase, allowing p53 to stabilise and activate the p21CIP1 cell-cycle inhibitor, inducing senescence in Pax8+ kidney-specific cells. The use of an endogenous tdTomato reporter allows visualisation of cells undergoing successful recombination upon the administration of tamoxifen (TAM).

**Results:** As expected, cell-cycle inhibitor/SC marker, Cdkn1a was upregulated by qPCR in TAM-treated young murine whole kidneys 10-fold compared to controls (p = 0.0173) (Figure 1). Ccl2 (monocyte chemoattractant) was up-regulated 20-fold in young (p = 0.0405) TAM-treated TG mice vs controls (Figure 1). In agreement with an increase of Ccl2 transcripts, there was a significant increase of renal macrophages as quantified by flow cytometry of kidney digests (p = 0.0141) in TAM treated young TG mice. Immunofluorescence staining of transgenic mice revealed an increase of Iba1 positive macrophages, correlated with staining of tdTomato tubules, suggesting that increase in macrophage numbers was in response to senescence induction (Figure 2). Iba1-p21 co-stains show a increases in p21 positive cells in TAM-treated transgenic mice, evidently a result of construct activation and appear in proximity to the macrophages (Figure 2).

**Conclusion:** Apparent increases in macrophages due to the presence of senescent cells may indicate one of the mechanisms by which AKI progresses to CKD, particularly if inflammatory macrophage phenotypes are present and persist. Macrophage and monocyte populations fluctuate with age and the use of this model allows analysis of macrophage recruitment/polarisation due to senescent cell burden in the absence of age/injury and possible confounding factors, in young mice.

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**Figure 1:**
Figure 1: Indicators of senescence and incipient SASP. (A) Transcripts for cell cycle inhibitor p21\textsuperscript{CIP1} (Cdkn1a) are significantly increased in the Pax8-creERT2;mdm2 \textsuperscript{fl/fl} transgenic mice treated with tamoxifen (TAM) compared to vehicle (VEH) treated wild type (WT) mice. (B) Transcripts for the potent macrophage/monocyte chemoattractant Ccl2 are significantly upregulated compared to vehicle treated young WT mice.

Figure 2: Recruitment of macrophages, and increase of p21 positive cells in response to construct activation. In response to tamoxifen (TAM) treatment, Pax8-creERT2;mdm2 \textsuperscript{fl/fl} transgenic (TG) mice show an increase of Iba1 positive cells (macrophages – red), localised around tdTomato positive (green) tubules, not observed in wild-type (WT) mice. Senescent marker p21\textsuperscript{kip1} was also seen at higher levels in TAM treated TG mice compared to age-matched TAM treated WT mice.
#5958
VALUE OF EXOME SEQUENCING “FIRST” FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common Mendelian kidney diseases, that can progress to end-stage kidney failure. Pathological variants in PKD1 or PKD2 genes are found in about 78% and 15% respectively. Additional variants in genes such as GANAB, DNaJB11, and ALG8/5 have been identified in ADPKD. The sequencing of PKD1 by short read sequencing technics with exome capture such as Exome sequencing (ES) has been describe as technically challenging given 6 pseudogenes with more than 98% homology in PKD1 exonic regions 1 to 33. Moreover, the presence of repeated motifs and GC-rich in PKD1/2 add difficulties. We study the relevance of exome sequencing (ES) “first-hand” during autosomal dominant polycystic kidney disease.

Method: ES was performed in 684 unrelated adult patients with kidney disease from the department of Nephrology of Sorbonne University, Paris, France. Genomic DNA was extracted and exonic coding regions (37 megabases) were enriched with the Twist Human Core Exome kit, and paired-end sequenced on NextSeq500 (Illumina) machine. Sequences were analyzed with in-house and the SeqOne v1.3, 2019 pipelines according to GATK4 best practices. If necessary, co-segregation of pathological variants was studied by Sanger sequencing in relatives.

Results: Of the 684 patients, 143 had renal cysts. Pathogenic or probably pathogenic variations in the PKD1, PKD2, and DNaJB11 genes have been identified in 26 patients, all with cystic disease; with respectively 17 variants in PKD1, 6 variants in PKD2 and 3 variants in DNaJB11. In this cohort, 18.2% of the 17 pathogenic variants are reported in PKD1, and 14 (82%) are included in exons 1 to 33. All variants were eventually confirmed by Sanger sequencing without false positive. Moreover, in 5 of the 26 patients diagnosed (19%), meaningful additional genetic data have been found, falling either in CFTR, DHCNR7, HFE, F8, or ACTA2 gene.

Conclusion: ES highlights PKD1 and PKD2 pathogenic variants detection without false positive. This strategy allowed us to provide appropriate genetic counseling (CFTR, DHCNR7), as management of yet unexpected additional genetic diseases that can affect ADPKD (F8, HFE, and ACTA2) phenotype. Given these preliminary data, ES appears effective for PKD1/PKD2 variant detection, providing additional information for ADPKD management in 20% of cases.
#5885
HYPOXIA INDUCES COMPLEMENT ACTIVATION ON HUMAN KIDNEY EPITHELIAL CELLS
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Background and Aims: Ischemia-reperfusion injury is an inevitable event associated with kidney transplantation (Tx) and has a major impact on short- and long-term graft survival. Proximal tubular epithelial cells are both a source of complement during Tx and a target of complement activation. The normal kidney has a capacity to protect itself from complement activation through cellular expression of complement regulatory proteins. In this study we investigated whether hypoxia and reoxygenation increase C3 deposition and alter complement regulatory protein expression (CD46, CD59 and CD55).

Method: In vitro, HKC-8 renal proximal tubular epithelial cells were subjected to 24h of hypoxia (1% O₂) and then reoxygenated for 4h (O₂ = 21%) in the presence of 40% normal human serum. qRT-PCR was used to estimate the level of VEGF-A (as a positive control), C3, CD46, CD59 and CD55 expression. Similar analysis was performed in untreated, normoxic cells. Immunofluorescence staining was used to determine C3 deposition on the cell surface and intensity quantified by ImageJ. Experiments were repeated three times.

Results: qRT-PCR analysis of HKC-8 cells in hypoxia revealed significant increases in the expression of VEGF-A after 24h (p = 0.0113). C3 expression...
following hypoxia and reoxygenation increased insignificantly. Increased expression of CD59 with the presence of serum was observed in epithelial cells (p = 0.026). However, no significant change was seen in the expression of CD55 and CD46. Reoxygenation in human serum led to significantly greater deposition of C3 on hypoxic cells compared with normoxic HKC-8 cells (Figure 1, 2).

**Conclusion:** Our preliminary data suggests that hypoxia and reoxygenation significantly increases C3 deposition on the proximal tubular cell surface. CD59, as one of the regulators of complement activation is upregulated at mRNA level after hypoxia followed by 4h reperfusion in the presence of serum. These data demonstrate that hypoxia and reoxygenation activate complement system with upregulation of CD59 as a cell defence. However, expression of CD46 and CD55 do not change. Further study is needed to identify the impact of hypoxia on complement regulation in primary epithelial cells and kidney tissues.

### A3 - GENETIC DISEASES (INCLUDING CYSTIC DISEASES)

### #3023

**KARYOMEGALIC INTERSTITIAL NEPHRITIS SECONDARY TO FAN1 VARIANTS: CHARACTERIZATIONS AND OUTCOMES. RESULTS OF THE FAN1 STUDY GROUP**

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**Background and Aims:** Karyomegalic Interstitial Nephritis (KIN) is a rare monogenic disorder caused by biallelic variants in Fanconi Anaemia-associated Nuclease 1 (FAN1), a gene involved in DNA repair. Less than 50 cases have been reported in the literature. Affected individuals suffer from kidney and pulmonary disease and increased susceptibility to cancer. In this international study, we report comprehensive clinical and genetic data on 32 individuals with FAN1-defined KIN.

**Method:** We performed a comprehensive literature review and an online survey to compile updated data of new and published cases via the FAN1 Study Group. Data collected included genotype, age at diagnosis, initial cause of presentation, kidney progression, transplantation status, and occurrence of cancer and pulmonary disease.

**Results:** Clinical and genetic data were obtained on 32 individuals, 20 previously unpublished. A total of 27 disease-causing variants in FAN1 were identified, predominantly protein-truncating alleles (see table 1). The median age of initial presentation was 39 years (range 1–69), and 26 (81%) were males. Kidney biopsy was performed in 15 individuals, where characteristic tubular karyomegaly was observed in all biopsies. Extrarenal manifestations were observed in 13/32 (40%) individuals and included liver dysfunction (9%), respiratory disease (22%) and malignancy (9%). At last assessment, 15 (46%) individuals progressed to end-stage kidney disease at an average age of 37.2 years (range 27 to 48 years). Eight (25%) individuals received a kidney transplant at a mean age of 45.1 years (range 34 to 62 years). 25% of individuals with a FAN1 variants developed a malignancy post-transplant. Overall mortality in this group was 12.5% (n = 4). 37.5% (n = 3) of transplant recipients died. One patient died from lung cancer 2.5 years post-transplant, another died from pulmonary aspergillosis 10 years post-transplant and a third died 10 years post-transplant due to interstitial lung disease. Post infectious respiratory failure was the cause of death for the remaining non-transplanted patient.

**Conclusion:** FAN1 variants result in a high burden of kidney failure and extrarenal comorbidities in this young population group. Incidence of malignancy was almost double that which has been reported in the general transplant population. This result may suggest that careful consideration and counselling should be provided to patients with FAN1 prior to transplantation given their potential for increased risk of malignancy and respiratory failure. In this study, international collaboration has provided new clinical and genetic data for 20 cases of FAN1 not previously published adding to our understanding of the natural history of a very rare disease. Please contact michelleclince@gmail.com if you have a case that you could contribute to our survey.

### Table 1: Clinical, biological, and genetic characterization of 32 individuals with FAN1 variants.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>32</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>26 (81)</td>
</tr>
<tr>
<td>Age at initial Presentation, median (range) in years</td>
<td>39 (1 – 69)</td>
</tr>
<tr>
<td>Serum Cr at initial presentation (μmol/L), median (range)</td>
<td>176 (16 – 1229)</td>
</tr>
<tr>
<td>(27 cases) Median eGFR at initial presentation (ml/min)</td>
<td>38.5 (4 – &gt;120)</td>
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<tr>
<td>(28 cases) Kidney Biopsy, n</td>
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<tr>
<td>Megakaryotic cells seen on biopsy, n</td>
<td>15</td>
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<tr>
<td>Age at ESKD, mean ± SD, years</td>
<td>39.3 ± 14.3</td>
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<tr>
<td>Kidney transplant, n</td>
<td>8</td>
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<td>Biallelic Compound heterozygous variants: 6</td>
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Method: PEG-CZNPs were synthesized using a non-hydrolytic sol-gel reaction method. HK-2 cells were transfected with α-galactosidase A (α-GLA) siRNA for permanent cellular model of FD. For in vivo study 4-week-old male B6.129-Gla<sup>min10ld</sup> mice were treated for 48 weeks with 10mg/kg of PEG-CZNPs twice per week via intraperitoneal injection. PCR, immunoblotting, immunofluorescence assay, electron microscopy analysis, ICP-MS, biochemical and histological analysis were done.

Results: TFEB translocated to the nucleus by treatment with PEG-CZNPs. Autophagy flux was evaluated with chloroquine. Autophagy flux was enhanced by PEG-CZNPs treatment. To show whether TFEB plays the important role in autophagy flux, we transfected HK-2 cells with siTFEB. Autophagy flux significantly decreased after knockdown of TFEB with PEG-CZNPs treatment. We next assessed upper signaling pathway of TFEB by PEG-CZNPs. TFEB dephosphorylation was independent of both mTOR and ERK but GSK3β signaling pathway showed massive impact on TFEB dephosphorylation by PEG-CZNPs. PEG-CZNPs decrease intracellular globothriaosacercyamide (Gb3) accumulation and decreased the levels of Collagen type IV, αSMA and MMP9 expression in cellular model of FD. Gb3 levels were significantly reduced in the kidney tissues and the levels of Fibronectin, Collagen type 4 and αSMA was decreased by PEG-CZNPs in animal model of FD.

Conclusion: These results suggest PEG-CZNPs promote autophagy flux through GSK3β -TFEB signaling pathways, showed the beneficial effect on renal fibrosis in cellular and animal models of FD. It thus provided a new insight of the potential therapeutics on FD.

Table 1: Variables and results collected. N: number of patients. IQR: interquartile range. CKD: chronic kidney disease. ADTKD: Autosomal dominant tubulointerstitial nephropathy.
FOCAL SEGMENTAL GLOMERULOSCLEROSIS DUE TO A3243G POINT MUTATION IN THE MTDNA CODING FOR TRNALEU(UUR)

Michele Marchini¹, Valentina Blanco², Michela Ardini¹, Laura Panaro¹, Sonila Mocka¹, Matteo Trezzi¹, Nadia Chiappini¹, Francesca Lauria¹ and Davide Rolla¹

¹Ospedale Sant’Andrea, U.O.C. Nefrologia e Dialisi, La Spezia, Italy and
²Piacenza, Nefrologia e Dialisi, Piacenza, Italy

Background and Aims: Mitochondrial Diseases represent a heterogeneous set of maternally inherited diseases that arise by mutations either of the mitochondrial DNA (mtDNA) or in genes of nuclear DNA (nDNA) linked to the cell mitochondrial cross-talk. Many mutations in mtDNA that code for different genes are linked to a wide spectrum of kidney manifestations ranging from focal segmental glomerulosclerosis (FSGS), tubule-interstitial disease (TIN), nephrotic syndrome (NS), and proximal or distal tubulopathy. Renal manifestations of mtDNA disorders are poorly recognized in clinical practice and often misdiagnosed for other conditions like FSGS, Alport Syndrome, steroid-resistant nephrotic syndrome. The guanine for adenine point mutation (A–G) at position 3243 in the mtDNA has emerged as the most common mutation found in patients with FSGS often accompanied by diabetes mellitus and deafness. Focal Segmental Glomerulosclerosis, (FSGS) is the prevalent histologic finding in patients with FSGS often accompanied by diabetes mellitus and deafness. Focal Segmental Glomerulosclerosis is the prevalent histologic finding in patients with FSGS often accompanied by diabetes mellitus and deafness. Focal Segmental Glomerulosclerosis is the prevalent histologic finding in patients with FSGS often accompanied by diabetes mellitus and deafness. Focal Segmental Glomerulosclerosis is the prevalent histologic finding in patients with FSGS often accompanied by diabetes mellitus and deafness. Focal Segmental Glomerulosclerosis is the prevalent histologic finding in patients with FSGS often accompanied by diabetes mellitus and deafness. Focal Segmental Glomerulosclerosis is the prevalent histologic finding in patients with FSGS often accompanied by diabetes mellitus and deafness.

Method: A 34-year-old man presented for evaluation with recently diagnosed Type II diabetes mellitus and serum creatinine of 3.9 mg/dL with nephrotic range proteinuria (3.2 gr/die). His family history included Type II diabetes mellitus, chronic kidney disease, coronary artery disease, and hypertension. The patient medical history included hypertension, dyslipidemia, and sensorineural hearing loss which had initially developed during adolescence. Serum creatinine was reportedly elevated years before this presentation, and urinalysis showed mild proteinuria with no microhematuria, white cells, or casts.

Results: On evaluation his blood pressure was 150/90 mmHg, presented mild peripheral leg edema. Laboratory results showed serum creatinine 3.4 mg/dl (eGFR 23 ml/min), HbA1c of 7.2%, albumin 2.8 gr/dL. Urinalysis showed protein (3+), glucose (+1) and no hematuria. Urinary protein-creatinine ratio was 3 mg/g. Serum C3 and C4, immunoglobulins, liver enzymes were normal; autoimmunity tested negative (ANCA, Anti-PLA2r, Anti nuclear antibodies). A kidney biopsy was performed. Light microscopy revealed glomeruli with segmental obliteration of glomerular capillaries by collagenous sclerosis (Fig. 1). Both the Jones methenamine silver stain and Masson’s trichrome stain (Fig. 1B, C) showed segmental collagen deposition and sclerosis of glomerular capillaries. Tubular atrophy and fibrosis were also present. Immunofluorescence microscopy was negative. A diagnosis of not otherwise specified focal segmental glomerulosclerosis (NOS FSGS) was made. Interestingly electron microscopy showed mitochondrial abnormalities in the tubular cells. In particular, the cytoplasm of a tubular cell appears to be whiffed by mitochondria of enlarged size and altered shape (Fig. 2). Mitochondria appeared dysmorphic with extensive reduction of mitochondrial cristae (Fig. 2 arrows). The patient was screened for mtDNA mutations and guanine for adenine substitution (A–G) at position 3243 was detected. The patient received a diagnosis of chronic kidney disease with histological features of FSGS due to an A3243G point mutation in the mtDNA with associated diabetes mellitus and sensorineural deafness.

Conclusion: This case underscores the role of electron microscopy in identifying mitochondrial related nephropathies. Even more important is to evaluate mtDNA mutations in cases with familial FSGS, sensorineural hearing loss, cardiomyopathy and diabetes.
INTRAFAMILIAL HETEROGENEITY AND IMPACT OF FAMILY SCREENING IN PRIMARY HYPEROXALURIA TYPE 1

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Emma children’s hospital, Amsterdam UMC, Department of pediatric nephrology, Amsterdam, Netherlands

Background and Aims: Primary hyperoxaluria is a rare genetic disease, caused by an autosomal recessive mutation of the AGXT gene. Clinical variability in outcome is reported within families with primary hyperoxaluria type 1 (PH1) with identical genotypes, leading to the question which differences in the disease course between affected family members can be attributed to environmental factors and which to early diagnosis or therapy. The limited research on this subject results into prognostic challenges and leads to difficult decision-making concerning the timing of transplantation and therapy. Therefore, the objective of this study was to determine whether and to what extent intra-familial heterogeneity is present, based on a clear definition of intra-familial heterogeneity in PH1 and to analyse the impact of therapeutic intervention and early diagnosis via family screening on the prognosis of siblings.

Method: A retrospective registry study was performed using data from the OxalEurope registry. All families with PH1 were identified and analyzed. A six-point PH1 scoring system was developed to calculate the heterogeneity score within a family, based on the clinical outcome of siblings (Table 1). A score ≥2 was considered as significant intra-familial heterogeneity. Assessment of the impact of family screening was conducted by stratification of the patients based on family screening and symptoms. The Fisher-Freeman-Halton exact test, Mann-Whitney U test, Kruskal Wallis test and Kaplan Meier analysis were used for statistical testing.

Results: A total of 88 families were included in this study, including a total of 193 patients with PH1. The median (IQR) follow-up time was 7.8 (1.9–17) years. Family screening was conducted in most families (77%), although not all. Intra-familial heterogeneity was found in 38 (43%) families. A (partly) B6-responsive mutation did not lead to a significant difference in intra-familial heterogeneity score. In more than half of the families (54%), affected siblings had a better outcome than the index case and in 67% of families one or more cases of kidney failure occurred. Asymptomatic siblings had a significant better clinical outcome compared to symptomatic siblings and index cases based on clinical outcome score (p < 0.001). Kaplan-Meier analyses (Figure 1) revealed that index cases reached kidney failure at an earlier age and earlier in follow-up compared to siblings (Log-rank; p < 0.0001).

Conclusion: Intra-familial heterogeneity is found in nearly half of families with PH1. These findings confirm that intra-familial heterogeneity is present in PH1, in line with previous reports. Asymptomatic siblings found by family screening had a significant better outcome based on clinical outcome score and kidney survival, substantiating the benefit of family screening. Although the exact cause of heterogeneity in PH1 could not be identified, family screening is essential and strongly recommended since it may improve kidney survival in siblings.

Figure 1: Kaplan-Meier analysis of death-censored kidney survival by age, stratified by index case, sibling asymptomatic at time of diagnosis and sibling symptomatic at time of diagnosis. Log-rank test analysis showed a significant difference (p < 0.0001) between the groups.

Table 1: 6-point PH1 clinical outcome scoring system for calculating intra-familial heterogeneity.

<table>
<thead>
<tr>
<th>Patient type</th>
<th>1 Asymptomatic</th>
<th>2 Symptomatic (nepholithiasis/ nephrocalcinosis)</th>
<th>3 Kidney failure &gt;40 years</th>
<th>4 Kidney failure 20–40 years</th>
<th>5 Kidney failure &lt;20 years</th>
<th>6 Infantile oxalosis</th>
<th>Total follow-up (years)</th>
<th>Age last follow-up (years)</th>
<th>Heterogeneity score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1B</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.29</td>
<td>0.47</td>
<td>4*</td>
</tr>
<tr>
<td>1C</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>36.90</td>
<td>37</td>
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<td></td>
<td></td>
<td>34.00</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

U: index case is highlighted in bold.
Y: siblings of the index case.
Z: heterogeneity score of family 1 (6-2 = 4).
MT-TL1 M.3243A>G MITOCHONDRIAL DNA VARIANT DETECTED FROM WHOLE EXOME SEQUENCING CAN EXPLAIN CASES OF ADULT UNKNOWN NEPHROPATHIES
Ilia Bensouma1, Marine Dancer2, Anne-Sophie Lebre3, Laure Raymond2, Alice Doreille1, Florence Lauteri-Badin1 and Laurent Mesnard1
1APHP, Sorbonne University, Tenon Hospital, SINRA Nephrology Department, Paris, France; 2Biominis, Genetics, Lyon, France and 3APHP, Sorbonne University, Pitié-Salpêtrière Hospital, Genetics, Paris, France

Background and Aims: In a population-based study, mainly constituted of unknown nephropathies (cohort Sorbonne University, Paris, France N = 1197 patients), beyond reporting the diagnostic yield of nuclear genes, we also investigated the incidence of the mtDNA pathogenic variant MT-TL1 m.3243A>G. This variant was systematically searched from whole exome sequencing (WES) data. In retrospect, we described the renal phenotype and studied the heteroplasmy level of the mtDNA variation in urine or kidney tissues compared to its blood fraction. The prevalence of m.3243A>G has been estimated ranging from 0.08% to up to 0.25%.

Method: From September 2018, to February 2023, WES has been prospectively performed, as a first exploration of adult nephropathies of unknown origin or when a genetic renal disease was clinically suggested. As off-target result, we retrieved m.3243A>G variation in blood DNA and then determined the mtDNA heteroplasmy level respective from urine sample or kidney tissue when available with an orthogonal method.

Results: We report a molecular diagnosis in 294 over 1197 adult patients sequenced (diagnostic yield: 24%, Age 43 y/o in average). Among these 294 patients with molecular diagnoses, 48 were distinct monogenic disorders, out of which 47% accounted for 52% of the genetic diagnoses. MT-TL1 m.3243A>G pathogenic variant was detected in 1.7% of the patients (20 patients over 1197 patients). An orthogonal method confirmed the presence of m.3243A>G variant in 10 patients supporting the possibility to diagnose from blood DNA analysed by WES. In all cases, the presence of m.3243A>G had major clinical implications for the patients and their families: living related donor aborted for two patients, a molecular diagnosis in three patients with unknown nephropathies and in three patients with histological diagnosis of focal segmental glomerulosclerosis. Other mitochondrial diseases appeared less likely involved in our adult cohort (only one patient with COQ2 pathogenic variants).

Conclusion: This population-based study reinforces the place of WES as first-tier exploration for adult patients with chronic kidney disease in whom phenotypes are often poor and/or atypical. The mitochondrial genome analysis with the same assay allowed the detection of yet unsuspected MT-TL1 m.3243A>G variant in 1.7% of patients suggesting enrichment compared to current prevalence observed in other population. Our data suggest that the entity "mitochondrial nephropathy" can represent a significant part of adult unknown nephropathies.

TOlvaptan dose adjustment in ADPKD based on urinary osmolality: similar efficacy and low dropout rate
Francisco Roca Oporto1, Cristina Andrade Gómez2, Gema Montilla Cosano1, Alicia Luna Aguilara2 and José Luis Roche Castilla1
1Hospital Universitario Virgen del Rocio, Nefrología, Sevilla, Spain and 2Hospital Puntal de Europa, Nefrología, Algeciras, Spain

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disease. Tolvaptan is the only treatment that has been shown to slow disease progression. The current recommendation is to reach the maximum tolerated dose while controlling side effects such as hepatotoxicity. There are data suggesting a marked decrease in tolerability at high doses of the drug. We explored the possibility of an individualized tolvaptan dose adjustment, based on urinary osmolality (Uosm), as an indirect indicator of treatment efficacy.

Method: A single-center prospective cohort study of tolvaptan in patients with ADPKD and rapid progression, with dose adjustment according to Uosm, with dose increase if Uosm > 200 mOsm/kg. Glomerular filtration rate (GFR) estimated by CKD-EPI, Uosm, adverse effects and dropouts were analyzed.

Results: 40 patients: 35 patients with more than 2 years treatment, mean follow-up 30±6 months. Mean age 45±7 years, 82% hypertensive and 47% male.

Evolution: mean annual fall in GFR during the previous 3 years without treatment -7.24 ± 1.5 ml/min/year. Baseline GFR 51.05±12.5 ml/min and baseline Uosm 391±87 mOsm/kg. Average annual drop in GFR over 3 years with treatment -3.18±1.3 ml/min/year. Average Uosm achieved during treatment 171±47 mOsm/kg. Maximum tolvaptan dose reached 60 mg (90%) and 90 mg (10%). The adverse events recorded highlight that there were no cases of hepatotoxicity (0%). The most frequent alterations were hyperuricemia (18%) and hypernatremia (11%), but in all cases asymptomatic. Polyuria was recorded in all our patients (100%), with a median diuresis 6000 ml/day (7000-5500), but the dropout rate due to aquaretic effects was minimal, only 2 patients (5%).

Conclusion: In our series of patients, treatment with tolvaptan at a dose adapted to Uosm, seems to show a similar efficacy to the reference studies in the annual fall of GFR, with a low rate of adverse events and very low dropout rate.
ADPKD is the most common form of inherited renal disease worldwide. ADPKD care has advanced over the past decade by the identification of several clinical/genetic risk factors of progression and approval of first disease-modifying drug. Further clinical outcomes research is needed to improve patient-centered clinical care; in addition new disease-modifying therapies are in pipeline, requiring a growing need for patient enrolment in clinical trials. To advance these goals, the Italian Society of Nephrology, therapies are in pipeline, requiring a growing need for patient enrolment in clinical trials. To advance these goals, the Italian Society of Nephrology, supported by the Italian PKD Foundation (AIRP) established in 2020 the creation of a National web-based ADPKD Registry. Here we present the design of this Registry and the preliminary results.

Method: Adult patients with clinical or genotypically confirmed diagnosis of ADPKD have been enrolled in the Registry, hosted by a secure online platform including both a clinical and genetic database. Databases have modular design collecting clinical features, including demographic data, type of diagnosis, e-GFR at onset and at time of first and last nephrological referral, age at onset of hypertension (HTN) and major urological complications (UC), Total Kidney Volume (hTKV) and Mayo Imaging Classification of ADPKD, age at ESRD, use of aspecific renal-protective and disease-modifying drugs, additional risk factors for CKD progression (smoke, diabetes, NSAID), extra-renal manifestations. Genetic data collected include type of PKD1/2 variant using linear-mixed modelling.

**Table 1: Clinical characteristics of ADPKD patients enrolled in Italian Registry.**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>%</th>
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<td>female screening</td>
<td>633</td>
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<tr>
<td>incidental</td>
<td>199</td>
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<tr>
<td>for symptoms</td>
<td>98</td>
<td>10.5</td>
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<tr>
<td>age at onset (M,SD) before 35 yo</td>
<td>41.8</td>
<td>±15.5</td>
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<tr>
<td>CKD stage</td>
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<tr>
<td>III</td>
<td>257</td>
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</tr>
<tr>
<td>IV</td>
<td>113</td>
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</tr>
<tr>
<td>V</td>
<td>77</td>
<td>10.0</td>
</tr>
<tr>
<td>hTKV (M,SD) ml/m³</td>
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<td>±996</td>
</tr>
<tr>
<td>Mayo Classification</td>
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<tr>
<td>1C</td>
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<tr>
<td>1E</td>
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<tr>
<td>high</td>
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**Results:** By January 2023, the Registry had recruited 985 ADPKD patients across 21 Italian Nephrology Unit; 513 (52.1%) were females; 967 (98.2%) Caucasians. Familiar history of ADPKD was reported in 738 patients (79%). All CKD stages were represented and 105 (14.1%) patients reached ESRD (median age 57.4 ± 11.5). hTKV was available for 353 (35.9%) patients, with a median value of 1100 ± 996 ml/m³; a Mayo class of 1C or higher was found in 221 (70.4%). PROPKD score was evaluated in 162 patients, and in 50% of them it was associated with low risk of progression. A total of 191 (21.6%) were receiving Tolvaptan. Demographic and clinical characteristics are summarized in Table 1.

Genetic testing was performed in 288 patients; 111 (38.5%) had PKD1 truncating (T) variants; 66 (23.3%) PKD1 non truncating variants; 69 (24.2%) PKD2 variants. In 41 patients (14.2%) no pathogenic variants were detected. In our cohort deterioration of renal function over time, estimated using eGFR slope was significantly associated with Mayo Imaging classes, high-medium (p = 0.014). Conclusion: The Italian ADPKD National Registry is an important research tool collecting clinical and genetic information. Our preliminary data confirm that in the Italian population genotype, early onset HTN or UC, Mayo Imaging classification and PROPKD score are able to predict deterioration of GFR in ADPKD. The future empowerment of the Registry will provide a comprehensive description of clinical features and genetic variants related to ADPKD in a large cohort of Italian patients, enabling us to better understand genotype-phenotype correlation. Furthermore, the Registry could be an opportunity to identify patients suitable for future clinical trials or observational studies concerning specific aspects of the disease.
INVESTIGATION OF NOTCH PATHWAY ACTIVATION AND ITS RELATION TO GREMLIN IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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1IIS-Fundación Jiménez Díaz, Madrid, Spain, 2Facultad de Medicina UAM, Madrid, Spain, 3Institut de Investigación Sanitaria de Santiago, Santiago de Compostela, Spain and 4Fundación para la Investigación y la Innovación Biosanitaria de Asturias, Oviedo, Spain

Background and Aims: Activation of the NOTCH signalling pathway has been described in several progressive kidney diseases. Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a genetic disease caused by PKD1 or PKD2 mutations, which codify for the Polycystin-1 and Polycystin-2 proteins, respectively. ADPKD prevalence is among 1:800 and 1:1000 of live births and is characterized by fluid-filled renal cysts. During this process the production of chemokines, cytokines and growth factors by epithelial cells, interstitial fibroblasts and inflammatory cells, such as macrophages, increases, leading to end-stage renal disease (ESRD). GREMLIN has been proposed as an important mediator of chronic kidney disease in preclinical studies. In addition, urinary levels of GREMLIN may be a biomarker in any renal disease. However, there are no studies on GREMLIN in polycystic kidney disease.

Method: We have done the studies in an orthologous murine model of polycystic kidney disease (Pkd1cond/cond;Tam-Cre+/−) where we investigated the role of GREMLIN and its related mechanisms (its receptor VEGFR2 and the Notch signalling pathway) in different stages of renal cystic progression. The polycystic phenotype was induced in lactating mice by administering tamoxifen to the mother on postnatal days 10 and 11, causing a deletion in

Figure 1: (A) Correlation between eGFR slope and early onset of hypertension (HTN); (B) Correlation between eGFR slope and genotype (T = truncating, NT = non truncating); (C) Correlation between eGFR slope and Mayo Imaging Class; (D) Correlation between eGFR slope and PROPKD score.
usually in mid-adulthood. ADTKD has a progressive decline in kidney function, reaching end-stage renal disease (ESRD) as a common end-stage phenotype. Subforms, exclusively caused by a characteristic frameshift mutation, leading to MUC1-framedeleted (MUC1-fs) protein levels. MUC1-fs protein revealed a significantly shorter half-life than wildtype mucin 1, possibly due to its different cellular distribution.

**Conclusion:** Our data confirm and extend previously published information on intracellular MUC1-fs localization and regulation (Dvela-Levitt et al., Cell 2019). The protein kinetics of MUC1-fs appear quite dynamic in terms of synthesis and decay, which should argue for it being a suitable pharmacological target. Both, BRD4780 and RNA interference potently downregulate MUC1-fs. Interestingly, in primary and immortalized patient derived cells MUC1-fs localization is not confined to the early secretory pathway. Should the effect of BRD4780 be restricted to TME-derived COP vesicles, this can suggest a possible reduced effectiveness. Therefore, RNA interference may be more efficient, since it reduces MUC1-fs at an earlier stage and is not dependent on intracellular processing.

### #4297

**AN ALTERNATIVE METHOD FOR SCREENING FABRY DISEASE IN WOMEN - PARTIAL RESULTS OF A BRAZILIAN STUDY**


1 Universidade Estadual Paulista (UNESP), Postgraduate program, Botucatu, Brazil, 2 DLE, Brazil, 3 UFRN, Brazil, 4 Instituto de Medicina Integral Fernando Figueira - IMIP, Brazil, 5 UFBAM, Brazil, 6 Santa Casa de Maringá, Brazil, 7 Metta Saúde Clínica do Rim, Brazil, 8 Serviço de Terapia Renal de Ourinhos, Brazil, 9 USP, Brazil, 10 Fundação Ipy-Rim, Brazil, 11 Santa Casa da Misericórdia de Itabuna, Brazil, 12 Grupo Instituto do Rim do Paran, Brazil, 13 Universidade Federal de Goiás, Brazil, 14 Clirenal, Brazil, 15 Centro de Nefrologia de Nova Friburgo, Brazil and 16 Universidade Federal do Paraná, Brazil

**Background and Aims:** Fabry disease (FD) is a rare X-linked lysosomal storage disease that can affect multiple organs, including the kidneys. The main objective of this study was to evaluate the effectiveness of a combination of α-GAL enzyme activity and plasma levels of lysosomal α-GAL enzyme activity.

**Conclusion:** Preliminary results suggest that the combination of α-GAL enzyme activity and lysosomal α-GAL enzyme activity may be a good alternative for screening FD in women with chronic kidney disease (CKD).

### #3632

**CHARACTERIZATION AND REGULATION OF THE PATHOGENIC MUCIN1 FRAMESHIFT PROTEIN IN PATIENT DERIVED CELLS CAUSED BY ADTKD-MUC1**

Karl Knauß1, Karen Schneider1, Sonja Rehrl1, Florian Wopperer1, Mario Schiffer1, Maike Büttner-Herold2, Kerstin Amann2, Ursula Schloetzer-Schrehardt3 and Michael Wiesener4

1 University Hospital Erlangen, Department of Nephrology & Hypertension, Erlangen, Germany, 2 University Hospital Erlangen, Division of Nephrology, Erlangen, Germany and 3 University Hospital Erlangen, Department of Ophthalmology, Erlangen, Germany

**Background and Aims:** Autosomal Dominant Tubulointerstitial Kidney Diseases (ADTKD) are caused by mutations in one of at least five genes (UMOD, MUC1, HNF1B, REN and SEG61A1) and are characterized by progressive decline in kidney function, reaching end-stage renal disease (ESRD) usually in mid-adulthood. ADTKD-MUC1 is one of the most frequent subforms, exclusively caused by a characteristic frameshift mutation, leading to the de novo protein MUC1-fs. MUC1-fs is believed to play the distinct pathogenic role in terms of a toxic proteinopathy, accumulating in the early secretory pathway. The substance BRD4780 was reported to re-route MUC1-fs towards lysosomal degradation (Dvela-Levitt et al., Cell 2019), with interventional trials being in preparation. Therefore, we aimed to gain more insights into MUC1-fs temporal and spacial regulative characteristics, comparing pharmacological intervention vs. RNA interference in patient derived tubular cells.

**Methods:** Cells culture (HCK-8 cells and patient derived human urinary Primary Tubular Cells, huPTC); siRNA knockdown; Transient transfection; Immunofluorescence; immunogold electron microscopy (EM); Immunoblotting (IB); Lentiviral SV40/Large-T antigen immortalization of huPTC; Generation of a novel polyclonal MUC1-fs antibody with an independent antigen downstream of the VNTR.

**Results:** To analyze MUC1-fs protein in more detail, we generated iTCs (immortalized tubular cells) from huPTC of patients with ADTKD-MUC1. Clonal selection of cells was performed to gain immortalized clones with MUC1-fs expression. MUC1-fs mainly localizes to the secretory pathway. Co-localization was only partially observed with TMED9, which localizes to COP vesicles, being involved in protein trafficking within the early secretory pathway. TMED9 negative components of this pathway also showed MUC1-fs staining, such as the Golgi apparatus and Early Endosomes. Immunogold EM of huPTC reveals MUC1-fs expression within the ER (and secretory) vesicles. Ultrastructural analyses of biopsies by EM from ADTKD-MUC1 patients did not show specific protein accumulation, as previously described in ADTKD-MUC1 and pharmacological application of BRD4780 was performed in huPTC and iTCs, with detailed description of MUC1-fs regulation kinetics. Both approaches led to strongly reduced MUC1-fs protein levels. MUC1-fs protein revealed a significantly shorter half-life than wildtype mucin 1, possibly due to its different cellular distribution.

**Conclusion:** Our data confirm and extend previously published information on intracellular MUC1-fs localization and regulation (Dvela-Levitt et al., Cell 2019). The protein kinetics of MUC1-fs appear quite dynamic in terms of synthesis and decay, which should argue for it being a suitable pharmacological target. Both, BRD4780 and RNA interference potently downregulate MUC1-fs. Interestingly, in primary and immortalized patient derived cells MUC1-fs localization is not confined to the early secretory pathway. Should the effect of BRD4780 be restricted to TME-derived COP vesicles, this can suggest a possible reduced effectiveness. Therefore, RNA interference may be more efficient, since it reduces MUC1-fs at an earlier stage and is not dependent on intracellular processing.

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Figure 1: Pkd1 gene. Studies were performed considering different sacrifice points: at 18, 30 and 45 days. Furthermore, in urine and renal tissue from ADPKD patients, we studied the expression of GREMLIM.

**Results:** We have been able to see how in Pkd1-/- mutant mice, greml-1 renal expression (that encoding GREMLIN protein), was increased from 18 days, with a significant increase at 30 days. This increase was associated with progressive cysts expansion and detritum in renal function measured by BUN. These results were confirmed at the protein level by western blot. Immunohistochemistry revealed positive GREMLIN staining since pre-cystic tubulopelithelial cells, which remained elevated in the tubules at later times. Positive GREMLIN expression was observed in biopsy samples of cysts from ADPKD patients as well as GREMLIN protein presence in urine samples. In the polycystic model, GREMLIN induction was correlated with VEGFR2 activation in the same tubular segments. Cyst formation was associated with activation of the NOTCH pathway, characterized by NOTCH1 and NOTCH3 activation.

**Conclusion:** Thus, we can suggest that GREMLIN expression may be an important mediator of renal damage progression in ADPKD and this protein would act through the Notch pathway.

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**Abstracts**
Recogni6on of Renal Tubular Dysgenesis in Ado5lescent Ckd by Biallelic Agt Variants Required Broad Genetic Analysis

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Background and Aims: Autosomal recessive renal tubular dysgenesis (ARRTD) is a rare inherited disorder of renal (tubular) development, clinically characterized by fetal oligo-/anuria leading to oligohydramnion and Potter sequence, resulting in high mortality within the prenatal and neonatal period. Variants in genes encoding components of the renin-angiotensin system (RAS) are causative for this disorder. Herein, we report 2 European families with biallelic variants within AGT and aim to provide novel insights into disease understanding.

Method: The study was approved by our institutional ethics committee (approval number: 251_18 B). Clinical, histological and pedigree analyses were performed. Exome sequencing of a preselected gene panel (nephrop7y, 560 genes associated with renal disease) was analysed on the HiSeq System 2500 (Illumina) after enrichment by TWIST human core technology (TWIST Bioscience). Immunohistochemistry staining (IHC) and in-situ hybridization (ISH) for expression of renin were performed on kidney biopsy. In addition, renin expression was determined in primary tubular cells of the index patient by qPCR. Allele frequencies of heterozygous and biallelic predicted deleterious variants were determined by analysis of the Genomics England 100,000 Genomes Project.

Results: The first family was identified after transition from pediatric to adult nephrop7y at the University Hospital Erlangen. Initially, the male index patient of consanguineous Turkish descent presented with oligohydramnion in the prenatal period. Directly after birth (32nd gestational week) he suffered from profound hypotension, pulmonary hypoplasia and pulmonary stenosis, as well as third degree acute kidney injury leading to ICU treatment, but no need of hemodialysis. He survived the perinatal period. It is not reported if these individuals reached adulthood.

Conclusion: We hereby demonstrate two extremely rare cases, affected by biallelic variants within AGT, that survived the perinatal period and eventually led to chronic kidney disease. Since the phenotypes may be variable, a contemporary approach by broad genetic analysis is the only option to decode the genetic background in individuals with a suspected genetic disorder. Upregulation of renin in tubular cells by inactivation of AGT in the germline may drive tubulointerstitial fibrosis, which is a theoretical concern regarding ongoing targeted pharmacological approaches against AGT for arterial hypertension.

Monoallelic Ift140-related Polycystic Kidney Disease in an Italian AdPkd Cohort

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Background and Aims: Autosomal-dominant polycystic kidney disease (ADPKD) is the most common inherited renal disorder characterized by progressive bilateral renal cysts development and extrarenal phenotype, i.e. liver and/or pancreatic cysts, intracranial aneurism, hernias, mitral valve prolapse and diverticulosis. More than 90% of patients harbour heterozygous pathogenic variant in PKD1 or PKD2 genes, rarely in other cystogenes (e.g. GANAB, DNAJB11, ALG8, ALG9). Recently, NGS genetic testing protocol for ADPKD has been updated with IFT140 gene, thus the ADPKD gene panel included: ALG8, ALG9, ANKS6, DNAJB11, GANAB, IFT140, LRP5, PARN, PKD1, PKD2, PRKCSH, SEC61A1, SEC63. The new protocol has been offered to patients evaluated since January 2022 and to all genetically unresolved patients evaluated in 2021. All patients performed also multiple ligation probe amplification (MLPA) analysis of PKD1 and PKD2.

Results: In 2021 and 2022 ADPKD genes testing has been performed in 129 patients. Pathogenic variants in PKD1 or PKD2 genes were detected in 110/129 patients (85%); among the negative cases (19/129, 15%), 3 patients (P1, P2, P3) resulted heterozygous carrier of LoF variants in IFT140 gene: p.Arg307*, p.Lys1275Argfs*23 and p.Arg834* respectively. Overall 2.3% of ADPKD patients harboured IFT140 pathogenic variant; considering unresolved cases only, the prevalence was 15.7% (3/19). Segregation analysis identified the LoF variant in 3 daughters of P1 and in a son of P2. The 3 probands were diagnosed with renal disease in adulthood from fourth to sixth decade. In P1 eGFR (CKD-EPI formula) slowly declined from 104 ml/min/1.73 at onset (43 year-old) to 74.6 ml/min/1.73 at age 55. In P2 eGFR at first evaluation was 38 ml/min/1.73 (68 year-old); at last follow-up 32.9 ml/min/1.73 (73 year-old). In P3 eGFR declined from 51.7 ml/min/1.73 (55 year-old) to 42 ml/min/1.73 at age 67. Renal imaging in P1 at and P2 disclosed increased total kidney volume (TKV 1042 and 5520 cc respectively), large cysts and absence of cystic liver disease. P3 had slightly increased kidneys (TKV 447 cc) with large renal cysts and few liver cysts. Hypertension was present in 4 patients, all with adult-onset (46-60 years). Two patients had an early diagnosis of kidney stones (age 24 and 18). No macroscopic hematuria or cyst infections were reported. In accordance with ADPKD-like disease form, P1 presented inguinal hernia. Imaging data are summarized in Figure 1.

Conclusion: In this Italian cohort, heterozygous LoF variants in IFT140 gene is confirmed to be the third most common genetic cause of ADPKD spectrum disease, the prevalence being 2.3%. The major features are late onset hypertension, increased kidney volume due to large cysts and slow progressive renal failure. IFT140 gene must be included in diagnostic protocol of ADPKD patients to better define renal prognosis, therapy and familial screening.
#CLINICAL UTILITY OF GENETIC TESTING IN A KIDNEY TRANSPLANT CLINIC

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Background and Aims: Inherited kidney disease (IKD) is one of the leading causes of end-stage of kidney disease. Genetic diagnosis plays an important role in the counseling and management of kidney transplant patients or those on the waiting list, as it makes it possible to identify the cause of CKD, help in the selection of living donors, carry out genetic counseling and find out the prognosis around the graft survival and the risk of recurrence of the primary disease. The objective of the following study is to analyze the prevalence of IKD in our kidney transplant population and those on the waiting list, the phenotypic characteristics, genetic findings, and the diagnostic reclassification performed after the genetic study.

Method: This retrospective study has included all genetic test (by next-generation sequencing (NGS) until 529 genes associated with kidney disease) performance between January 2018 and January 2023 in kidney transplant patients or on the waiting list for kidney transplant at Doctor Peset Hospital, using a multidisciplinary team approach. The patients were considered for genomic evaluation if they met one of the inclusion criteria: CKD of unknown etiology, family history of CKD, glomerular disease or chronic tubulo-interstitial disease with no recognized cause, suspicion of aHUS, CKD and other extrarenal syndromic signs or with renal malformations or nephrocalcinosis. Demographic data, family burden and screening, CKD phenotype, urinary anormalities, hypertension, diabetes, results of genetic test, were analyzed.

Results: We performed genetic testing in 76 patients (43.4% women; 88% Caucasian). Median age at time of kidney failure was 37 years (range: 17–77), 62% of patients had a positive family history of CKD and 29% presented extrarenal manifestations. The majority were male patients (56.6%) and Caucasian patients (88.2%). Most patients presented with an original clinical diagnosis glomerular disease 52.6% (FSGS lesion on biopsy (8/27) and non-diagnostic histology (10/27)), followed by ciliopathy (13%), aHUS (10.5%), and chronic kidney disease of unknown cause (6.6%), tubulointerstitial nephritis (6.6%), and with congenital anomalies (6.6%). In 46 patients had a genetic diagnosis defined as finding a pathogenic or likely pathogenic gene variant that explained the patient’s kidney disease. With majority being COL4 variants (26.3%), followed by autosomal dominant polycystic kidney disease (ADPKD) (10.5%), podocytopathy and autosomal dominant tubulointerstitial kidney diseases. There were confirmed within a clinical diagnostic in 28% (above all ADPKD) and resulted in reclassification of the clinical diagnosis in 33% (above all COL4-related nephropathy) and there are more frequently a negative result if clinical diagnosis was unknown etiology, congenital anomalies or aHUS until 60%. With this data, 78% of the patients could have avoided a biopsy and 50% an immunosuppressive treatment with the diagnosis by genetic test. A genetic cause was identified by family screening in 16 families comprising 19 patients. A genetic diagnosis were more likely to have a family history of kidney disease (47.4% versus 14.5%, P < 0.001). There was otherwise no statistically significant difference in any other clinical characteristic (age at onset of kidney disease, age at kidney failure, race, hypertension, diabetes, hematuria, renal cyst or stone).

Conclusion: Our study demonstrates the clinical utility of genetic study in kidney transplants with unknown etiology or glomerulonephritis or chronic tubule-interstitial disease with no recognized cause or with positive family history of kidney disease, getting a genetic diagnosis until 60%, with a reclassification of the clinical diagnosis in a one-third. A genetic diagnosis is necessary to evaluate to kidney transplant recipients, to identify the etiology of CKD, to perform a genetic counseling and to improve patient management and prognosis.
EARLY IDENTIFICATION OF PODOCYTOPATHIES AND COLLAGENOPATHIES REDUCE UNNECESSARY MEDICATION FOR PATIENTS AND ECONOMIC BURDEN ON HEALTHCARE SYSTEM

Luigi Cirillo1,2, Becherucci Francesca1,2, Tommaso Mazzieri1, Jacopo Lomi1, Eleonora Superchi1, Valentina Raglanti1, Gianmarco Lugli2, Samuela Landini1, Viviana Palazzo1, Benedetta Mazzinghi2 and Paola Romagnani1,2

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Background and Aims: Despite the efforts to improve guidelines on genetic testing of podocytopathies and collagenopathies, data on the economic burden of these diseases on healthcare systems is lacking, and economic studies have been identified as an unmet need. The lack of awareness about the genetic etiology can often lead to unnecessary procedures and treatments. We recently showed that many non-genomic examinations could be avoided using a “genetic-fist” approach. The aim of this study was 1) to quantify the healthcare resource utilization, including medications, and financial burden on the Healthcare System for the diagnosis of patients affected by collagenopathies and podocytopathies from real-life data 2) to evaluate the possible savings considering an early genetic testing.

Method: A collaborative network of regional nephrology centers was recently established by our group. Patients referred to our tertiary hospital for genetic testing from June 2014 to December 2022 were retrospectively enrolled in the study. All patients received a diagnosis of podocytopathy or collagenopathy; the length of follow-up was considered from the onset of symptoms to the genetic testing. Direct costs (medication use, in-hospital visits, invasive procedures, blood sampling, imaging studies, hospital admissions, and genetic tests) were collected from clinical records. Costs were calculated based on the Regional Health Reimbursement System, including supplies, staff, results reporting and overheads and expressed in euros. The costs were compared with those of “genomic first” approach (a basic panel of examinations according to genetic etiology can often lead to unnecessary procedures and treatments. The resulting hyperoxaluria can cause nephrocalcinosis, urolithiasis and renal failure. Conservative treatment options such as hydration, citrate and pyridoxine aim to slow the progression of the disease with a liver transplant currently being the only curative treatment. Since November 2020 Lumasiran is approved for use in patients with PH 1. Lumasiran reduces the hepatic oxalate production by RNA interference and may hence reduce hyperoxaluria. To date there is limited real world data available on the effectiveness of the treatment with Lumasiran.

Method: This observational study looked at the outcome of Lumasiran treatment in 10 patients under the age of 18 years with genetically confirmed PH 1. The primary end point was percentage reduction in plasma oxalate in the two patients on haemodialysis and percentage reduction of urinary oxalate excretion in the patients with preserved renal function. Secondary end points were change in nephrocalcinosis, urolithiasis and renal function. The follow up time was 6 months in one patient and 12 months in the other nine patients.

Results: Four of the patients were girls and the median age at the start of treatment was 5.25 years (range 0.3-17.9 years). One of the two patients on haemodialysis showed a decrease in plasma oxalate which allowed for a reduction of dialysis frequency from 5x/week to 3x/week whilst the other patient’s dialysis had to be intensified due to worsening systemic oxalosis. In the patients with preserved renal function the median reduction of urinary oxalate was 71% (range 10–91%) after 6 months and 78% (range 61–86%) after 12 months. Two patients reached values in the age specific normal range (Matos et al.). Lumasiran was discontinued after 4 months in one patient and after 8 months in another one due to treatment failure. An improvement in nephrocalcinosis was seen in three patients and two patients showed a subjective reduction in urolithiasis. Renal function improved slightly in one patient and remained stable in the others. Injection site reactions were the only observed side effects.

Conclusion: Our data highlights the heterogeneity of the disease and treatment response to Lumasiran. Despite promising data regarding the benefits of Lumasiran 2 of 10 patients did not benefit from Lumasiran injections. Hence, it is imperative to regularly re-evaluate hyperoxaluria during treatment with Lumasiran. Ideally the data should be entered into a registry for PH 1 patients to monitor the effectiveness and side effects of this novel drug not only in the short- but also the long term.

REFERENCE

#6307

EARLY IDENTIFICATION OF PODOCYTOPATHIES AND COLLAGENOPATHIES REDUCE UNNECESSARY MEDICATION FOR PATIENTS AND ECONOMIC BURDEN ON HEALTHCARE SYSTEM

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Background and Aims: Despite the efforts to improve guidelines on genetic testing of podocytopathies and collagenopathies, data on the economic burden of these diseases on healthcare systems is lacking, and economic studies have been identified as an unmet need. The lack of awareness about the genetic etiology can often lead to unnecessary procedures and treatments. We recently showed that many non-genomic examinations could be avoided using a “genetic-fist” approach. The aim of this study was 1) to quantify the healthcare resource utilization, including medications, and financial burden on the Healthcare System for the diagnosis of patients affected by collagenopathies and podocytopathies from real-life data 2) to evaluate the possible savings considering an early genetic testing. The study enrolled 43 patients (23 female), 22 with a diagnosis of podocytopathy and 21 with collagenopathy. Four patients were followed-up by more than one nephrology department from different hospitals. The median length of follow-up was 3.5 years (range 1–33 years). 20 patients were treated with steroids, with 9 receiving more than one course, while others were treated with cyclosporine, tacrolimus, MMF, rituximab, cyclophosphamide, or abatacept. 11 patients received renal replacement therapy during the follow-up, and 2 underwent a renal transplant (one patient underwent two transplants). Each patient underwent a mean of 13 blood drawings and urinalysis (mean 4 times/year/patient), with 39 patients undergoing at least one imaging study, most commonly a renal ultrasound. 26 patients underwent a renal biopsy (5 needed more than one biopsy). On average, each patient needed 7 in-hospital visits (2 visits/year/patient). Each patient underwent one genetic test, mainly exome sequencing, with 4 patients undergoing Sanger and 11 undergoing a gene panel. The economic costs related to medication during the follow-up were 98,252 euros (mean 698 euros/patient/year). In-hospital visits cost 4,125 euros, while hospital admissions for biopsy cost in total 68,138 euros. Blood exams and urinalysis cost 68,926 and 2,560 euros, respectively (mean 532 and 31 euros/patient/year). Imaging studies cost 9,023 euros (mean 83.5 euros/patient/year), and genetic testing cost 146,000 euros (1,540 euros/patient/year) for exome sequencing, 21,398 euros for gene panels, and 2,216 euros for Sanger sequencing. In total, we recorded expenses of 3,897 (mean 83.5 euros/patient/year), and genetic testing cost 146,000 euros (1,540 euros/patient/year) for exome sequencing, 21,398 euros for gene panels, and 2,216 euros for Sanger sequencing. In total, we recorded expenses of 3,897 euros per patient per year of follow-up before the diagnosis. This was almost the amount of a basic panel of exams coupled with exome sequencing (3,878 euros); however, after the first year, the early genome sequencing approach is cost-saving since other medications and non-genomic examinations can be avoided.

Conclusion: This study highlights the substantial amount of unnecessary treatments and examinations the patients are exposed to in unsuspected genetic diseases with consequent economic impact on the Healthcare System. Early identification of these diseases can reduce this burden. These data are important for policy makers in resource allocation.
Table 1: Comparison between AS patients with and without cystic phenotype.

<table>
<thead>
<tr>
<th></th>
<th>Cystic (n = 36)</th>
<th>Non-cystic (n = 60)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>47%</td>
<td>63%</td>
<td>0.140</td>
</tr>
<tr>
<td>ADAS</td>
<td>80%</td>
<td>60%</td>
<td>0.085</td>
</tr>
<tr>
<td>Missense variants (ADAS only n = 47)</td>
<td>82%</td>
<td>48%</td>
<td>0.035</td>
</tr>
<tr>
<td>Hypertension</td>
<td>74%</td>
<td>38%</td>
<td>0.001</td>
</tr>
<tr>
<td>Age at imaging (years)</td>
<td>59 (46;65)</td>
<td>42 (33;52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR at imaging (mL/min/1.73m²)</td>
<td>42 (21;63)</td>
<td>93 (60;104)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 1: Number and proportion of patients with/without cystic phenotype stratified by age and eGFR.

An expanded phenotypic spectrum of AS has been described, including recent reports of multiple kidney cysts in affected patients. The aim of the study was to evaluate the prevalence and characteristics of renal cysts in a cohort of adult patients with AS.

Method: This retrospective study included subjects with AS followed at the Outpatient Nephrogenetic Clinic of Spedali Civili di Brescia (Italy) from 2002 to 2022 and with at least one available renal imaging study (Ultrasonography/CT scan). Genetic testing was performed by using a next generation sequencing multi-gene panel for kidney disease. Cystic phenotype was defined as the presence of ≥3 cysts in each kidney. The prevalence of renal cystic phenotype was compared between patients (pts) with AS and a group of age- and eGFR-matched pts with sporadic IgA nephropathy (IgA-N). Demographic and clinical features were compared between pts with or without cystic phenotype. Logistic regression was performed to test whether sex, age, type of variant and eGFR (CKD-EPI formula) were independently associated with the cystic phenotype.

Results: A total of 96 AS pts were studied. The pattern of inheritance was AD in the majority of the cohort (56%), XL in 25%, AR in 2% and unknown in the remaining 17%. The cystic phenotype was observed in 36 pts (38%). When compared to a matched IgA-N cohort (n = 79), the cystic phenotype was significantly more common in AS (42% in AS; 19% in IgA-N; p = 0.002). The majority of AS pts with cystic phenotype showed normal/reduced sized kidneys and multiple cortical and/or parapelvic renal cysts. Increased total kidney volume, in keeping with primary cystic kidney disease, was observed in three patients; however, pathogenic variants in known cysto-genes were excluded. At the time of renal imaging, AS pts with cystic phenotype were older and had a more marked reduction in kidney function than their non-cystic counterparts (Table 1). When stratifying patients based on age or eGFR, the prevalence of the cystic phenotype gradually increased in parallel with older age and declining eGFR (Figure 1). Independent predictors of the cystic phenotype were age (HR 1.96 [95% CI 1.31-2.94] per 10 years; p = 0.001) and eGFR (HR 0.75 [95% CI 0.64-0.89] per 10 ml/min/1.73m²; p = 0.001). Serial longitudinal ultrasounds were available for 15 cystic pts, among whom the cystic phenotype was first observed from 40 years of age onwards, at an overall median age of 59 (IQR 46–65).

Conclusion: Our data show that multiple bilateral kidney cysts, with no increase in kidney size, are frequently found in AS patients. The cystic phenotype is associated with older age and eGFR decline, suggesting that it can reflect the severity and/or duration of CKD. However, the higher frequency of cystic phenotype in AS than IgAN, the role of the collagen IV α3 to α5 chains in the basement membranes in the glomerulus and distal tubule, and the occurrence of kidney cysts in a canine model of ADAS, support a possible pathogenetic link between type IV collagen mutations and cystogenesis in AS. Finding kidney cysts should not discourage from considering the diagnosis of AS, particularly in adult patients and in the presence of familial CKD. Future prospective studies will be needed to shed light on the prognostic implications of the cystic phenotype and possible genotype-phenotype associations.
CLINICAL DIVERSITY OF STEROID-RESISTANT NEPHROTIC SYNDROME CAUSED BY TRPC6 MUTATIONS
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Background and Aims: Steroid-resistant nephrotic syndrome (SRNS) is a clinically and genetically heterogeneous disorder caused by either genetic or immunological factors or their combination. Approximately 30–40% of patients with SRNS make a fast progression to ESRD. SRNS represents the second leading cause of end-stage renal disease in individuals under the age of 25 years worldwide. More than 60 podocyte-related gene mutations have thus far been reported in monogenic SRNS. Recent studies indicate that almost 30% of patients with childhood-onset SRNS have monogenic causative variants in one of the 27 SRNS genes. Among these, a mutation in Transient Receptor Potential Canonical 6 (TRPC6) gene, encoding non-selective cation channel, accounts for 6% of familial SRNS and approximately 2% of sporadic cases. We recently detected eight patients with TRPC6 mutations in our SRNS cohort (n = 39, 21%) and found inter- and intra-familial heterogeneity of clinical phenotypes in terms of disease onset and progression.

Method: A total of 39 Japanese SRNS patients were studied according to the protocol approved by the institutional review board of each affiliation. Subjects who manifested SRNS at age one to 14-year-old with biopsy-proven FSGS were enrolled. A total of 39 SRNS patients, whose average onset of proteinuria at median age 4 (range 0.9 to 17 yr) and ESRD at median age 7 (49% of total n = 19, range 3.0 to 16.0 yr) were studied. Family history was found in 44% (n = 17), including 13 autosomal recessive, 3 dominant, and one X-linked transmission. Sixteen percent (n = 10) of the patients who underwent renal transplantation win no recurrence. Sequence analysis revealed the pathogenic variants in 62% (n = 24) of all cases. Library for whole-exome sequencing or targeted panel sequencing were prepared from genomic DNA by use of SureSelect Human All Exon V5 (Agilent) or a HaloPlex target enrichment system kit (Agilent Technologies), or Ampli-Seq (Thermo). Prepared samples were run on a HiSeq 2000, or MiSeq (illumina), or Ion PGM (thermo). The sequence reads with 101-bp paired-end reads and 7-bp index reads were mapped to the human reference sequence (hg19, GRCh38.p7). After filtering the superfluous begin variants, only variants that fulfill the “pathogenic” criteria of ACMG and/or ClinVar, Varsome were selected.

Results: Sequence analysis revealed the pathogenic variants in 62% (n = 24) of all cases. TRPC6 mutations were the most frequent cause of SRNS (n = 8), which was followed by NUP107 (n = 5), PLCE1 (n = 3), COL4A3 (n = 2), COL4A5 (n = 1), and others were identified in only single case. The eight TRPC6 mutations clustered into the two distinctive cytoplasmic domains; N-terminal ANK (Y173D, R175W, R175G) and C-terminal coiled-coil domain (p.E875V, p.R867X, p.R866Del, p.S893N, p.R895C). The p.R895C is deposited as the pathogenic in ClinVar and may be a gain-of-function. The remaining 7 variants are of unknown functions: six have not yet been deposited in ClinVar, whereas one is VUS. Four patients were de novo occurrence, three followed the dominant transmission, and one arose from gonadal mosaicism. Two index patients exhibited SRNS in early childhood (< age 3), four manifested it in childhood (age 3–12), while the remaining two developed it in adolescence (age >12). In familial cases, for example, affected ones harboring R175W or p.E875V showed a remarkable discordant age onset and disease severity.

Conclusion: TRPC6 channelopathy was found to be the most frequent cause in our SRNS cohort, of which age onset ranges from age 0.9 to 17 year. Heterogeneity of disease severity may reflect that channel activity is regulated by the mode of action (gain- or loss-of-function), the combination of channel subunit assembly, and interaction with other modifying factors. Mutations in these TRPCs are associated with relatively common kidney diseases as well as other pathologies. Further expression studies will improve our mechanistic understanding of TRP channel pathology and may help the development of novel therapeutic targets.

#5496 EVALUATION OF THE PREDICTIVE ABILITY AND CONCORDANCE OF PROGNOSTIC SCORES FOR RAPID PROGRESSION IN ADPKD: A MULTICENTER COHORT
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1Nephrology, Dialysis and Transplantation Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, 2Department of Nephrology and Transplantation, Beaumont Hospital, Dublin, Ireland, 3Royal College of Surgeons in Ireland, Department of Medicine, Dublin, Ireland, 4IRCCS Sant’Orsola-Malpighi University Hospital, Medical Genetics Unit, Bologna, Italy, 5Alma Mater Studiorum, University of Bologna, Bologna, Italy, 6School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons, Dublin, Ireland, 7Radiology Unit, S. Orsola-Malpighi University Hospital, Bologna, Italy, 8Charité Universitätsmedizin, Department of Nephrology, Berlin, Germany and 9Nephrology, Dialysis and Transplantation Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is a common cause of end-stage kidney disease (ESKD). It is characterized by the progressive development of bilateral renal cysts, resulting in enlargement of the kidney volume, hypertension (HBP), and ESKD. Recently, a position statement of the ERK-NET was published to assess indications for Tolvaptan according to 3 algorithmic criteria: total kidney volume (HTKV) and Mayo Clinic Imaging Class (MCIC), rate of decline in eGFR, and the Predicting Renal Outcome in Polycystic Kidney Disease (PROPKD) score, combining clinical and genetic variables. In this scenario, these scores (MCIC and PROPKD) are alternatively used to define rapid progressor patients. In this retrospective multicentric cohort, the primary outcome was to evaluate and improve the concordance of sensitivity and specificity of MCIC and PROPKD predictive abilities for rapid disease progression.

Method: Data from adult ADPKD patients were obtained from 3 different renal centers (Bologna, Dublin, Berlin/Leipzig). We defined rapid disease progression as individuals with eGFR slope ≥ 3 mL/min/1.73m2/yearly over 4 years (Clinical Score), or MCIC classes 1C-D-E (Image Score), or high-risk PROPKD score (7 to 9 points). Descriptive statistics were used to summarize clinical parameters. The concordance between MCIC and PROPKD was assessed using kappa statistics. In individuals with PKD1 missense variants, the REVEL score was obtained and treated as a continuous variable; score greater than 0.65 were considered ‘pathogenic’ and regarded as PKD1-truncating variants for PROPKD score calculation.

Results: We evaluated 298 ADPKD patients, demographic and clinical data are summarized in Table 1. After 4 yr of follow-up, MCIC (p = 0.041), HBP (p = 0.031), and urolological events (p < 0.001) result were statistically significant on multivariate analysis (Table 1). Assessment of rapid disease progression using PROPKD and MCIC scores yielded Kappa Cohen of 0.149; 47.9% (n = 143) were concordant, 49.32% (n = 148) patients identified as rapid progressor (RP) for MCIC were non-RP for PROPKD, while 2.3% (n = 7) of PROPKD score considered RP using PROPKD score were considered non-RP using MCIC classes. Following the reclassification of PKD1 missense variants by REVEL score, K of Cohen improved to 0.174, and PROPKD becomes predictive of fast progression also at multivariate (p = 0.010).

Conclusion: Concordance between scores results low (K of Cohen 0.149). The PROPKD is more selective compared to the Mayo. Nevertheless, PROPKD allows the identification of some rapid progressor patients excluded from using the Mayo score only. The combined use of scoring may increase the ability to identify progressive patients. REVEL score could improve the agreement.
Table 1: Clinical features, univariate & multivariate analysis.

<table>
<thead>
<tr>
<th></th>
<th>eGFR slope &lt; 12 ml/min*</th>
<th>eGFR slope &gt; 12 ml/min*</th>
<th>Univariate**</th>
<th>Multivariate**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 56</td>
<td>n = 52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- M</td>
<td></td>
<td></td>
<td>0.699</td>
<td></td>
</tr>
<tr>
<td>- F</td>
<td>24 (42.9%)</td>
<td>25 (48.1%)</td>
<td>0.702</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>45.0 ±14.0</td>
<td>44.0 ±13.0</td>
<td>0.691</td>
<td></td>
</tr>
<tr>
<td>eGFR</td>
<td>75.4 ±32.8</td>
<td>73.0 ±28.2</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>HtTKV</td>
<td>1057 ±730</td>
<td>2028 ±1465</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>HBP</td>
<td>27 (48.2%)</td>
<td>38 (73.1%)</td>
<td>0.011</td>
<td>0.031</td>
</tr>
<tr>
<td>HBP(&lt;=35 yr)</td>
<td>14 (25.0%)</td>
<td>26 (50.0%)</td>
<td>0.010</td>
<td></td>
</tr>
<tr>
<td>&gt; 1 HBP drugs</td>
<td>5 (8.9%)</td>
<td>14 (26.9%)</td>
<td>0.022</td>
<td></td>
</tr>
<tr>
<td>Urological events (&lt;35 yr)</td>
<td>9 (16.1%)</td>
<td>28 (53.8%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- PKD1 NT</td>
<td>24 (42.9%)</td>
<td>19 (36.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PKD1 T</td>
<td>14 (25.0%)</td>
<td>27 (51.9%)</td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>- PKD2</td>
<td>18 (32.1%)</td>
<td>6 (11.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROPKD</td>
<td></td>
<td></td>
<td>0.016</td>
<td></td>
</tr>
<tr>
<td>- 0–6</td>
<td>50 (89.3%)</td>
<td>36 (69.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 7–9</td>
<td>6 (10.7%)</td>
<td>16 (30.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROPKD+REVEL</td>
<td></td>
<td></td>
<td>0.003</td>
<td>0.010</td>
</tr>
<tr>
<td>- 0–6</td>
<td>50 (89.3%)</td>
<td>33 (63.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 7–9</td>
<td>6 (10.7%)</td>
<td>19 (36.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCIC</td>
<td></td>
<td></td>
<td>0.003</td>
<td>0.011</td>
</tr>
<tr>
<td>- 1A-1B</td>
<td>24 (42.9%)</td>
<td>8 (15.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1C-1E</td>
<td>32 (57.1%)</td>
<td>44 (84.6%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* After 4 yr
** p-value

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is a ciliopathy which is characterized by abnormal tubular epithelial proliferation and fluid secretion. Anoctamin 1 (ANO1) is a calcium-dependent chloride channel, which has recently been shown to be involved in ADPKD progression. However, how ANO1 contributes to ADPKD is largely unexplored.

Method: 1. Based on mRNA gene chips, the expression of ANO1 abnormally increased in human ADPKD kidneys. 2. Immunohistochemical staining showed ANO1 location. 3. Real-time PCR and Western blot showed mRNAs and protein of ANO1 in ADPKD patients and animal model-PKD1RC/RC.

Figure 1: ANO1 is up-regulated in mouse and human ADPKD kidneys. (A) QT-PCR analysis of ANO1 expression in kidney tissues of PKD1RC/RC mice with different ages. (B) QT-PCR analysis of ANO1 expression in human normal control and ADPKD patients renal tissues. (C,D) WB analysis of ANO1 expression in human normal and ADPKD patients renal tissues and was further quantified. (E) Immunohistochemistry analysis of ANO1 (in brown) expression in human normal and ADPKD patients renal tissues. Scale bars, 200 μm. *p < 0.05. **p < 0.01.
Figure 2: ANO1 is localized in primary cilia. (A,B) IF staining for ANO1 and Glu-tubulin was performed on RCTE and ADPKD cells (PKD1+/− cells) and further quantitatively analyzed by confocal microscopy. Scale bars, 10 μm. (C) Super-resolution 3D structured illumination microscopy analysis of ANO1 in RCTE cells.

Figure 3: Knockdown of ANO1 increases the cilium length and the expression of polycystin 2 (PC2). IF: nonsense control (NC) siRNA or siRNA against ANO1 was transfected in human PKD1+/− cells. IF for PC2 and AC-tubulin was performed on RCTE and PKD1+/− cells and further analyzed by confocal microscopy. Cilia length and intensity of PC2 were quantified. The knockdown efficiency of siRNA was determined by RT-PCR. Scale bars, 5 μm.

Figure 4: Knock-down of ANO1 inhibits renal cyst formation in 3D culture models. (A,B) 3D culture model of cyst formation was established using IMCD3 cells which were treated with two different ANO1 inhibitors (Tinh16-A01 or Tannic acid). After 2 weeks of culture, the Surface area of cysts (SA) was measured. Scale bars, 300 μm. (C,D) 3D culture model of cyst formation was established using MDCK cells which were transfected with siRNA against ANO1. Knock down efficiency was measured by RT-PCR before MDCK cells were planted into the collagen gel. After 2 weeks of culture, the diameter of cysts was measured. Scale bars, 100 μm.

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formation in 3D culture models. Moreover, inhibition of ANO1 abolished the activation of STAT3 and ERK pathways in PKD cells.

**Conclusion:** Our data indicate ANO1 may aggravate ADPKD by regulating the cilia length and PC2 expression. Moreover, ANO1 could support cyst growth by activating STAT3 and ERK pathways. Thus ANO1 is a negative regulator for both cilia formation and cilia trafficking of polycystins and provide mechanistic insights regarding the therapeutic potential of ANO1 pathway in ADPKD treatment.

#4440

**PREVALENCE OF GENES INVOLVED IN HEREDITARY KIDNEY DISEASE AS A TOOL FOR THE DEVELOPMENT OF A GENE PANEL**

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Hospital Universitario Virgen del Rocío, Nephrologist, Seville, Spain

**Background and Aims:** Genetic study is the fundamental tool for the diagnosis of Hereditary Kidney Diseases (HKD). The proliferation of its use has led to an increase in diagnostic complexity due to phenotypic overlap and genotypic heterogeneity. The aim of this study is to evaluate the prevalence of genes in our series of adult patients with suspected monogenic kidney disease in order to develop the basis for the elaboration of a gene panel that will make its usefulness in our routine clinical practice profitable.

**Method:** A retrospective descriptive observational study was performed with the collection of all genetic studies that were positive in the period between October 2014 and December 2020 in our center. With a description of the causative genes involved, as well as the clinical data of the proband patients who turned out to be carriers of these variants. Descriptive results of continuous variables are expressed as mean and standard deviation (SD) or median and interquartile range (IQR) according to their distribution. For categorical data, frequency and percentage are reported.

**Results:** The results of a total of 77 genetic studies on probands were collected, of whom 51% were women with a mean age at diagnosis of 46 years (SD ± 13.4) and 64.9% had a family history of kidney disease. Renal function measured by mean estimated glomerular filtration rate (eGFR) using the CKD-EPI (CKD Epidemiology Collaboration) was 90.1 ml/min/1.73 m² (SD ± 29.64) with a mean proteinuria quantified in 24-hour urine of 627.9 mg (SD ±43.7) and 7.7% were on renal replacement therapy. (Table 1) 40.25% of probands were carriers of a mutation for Alport syndrome, in this group the most frequent gene was COL4A3 in 50% of cases. The second most frequent entity was autosomal dominant polycystic kidney disease (ADPKD) with 37% of the studies and among these the great majority were carriers of a variant in the PKD1 gene with 96.5%. The remaining diagnostic entities in order of frequency were Fabry disease, autosomal dominant tubulointerstitial nephropathy (ADTKD), congenital anomalies of the kidney and urinary tract (CAKUT), nephrotic syndrome, hereditary angiopathy with nephropathy, aneurysm and cramps syndrome (HANAC) and tuberous sclerosis (Figure 1).

**Conclusion:** Alport syndrome was the most frequently identified entity in patients with suspected monogenic renal disease in whom the genetic study was performed. Based on the results of our series, a proposal has been made for the genes to be included in a panel for hereditary renal diseases in our center. The development of these panels increases the efficiency and increases the cost-effectiveness of genetic studies in the diagnosis of these patients.

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**Table 1: Variables and results collected. N: number of patients. SD: standard deviation. CKD: chronic kidney disease. CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration**

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Age at diagnosis (mean, SD), years</td>
<td>46 ± 13.4</td>
<td></td>
</tr>
<tr>
<td>Sex (n, %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>38 (49)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>39 (51)</td>
<td></td>
</tr>
<tr>
<td>Family history of CKD (n, %)</td>
<td>50 (64.9)</td>
<td></td>
</tr>
<tr>
<td>Glomerular filtration rate CKD EPI ml/min/1.73 m² (mean, SD)</td>
<td>90.1 ± 29.64</td>
<td></td>
</tr>
<tr>
<td>24-hour urine protein mg/dl (mean, SD)</td>
<td>627.9 ±43.7</td>
<td></td>
</tr>
<tr>
<td>Renal replacement therapy (n, %)</td>
<td>6 (7.7)</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1:** HNF1β: Hepatocyte Nuclear Factor 1b. ADPKD: autosomal dominant polycystic kidney disease. ADTKD: autosomal dominant tubulointerstitial nephropathy. CAKUT: kidney and urinary tract.
THE GENOTYPE DISTRIBUTION IN A SINGLE-CENTRE COHORT OF PATIENTS WITH POLYCYSTIC KIDNEY DISEASE

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Background and Aims: Polycystic kidney disease (PKD) is one of the most common causes of chronic kidney disease (CKD) and could lead to the end-stage kidney disease (ESKD) both in adulthood and in childhood. In the last few years many genes were discovered to be associated with PKD beyond the classical genes PKD1 and PKD2, that account for the majority of patients with ADPKD (Autosomal Dominant Polycystic Kidney Disease), and PKHD1 and DZIP1 that are responsible of ARPKD (Autosomal Recessive Polycystic Kidney Disease). The new genes are associated with different type of extra-renal involvement and with variable chance to develop CKD or ESKD. Thus, it is important for clinicians to define what mutation is involved in each patient to improve care in a context of precision medicine. We here describe a cohort of 65 consecutive patients followed at our PKD outpatient clinic who underwent genetic analysis.

Method: We conducted a retrospective study of patients followed at our PKD outpatient clinic who underwent a genetic test for clinical reasons. We recorded why test was performed, with which modality and what was the result. If the analysis was positive we analyzed if only one or more genes were found mutated and if they belong to new genes described as being involved in PKD or if they are usually described in association with different diseases. Then, we collected demographic and clinical information (age, sex, renal function/presence of absence of ESKD) and the radiological description of kidneys in order to distinguish between typical and atypical PKDs.

Results: Among the 65 patients of our cohort 28 (43%) were males and 37 (57%) were females, the mean age was 56±18.6 years old; 20% had ESKD. They underwent genetic analysis for different reasons: 31 because of atypical PKD forms, 6 to define a suspected de novo mutation, 14 as a familiar screening and 14 for a better prognosis definition or when they approached the kidney transplant. The genetic analysis was conducted in two main ways: sequencing of PKD1 and PKD2 genes according to modern standards or exome sequencing. The first type of analysis was used for typical ADPKD forms whereas the second type was used when patients displayed an atypical presentation for both cysts distribution and kidney diameter (usually not enlarged kidneys with multiple bilateral cysts) and in two patients in which PKD1 and PKD2 sequencing was negative despite the PKD phenotype. We found that 25% of patients were negative, and the others are almost equally distributed between typical gene mutations and mutations in other genes (40% and 35% respectively) (Figure 1A). Of those with typical mutation, 81% was PKD1 positive and 19% PKD2 positive, a distribution that reflects that of literature (Figure 1B). Of those with other genes positivity: 52% had a DNAJB11 mutation, 17% a mutations in other PKD genes (ALG8, LRP5, PKHD1, COL4A1, IFT140), 32% had a mutation in genes usually associated with CAKUT (congenital anomalies of kidney and urinary tract) or with syndromic or extra-renal diseases (Figure 1C). 18 patients presented with multiple mutations, usually 2, in one case three and in another 4. Of them, the 22% had a double PKD1 mutation, while the others showed mutations in different genes associated with syndromic or extra-renal diseases (Figure 1D).

Conclusion: Our cohort revealed a wide variety of genetic mutations and also an almost equal distribution between typical genes and atypical/other genes. This could be the result of the small number of patients involved and of the monocentric design of the study (we have a cluster of patients with DNAJB11 belonging to the same small geographical area), but also of the larger inclusion of patients presenting with atypical PKDs. Unfortunately a 25% of patients remained genetically unresolved despite the use of exome sequencing.

Figure 1: A: The distribution of patients between negative and positive genetic analysis with distinction between typical and atypical/other genes; B: PKD1 and PKD2 division of typical mutated patients; C: the division among patients with atypical/other genes mutations; D: the distribution of double mutations.
#5842

ULTRASOUND AND 3D IMAGING CHARACTERISATION OF A RAT MODEL OF POLYCYSTIC KIDNEY DISEASE

Michael Christensen, Trine Porsgaard, Johanne Perens, Frederikke Emilie Sembach, Henrik Bjirk Hansen and Maria Ougaard

Gubra aps, Denmark

Background and Aims: Polycystic kidney disease (PKD) is a congenital fibrocystic disorder where cysts are primarily forming within the kidneys causing enlargement, loss of kidney function and resulting in chronic kidney disease for which there is no curative treatment. Consequently, PKD is classified as a medical condition with high unmet therapeutic need. Animal models with improved clinical translatability can optimally inform about potential clinical efficacy of novel drug candidates for PKD. The polycystic kidney (PKC) rat is an established genetic model of PKD with natural history and renal histologic abnormalities that resemble the human disease. Gubra has established a PKC rat breeding program to enable fast turnaround time of preclinical drug discovery studies for PKD. In this study, we have characterised disease progression in the PKC rat to aid in designing future pharmacological intervention studies.

Method: Male PKC (PKC/CrlCr-Pkhdl/pck/Crl) and control (CRL:CD(SD)) rats (Charles River) were randomised into groups based on body weight at the age of 10 weeks. At the age of 17 and 25 weeks, rats underwent ultrasound assessment of kidney volume, urine collection for quantification of albuminuria, and plasma sampling for analysis of urea and creatinine levels. At termination, whole kidneys were harvested and total kidney volume, cyst number and cyst volume were analysed using quantitative 3D light sheet imaging.

Results: Compared to age-matched control rats, PKC rats displayed marked albuminuria which was significantly increased at week 25 of age. Whereas plasma urea was progressively increased at both time points, plasma creatinine increased at week 25. Ultrasound measurements revealed that total kidney volume progressive increased compared to control rats. 3D Light sheet imaging enabled whole-kidney counting of cysts and quantification of cyst volume as well as the total kidney volume that closely correlated to kidney ultrasound results.

Conclusion: The PKC rats displays histological hallmarks of PKD, characterized by age-dependent progressive increases in biomarkers of kidney injury, kidney hypertrophy and cyst formation. In vivo ultrasound and ex vivo quantitative whole-kidney 3D light sheet imaging is highly instrumental for detailed assessment of progressive disease in the PKC rat. The renal histopathological markers may serve as key histological endpoints for assessment of therapeutic effects of preclinical drug candidates in this translational rat model of PKD.

#6120

MIRNA PROFILING OF URINARY EXTRACELLULAR VESICLES (EVS) IN TBMN AND CFHR5 NEPHROPATHY FOR THE IDENTIFICATION OF NOVEL DISEASE BIOMARKERS

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Background and Aims: Thin basement membrane nephropathy (TBMN) and complement factor-H related protein 5 (CFHR5) nephropathy are two of the most common renal monogenic diseases with high phenotypic heterogeneity that is only partly accounted for by locus and allelic factors. Intra-familial variability in the age of ESKD onset for some patients particularly exemplifies that is only partly accounted for by locus and allelic factors. Intra-familial variability in the age of ESKD onset for some patients particularly exemplifies that is only partly accounted for by locus and allelic factors. Intra-familial variability in the age of ESKD onset for some patients particularly exemplifies.

Method: MiRNA profiling of human urinary EVs was carried out by small RNA-sequencing in an initial discovery cohort of 54 patients with TBMN and 44 patients with CFHR5 nephropathy, each classified further into three subgroups based on disease severity (Grey-zone: eGFR >60 ml/min/1.73m² and age <50 y/o; Mild: eGFR >60 ml/min/1.73m² and age <50 y/o; Severe: eGFR <60 ml/min/1.73m² independently of age). Differential expression of miRNAs from urine-derived EVs was compared with 30 age and sex matched healthy controls, whilst bioinformatic analysis was performed to delineate their associated mechanisms.

Results: Kidney-enriched candidate miRNA families were identified in urine-derived EVs for both TBMN and CFHR5 patients and further verified by RT-qPCR in the respective validation cohorts. Distinct miRNAs with significantly differentiated expression levels, compared to that of healthy control cohort, showed significant correlations with some of the evaluated clinical characteristics both for TBMN and CFHR5 patients suggesting a possible diagnostic and prognostic value on long follow-up. Finally, inverse correlations of miRNA expression with their predicted targeted genes identified dysregulated pathways and transcriptional networks for further investigation.

Conclusion: Collectively, distinct profiles of miRNAs from urine-derived EVs were identified in TBMN and CFHR5 nephropathy suggesting that a subset of differentially expressed miRNAs could serve as novel non-invasive biomarkers of disease progression and/or targets for the development of novel therapeutic approaches.

#3812

ARE KIDNEY CYSTS MORE COMMON IN PEOPLE WITH COLA3/COLA4 PATHOGENIC VARIANTS?

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1Fundación Puigvert, Nephrology, Barcelona, Spain, 2Fundación Puigvert, Genetic Laboratory, Barcelona, Spain, 3Hospital Universitario Virgen de Arrixaca, Nephrology, Murcia, Spain, 4Hospital General de Castellón, Nephrology, Castellón de la Plana, Spain and 5Fundación Jiménez Diaz, Nephrology, Madrid, Spain

Background and Aims: Individuals with pathogenic heterozygous variants in the COLA3/COLA4 genes are usually asymptomatic or present only with microhaematuria, although some may develop proteinuria and chronic kidney disease (CKD). Simple renal cysts are common in healthy individuals, with an increasing incidence with age and CKD grade. A possible association between pathogenic variants of collagen type IV and renal cysts has been described. This study investigates the presence of renal cysts in a large cohort of individuals with heterozygous pathogenic variants in COLA3/COLA4.

Method: We evaluated the presence of kidney cysts, kidney size and lithiasis by ultrasound in 162 individuals with pathogenic variants in COLA3/COLA4 without kidney replacement therapy. The correlation between kidney cysts and age, proteinuria, eGFR, causing gene and type of variant, was analysed. Genetic testing had been performed in index cases by next generation sequencing (NGS) of a kidney-disease gene panel containing more than 400 genes including COLA3, COLA4 and COLA5 genes.

Results: 153 patients with a heterozygous disease-causing variant in COLA3 or COLA4 and 9 patients with digenic/complex inheritance were included. The mean age at renal ultrasound was 46.19 years (SD 14.93) and the mean eGFR was 75 ml/min/1.73 m² (SD 35 ml/min/1.73 m²). Renal cysts were present in 50% of patients (81/162) and were bilateral in 30.25%. The mean age of patients with renal cysts was 53.26 years vs. 39.12 years for those without, and the mean eGFR was 60ml/min/1.73 m² vs. 89ml/min/1.73 m² for patients with and without renal cysts. Only 2.5% (4/162) of patients had renal lithiasis. The mean kidney size was 104.05 mm (SD 13.86 mm) for the right kidney and 104.98 mm (SD 13.94 mm) for the left kidney. Cystic nephromegaly was observed in 3.7% (6/162). No correlation was found between renal cysts and gender (p = 0.632). Age and CKD stage had a positive correlation with the development of renal cysts (p = <0.001) (Tables 1 and 2). Proteinuria was more common in individuals with renal cysts 61% vs 39% (p = 0.012), but was related to age and CKD stage. The presence of a kidney cyst did not correlate with the mutated gene or the type of variant.

Conclusion: Individuals with COLA3/COLA4 pathogenic variants develop kidney cysts at a higher rate than age-matched healthy individuals, and their presence is also related to ageing, as in the general population. Gender is not relevant for the development of renal cysts, in contrast to the general population cohorts. Proteinuria and CKD grade correlate with the development of renal cysts but nephromegaly is rare. Renal cysts in heterozygous carriers of COLA3 or COLA4 pathogenic variants are common but have no clinical consequences.
**Table 1: Individuals with kidney cysts according to the age groups.**

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt; 30</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>&gt;70</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>21</td>
<td>32</td>
<td>38</td>
<td>41</td>
<td>25</td>
<td>5</td>
<td>162</td>
</tr>
<tr>
<td>Kidney cysts (KC)</td>
<td>3 (14.3%)</td>
<td>9 (28.1%)</td>
<td>18 (47.4%)</td>
<td>25 (61%)</td>
<td>21 (84%)</td>
<td>5 (100%)</td>
<td>81 (50%)</td>
</tr>
<tr>
<td>Unilateral KC</td>
<td>2 (9.5%)</td>
<td>2 (6.3%)</td>
<td>10 (26.3%)</td>
<td>5 (12.2%)</td>
<td>10 (40%)</td>
<td>3 (60%)</td>
<td>32 (19.8%)</td>
</tr>
<tr>
<td>Bilateral KC</td>
<td>1 (4.8%)</td>
<td>7 (21.9%)</td>
<td>8 (21.1%)</td>
<td>17 (41.5%)</td>
<td>14 (56%)</td>
<td>2 (40%)</td>
<td>49 (30.2%)</td>
</tr>
</tbody>
</table>

**Table 2: Individuals with kidney cysts according to chronic kidney disease (CKD) stage.**

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>1</th>
<th>2</th>
<th>3a</th>
<th>3b</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>63</td>
<td>38</td>
<td>17</td>
<td>26</td>
<td>12</td>
<td>6</td>
<td>162</td>
</tr>
<tr>
<td>Kidney cysts (KC)</td>
<td>20 (31.7%)</td>
<td>15 (39.5%)</td>
<td>13 (76.5%)</td>
<td>20 (76.9%)</td>
<td>8 (66.7%)</td>
<td>5 (83.3%)</td>
<td>81 (50%)</td>
</tr>
<tr>
<td>Unilateral KC</td>
<td>9 (14.3%)</td>
<td>9 (23.7%)</td>
<td>5 (29.4%)</td>
<td>6 (23.1%)</td>
<td>1 (8.3%)</td>
<td>2 (33.3%)</td>
<td>32 (19.8%)</td>
</tr>
<tr>
<td>Bilateral KC</td>
<td>11 (17.5%)</td>
<td>6 (15.8%)</td>
<td>8 (47.1%)</td>
<td>14 (53.8%)</td>
<td>7 (58.3%)</td>
<td>3 (30%)</td>
<td>49 (30.2%)</td>
</tr>
</tbody>
</table>

**#5559**

**BONE SPECIFIC ALKALINE PHOSPHATASE AS A POTENTIAL BIOMARKER OF AUTOSOMAL DOMINANT POLycystic KIDNEY DISEASE PROGRESSION**

Magdalena Jankowska1, Abdul Rashid Tony Qureshi2, Mathias Lobberg Haarhaus2, Alicja Debska-Slizien1, Peter Stenvinkel1, Pieter Evenepoel1 and Bengt Lindholm2

1Medical University of Gda´nsk, Department of Nephrology, Transplantology and Internal Medicine, Gda´nsk, Poland, 2Karolinska Institutet Clince, Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Sweden and 3University Hospitals, Department of Nephrology and Renal Transplantation, Leuven, Belgium

**Background and Aims:** Autosomal dominant polycystic kidney disease (ADPKD) is a systemic disease, resulting in a dysfunction of the primary cilium, a sensory organelle ubiquitously present in human cells. Ciliopathies are characterized by disorders of seemingly unrelated organs and functions, which depend on integrity of the primary cilium, among them the skeleton and the kidneys. A distinct bone phenotype has been reported in ADPKD patients in several cohort studies. Findings, however, were heterogeneous. Present study aimed to measure bone turnover biomarkers in patients with ADPKD across disease severity measured by eGFR and height-adjusted total kidney volume (HtTKV).

**Method:** In this cross-sectional study, we included 80 ADPKD patients with different chronic kidney disease (CKD) stages (G1 and G2 (n = 39), and G3 and G4 (n = 41)) with median age 44.0 (33.5–50.5) years, 62.5% men, and BMI 25.1 (23.3–28.7) kg/m². HtTKV was measured with magnetic resonance imaging. We measured biochemical parameters of mineral metabolism, including bone specific alkaline phosphatase (BALP) and total ALP, calcium (Ca), parathyroid hormone (PTH), and 25(OH) vitamin D (25(OH)D) and bone strength index (BSi) with microindentation, using an OsteoProbe® (Active Life Scientific, USA). Microindentation is minimally invasive technique assessing bone quality. The cortical bone at the mid-shaft of the tibia is penetrated with the indenters to measure bone resistance.

**Results:** Bone biomarkers expressed as median and interquartile range were as follow: Ca 9.6 (9.3–9.9) mg/dL, BALP 9.0 (7.0–12.5) ug/L, ALP 59.0 (46.0–72.0) U/L, PTH 43.5 (26.6–72.0) pg/mL, and 25(OH)D 25.8 (16.6–33.5) ng/mL. Median BSI was 79.1 (73.5–82.1) in men and 68.5 (62.1–78.6) in women (lower than the average score in healthy caucasians). Among analyzed bone markers only BALP significantly associated with severity of ADPKD. BALP - but not eGFR - associated with HtTKV and was different across HtTKV tertiles. BALP was also higher in the highest BSI group, but BSI did not associate with HtTKV (Figure 1).

**Conclusion:** In patients with ADPKD and different stages of CKD, BALP associates with bone strength and kidney volume, suggesting that it may be a sensitive marker of systemic ADPKD manifestations. Further studies should elucidate whether BALP may be a more sensitive marker for ADPKD progression than GFR.

**#5783**

**REAL-LIFE USE OF TOLVAPTAN IN ADPKD: A RETROSPECTIVE ANALYSIS OF A LARGE CANADIAN COHORT**

Luca Calvaruso1,2, Kevin Yan1, Pedram Akbari1, Fatemeh Nasri1, Shirley X. Deng1, Saima Khowaja1, Ning He1, Amirreza Haghigi1, Korosh Khalili2 and York Pei1

1Division of Nephrology, University Health Network and University of Toronto, Toronto, Canada, Toronto, Canada, 2U.O.C. Nefrologia, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Roma, Italy and 3Department of Medical Imaging, University Health Network and University of Toronto, Toronto, Ontario, Canada

**Background and Aims:** Tolvaptan is the first disease-modifier therapy proven to slow eGFR decline in high-risk patients with ADPKD. However, barriers to its use in real-life settings have not been examined.

**Method:** Single-center, retrospective study of 523 current or new patients with ADPKD followed at the Center for Innovative Management of PKD in Toronto, Ontario between January 1, 2016 to December 30, 2018. All patients had clinical assessment and total kidney volume measurements; those deemed to be at high risk based on their Mayo Clinic Imaging Class (MCIC) 1C, 1D, or 1E, were offered tolvaptan with their preference (yes or no) and reasons for their choices recorded.

**Results:** Overall, 315/523 (60.2%) patients had MCIC 1C-1E; however, only 96 (30%) of them were treated with tolvaptan at the last follow-up. Among these high-risk patients, those treated with tolvaptan were more likely to have a higher eGFR (61 ±27 vs. 82 ±26 ml/min/1.73 m²), CKD stages 1–2 (41% vs. 79%), and MCIC 1D-1E (69% vs. 37%). The most common reasons provided for not taking tolvaptan were lifestyle preference related to the aquaretic effect (51%), older age ≥60 (12%), and pregnancy or family planning (6%).

**Conclusion:** In this real-world experience, at least 60% of patients with ADPKD considered to be at high risk for progression to ESKD by imaging were not treated with tolvaptan; most of them had earlier stages of CKD with well-preserved eGFR. The most common reason for their refusal to consider tolvaptan is a concern for tolerability of the aquaretic side-effect; strategies to mitigate this side-effect may help to reduce the barrier to tolvaptan therapy.
Figure 1: Reasons for not using tolvaptan among ADPKD patients with Mayo Clinic Imaging Classification 1C, 1D, 1E (n = 219) from the cohort followed primarily or co-managed with their primary nephrologists by the Center for Innovative Management of Polycystic Kidney Disease.

<table>
<thead>
<tr>
<th>Reason for Not Using Tolvaptan</th>
</tr>
</thead>
<tbody>
<tr>
<td>a Unspecified: No reason provided in the response.</td>
</tr>
<tr>
<td>b Considering: Patients who are considering tolvaptan but remain undecided.</td>
</tr>
<tr>
<td>c Family planning: Planning pregnant or contemplating pregnancy.</td>
</tr>
<tr>
<td>d Advanced age: Age ≥ 60 with perceived reduced benefit of tolvaptan usage.</td>
</tr>
<tr>
<td>e Lifestyle: Patients who had refused tolvaptan due to being unable to handle the possible aquaretic effect of the medication due to either their occupation or social circumstances.</td>
</tr>
</tbody>
</table>

Table 1: Clinical Characteristics of High-Risk Patients with Mayo Clinic Imaging Class 1C, 1D, or 1E on tolvaptan vs. not on tolvaptan at last follow-up in December 2019 (n = 315).

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Tolvaptan</th>
<th>Not on Tolvaptan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, number</td>
<td>96</td>
<td>219</td>
</tr>
<tr>
<td>Male sex</td>
<td>55 (57.3%)</td>
<td>102 (46.6%)</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>46 ± 13</td>
<td>43 ± 14</td>
</tr>
<tr>
<td>eGFR (CKD-EPI, ml/min/1.73m²), mean ± SD</td>
<td>61 ± 27</td>
<td>82 ± 26</td>
</tr>
<tr>
<td>CrCl (ml/min), mean ± SD</td>
<td>76 ± 33</td>
<td>96 ± 6</td>
</tr>
<tr>
<td>CKD Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD 1/2</td>
<td>39 (40.6%)</td>
<td>173 (79%)</td>
</tr>
<tr>
<td>CKD 3</td>
<td>49 (51%)</td>
<td>42 (19.2%)</td>
</tr>
<tr>
<td>CKD 4/5</td>
<td>8 (8.3%)</td>
<td>4 (1.8%)</td>
</tr>
<tr>
<td>Genetic mutation - no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PKD1 PT</td>
<td>43 (44.8%)</td>
<td>72 (32.9%)</td>
</tr>
<tr>
<td>PKD1 NT</td>
<td>27 (28.1%)</td>
<td>54 (24.7%)</td>
</tr>
<tr>
<td>PKD2</td>
<td>17 (17.7%)</td>
<td>55 (25.1%)</td>
</tr>
<tr>
<td>No mutation</td>
<td>7 (7.3%)</td>
<td>31 (14.2%)</td>
</tr>
<tr>
<td>ht-TKV, median (IQR)</td>
<td>1328.5 (949.4 - 1772.4)</td>
<td>848.4 (609.1 - 1298.4)</td>
</tr>
<tr>
<td>Mayo Clinic Imaging Classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1C</td>
<td>30 (31.2%)</td>
<td>138 (63%)</td>
</tr>
<tr>
<td>1D/1E</td>
<td>66 (68.8%)</td>
<td>81 (37%)</td>
</tr>
</tbody>
</table>

PKD1, PT PKD1 protein truncating mutation; PKD1 NT, PKD1 non-truncating variants (i.e. indel small in-frame deletion/insertion, nonsynonymous missense, or atypical splice site variants); PKD2, PKD2 mutation.

aData are presented as the number (percentage) of patients, unless otherwise reported.

#5571

THERAPY WITH BUROSUMAB IN ADULT PATIENTS WITH X-LINKED HYPOPHOSPHATEMIA: A YEAR OF FOLLOW-UP

Silverio Rotondi, Lida Tartaglione, Adolfo Perrotta, Nadia Carroccia, Marzia Pasquali and Sandro Mazzaferr

Sapienza University of Rome, Roma, Italy

Background and Aims: X-linked hypophosphatemic rickets (XLH) is a genetic disorder secondary to the mutation of the PHEX gene that results in increased circulating levels of FGF23. Increased FGF23 causes hypophosphatemia secondary to renal phosphate loss. Clinically, the disease is characterized by reduced growth, bone alterations, weakness, chronic pain and reduced mobility. From a biochemical point of view, patients have hypophosphatemia, increased values of alkaline phosphatase, increased fraction excretion of phosphate (FEP). Recently, therapy with Burosumab, a monoclonal antibody against FGF23, has been introduced. Burosumab by reducing the receptor availability of circulating FGF23 reduces its activity. This leads to a normalization of serum phosphate and in paediatric patients an improvement of the clinical phenotype. In adult patients, the effectiveness of therapy in improving the clinical outcome and quality of life is being investigated. The purpose of the study was to evaluate the efficacy in improving the biochemical, bone and clinical picture of adult patients with XLH in therapy with Burosumab for one year.

Method: We enrolled patients with XLH naive for Burosumab therapy. In all we evaluated the biochemical aspects (phosphatemia, alkaline phosphatase, FEP), bone Radiographic Global Impression of Change score and clinical improvements (six-minute walk test, UP and go timed test, WOMAC Index) pre therapy and after a year of therapy. Burosumab was administered monthly at a dose of 1 mg/Kg.

Results: We enrolled 5 patients (45 ± 10 year old, weight 60 ± 10 Kg, Burosumab dose 60 ±10 mg) with genetic diagnosis of XLH. The comparison between pre therapy and post-one-year therapy showed in all patients: increase in average phosphatemia (pre 1.9±0.5 mg/dl vs post 3.4±0.6 mg/dl p = 0.003),
reduction in FEP (pre 50 ±15% vs 20 ±10% p = 0.004), reduction of UP and go test (pre 20 ± 5 sec vs post 11 ± 3 sec p = 0.005) increase of the distance in the six minutes’ walk test (pre 150 ± 30 meters vs post 250 ± 50 meters p = 0.01), improvement of the WOMAC test (pre 15± 3 vs post ± 2; p = 0.008) and reduction of the Radiographic Global Impression of Change score (pre -2 ±0.5 and post 2± 0.4; p = 0.001). The serum value of alkaline phosphatase was high and it did not change with the Burosumab therapy (pre 200± 50 U/L vs post 220± 60 U/L; p. n. s. n. v. 33–98 U/L). No patients had significant complications during the first year of treatment.

Conclusion: The therapy with Burosumab was well tolerated by patients. It resulted in a marked improvement in the biochemical picture associated with a better quality of life identified by increased strength (improved walk test and UP and go timed test) reduction of pain (best WOMAC test) and bone damage score. In conclusion, Burosumab may be a good and safe therapy option for adults’ patients with XLH.

#3593
COEXISTENCE OF 2 (DE NOVO) MUTATIONS IN 2 DIVERSE GENES (PKD1, LRPS) IN A PATIENT WITH RENAL AND LIVER POLYCYSTIC DISEASE
George Tsirpanlis1, Danai Palaiologou1, Leandro Lazaros2, Michaela Louka2, Eirini Evangelou1, Dimitra Gkalitsiou1 and Emmanouil Kanavakis2
1General Hospital of Athens “G. Gennimatas”, Athina, Greece and 2Genesia Genoma Lab (GenLab.gr), Chalandri, Greece
Introduction: In Autosomal Dominant Polycystic Kidney Disease (ADPKD) the genotype is variable. The most common extrarenal manifestation of the disease is the presence of hepatic cysts. Parallel cysts appearance in two different organs is possibly related to the genetic injury. We present in this report the case of a patient without family history of ADPKD and 2 different mutations related to cyst formation.

Case report: A 53 year old woman came to our outpatient ADPKD clinic with known multiple hepatic and renal cysts, diagnosed 11 years ago. She had no family history of ADPKD, both her parents aged 89 years old, had no renal or liver cysts on recent ultrasound scans. The patient had a background of recurrent UTIs, nephrolithiasis and hypertension diagnosed at 40 years old. Currently she was found to have e-GFR 49ml/min and liver function tests within normal range. Genetic testing and Magnetic Resonance Imaging (MRI) for estimating Total Kidney Volume (TKV) and hepatic imaging were conducted. In the genetic testing with a second generation sequencing, two heterozygous mutations in two different genes were depicted. The first was found in PKD1 gene: c.1396G>A (p.Val466Thr) and causes the replacement of the amino acid alanine by threonine at position 1196 of the produced protein (Low density lipoprotein Receptor-related Protein-5). It is also referred as a variant of uncertain clinical significance, and exhibits autosomal dominant inheritance also. The MRI shows a particularly high cystic load in the liver (innumerable cysts) and multiple renal cysts in the two large kidneys, in a quite atypical form (not innumerable but many large cysts). The TKV was 1842 ml (1071 ml/m) and classified her in the class 1C (or possibly 2C because of the atypical form) according to the Mayo Clinic imaging classification system for ADPKD. The estimated prediction of the End-Stage Chronic Kidney Disease (ESCKD) (as long as the disease is not atypical) was according to the Mayo Clinic formula, 11 years.

Discussion: In a recent publication, pathological nucleotide variants of the LRPS gene were associated with hepatic cystogenesis. Coexistence of PKD1 and LRPS mutations was also identified in 2 families with polycystic kidney and liver disease. The underlying pathogenetic mechanism appears to be related to the connection between Polycystin-1 (the product of PKD1 involved in the pathogenesis of ADPKD) and the Wnt signaling pathway (affected by LRPS gene mutations and linked to hepatic cystogenesis). The coexistence of the two mutations possibly means synergistic action. Unique facts and important phenotypic characteristics in this particular patient, is the de novo simultaneous appearance of the two mutations (the parents were not genetically tested but do not have cysts in very old age), the particularly large cystic liver load (which is also observed in typical ADPKD, especially in women), the atypical renal cyst imaging and the moderate to severe renal disease (expected ESCKD at 64 years, which is more than expected in a PKD1 mutation only, but less than in a solitary PKD2 mutation). In conclusion, genetic complexity appears to go hand in hand with phenotype diversity in ADPKD and polycystic liver disease.

#4033
RAPID COMPLEMENT INHIBITION WITH THE C5 INHIBITOR CROVALIMAB: A TIMING ANALYSIS USING ANIMAL MODEL AND COMPOSER TRIAL DATA
Cristian Brocchieri1, Leigh Beveridge2, Muriel Buri3, Niels Janssen4, Patty Leon5, Yoshihori Tsuboi6 and Simon Buatös6
1F. Hoffmann-La Roche Ltd., Basel, Switzerland, 2Genentech, Inc., South San Francisco, United States of America and 3Chugai Pharmaceutical Co., Ltd., Chuo City, Japan
Background and Aims: Atypical haemolytic uraemic syndrome (aHUS) is a life-threatening disease, characterised by acute kidney injury, thrombocytopenia, and microangiopathic haemolytic anaemia due to complement dysregulation. Currently approved treatments for aHUS include the anti-complement C5 monoclonal antibodies eculizumab and ravulizumab. Although currently approved therapeutic options are effective at both inhibiting complement-mediated thrombotic microangiopathy (TMA) and improving renal function, the regular intravenous (IV) infusion dosing regimens impose a significant treatment burden, particularly in paediatric patients (pts) with aHUS, who may need dialysis in the future due to chronic kidney injury and would benefit from preservation of vascular access. Crovalimab is a novel monoclonal antibody developed against complement C5, engineered to allow for small volume subcutaneous (SC) self-injection once a week, in a weight-based dosing regimen [1]. In the adaptive Phase II/I COMPOSER trial (NCT03157365) evaluating crovalimab in pts with paroxysmal nocturnal haemoglobinuria (PNH), that, like aHUS, is a complement disorder characterised by uncontrolled complement activation, crovalimab has shown maintained disease control and was well tolerated after a median exposure of 3 years. Further, a Phase III study evaluating crovalimab in previously untreated pts met its primary efficacy endpoints [2]. The efficacy and safety of crovalimab are currently being evaluated in adult and paediatric pts with aHUS, either treatment-naïve or switching from another complement inhibitor, in the ongoing Phase III single-arm COMMUTE-a and COMMUTE-p trials [3]. Due to the rapidly progressing nature of aHUS, pts experiencing a TMA require rapid suppression of complement activation upon diagnosis to shut down the complement cascade and avoid further kidney deterioration and organ damage. Here, data from in vivo models and the COMPOSER trial were used to determine the time to complete complement inhibition after first crovalimab IV dose.

Method: Crovalimab’s ability to suppress C5 function and complement activity rapidly was initially studied in in vivo models of cycnomolus monkeys. This study assessed the pharmacokinetics and pharmacodynamics of crovalimab in these monkeys after a single IV or SC dose. As part of this study, four animals per group were evaluated with single 4 mg/kg IV and 20 mg/kg IV doses. Crovalimab was also evaluated in the four-part, Phase II/I COMPOSER trial. Part 2 (n = 10) and Part 4A (n = 8) enrolled pts with PNH who were naïve to complement inhibition. Pts in Part 2 received crovalimab 375 mg IV on Day 1, 500 mg IV on Day 8, 1000 mg IV on Day 22 and 170 mg SC weekly from Day 36 for 20 weeks. Pts in Part 4A received an optimised crovalimab dosing regimen of 1000 mg IV on Day 1, 340 mg SC on Days 2, 8, 15, and 22 and 680 mg SC Q4W from Day 29 onwards for 20 weeks. Crovalimab concentration, free C5 and complement activity were measured using validated assays in cynomolgus monkeys and in pts with PNH.

Results: Compared with baseline values in cycnomolus monkeys, a single crovalimab IV dose of 4 mg/kg reduced mean free C5 concentration by 99.6% and terminal complement activity by 81.4%, within 5 minutes after administration. In treatment-naïve pts from COMPOSER Parts 2 and 4, mean free C5 concentration dropped to below 1 µg/mL, indicating a high level of target engagement within 1–6 hours from the first IV dose (Figure 1). Correspondingly, inhibition of terminal complement activity was reached within 1 hour, with values near or below the limit of quantification (10 U/mL; Figure 2). Complete complement blockade was generally maintained long-term, up to Week 20, in both Parts 2 and 4, regardless of dose.

Conclusion: Crovalimab induced a complete, rapid, and sustained blockade of terminal complement activity in both non-human primates and pts with PNH, within hours from first dose. The dosing schedule of crovalimab included an initial IV loading dose, allowing for a rapid onset of action, followed by a convenient long-term SC maintenance regimen.

REFERENCES

Abstracts
#3639
WHEN WHOLE EXOME SEQUENCING IS NOT GOOD ENOUGH: BACK TO THE ROOTS OR FORWARD TO THE FUTURE
Arif Ekici1, Karl Knaup1, Karen Schneider1, Florian Wopperer1, Antje Wiesener1, Anne Dieterle2, Mario Schiffer2, Andre Reis1, Francesca Pasutto1 and Michael Wiesener2
1Institute of Human Genetics, University Hospital Erlangen, Erlangen, Germany, 2Dept. Nephrology and Hypertension, Erlangen, Germany and 3Dept. Nephrology and Hypertension, University Hospital Erlangen, Erlangen, Germany

Background and Aims: Over the last few years, massively parallel sequencing (MPS) has been established in genetic diagnostics, where large virtual panels of candidate genes can be screened on a whole exome basis. This has enabled large analyses for most medical indications, including renal genetic diseases. The 25 year old, index female patient was referred for disease clarification. Both non-related parents suffered from end-stage renal disease, with kidney failure in mid adulthood and familiar cystic disease in both the maternal and paternal lines. An external genetic analysis applying MPS on a restricted panel of genes retrieved no conclusive result, apart from two variants in the UMOD gene, classified as class 3 and 4 following ACMG criteria.

Method: Whole exome sequencing (WES), linkage analysis, haplotype reconstruction, whole genome sequencing (WGS), long-range PCR (LR-PCR).

Results: The detailed pedigree of the family displayed an autosomal dominant disease with several family members reaching end-stage kidney disease on both the maternal and paternal sides. The maternal family is characterized by polycystic disease of the kidney and most profoundly the liver, with two female members already liver transplanted and one on the waiting list. The paternal family shows more unspecific chronic kidney disease (CKD) with multiple cysts in the kidney, but not in the liver. Two male members reported gout attacks, before the knowledge of CKD. We consented 12 family members for research studies and collected blood for DNA. Contemporary MPS of a virtual
### #3320

**GENETIC TESTING FOR MOLECULAR DIAGNOSIS OF NEPHROLITHIASIS AND NEPHROCALCINOSIS IN ADULT PATIENTS: A SINGLE-CENTER COHORT**

Elena Emanuela Rusu1,2, Adrián Catalin Lungu1,3, Gabriel-Robert Pandele1, Alexandru Iordache4, Raluca Bobeica2, Lucia PKD1

**Conclusion:** ADPKD is one of the most frequent genetic diseases of the human genome, with PKD1 being involved in > 80% of cases. With the apparent ease of modern technology, increasingly ADPKD families are presented for genetic consultation, also to non-specialized centers. It is tempting to use MPS considering the number of candidate genes and the size of PKD1 (46 exons). However, a negative result should be supported either by LR-PCR or WGS, taking the profound difficulties with the 6 pseudogenes of PKD1 into consideration. It is hard to explain why the positive correlation of liver disease in this family with the PKD1 c.2180T>C variant implies a genotype-phenotype correlation, or whether other (genetic) modifiers may play for a liver phenotype. The renal prognosis of the index case is feared to be worse among both diseases, even with the pathogenes being different with a ciliopathy (ADPKD) and a toxic proteinopathy (ADTKD-UMOD), respectively. Since both affected genes are situated on the respective chromosomes 16, the patient bears a 100% risk of receiving children with an adult onset kidney disease, where pre-implantation technology will not solve this specific problem.

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**#6086 NEUTRAL LIPID STORAGE DISEASE WITH RENAL INVOLVEMENT: A CASE REPORT**

Olivieri Antonella1, Rosamaria Roperto2, Federica Allegrotta2, Sarah Ecoorte3, Fiamentta Ravaglia3, Francesca Massaro1 and Campolo Gesualdo2

1Università degli Studi di Firenze, Scienze Biomediche, Sperimentali e Cliniche “Mario Serio”, Florence, Italy, 2Ospedale Santo Stefano, Nefrologia e dialisi, Prato, Italy and 3Ospedale Santo Stefano, Neurologia, Italy

**Background and Aims:** Neutral lipid storage diseases (NLSD) are rare conditions caused by an inborn error of neutral lipid metabolism that results in a deficit in the degradation of cytoplasmic triglycerides and a consequent abnormal storage of the neutral lipids. Their accumulation in cytoplasmatic lipid droplets in most tissues of the body results in a very heterogeneous phenotype: myopathic syndrome, intellectual deficit, cataract, nephrocalcinosis, cardiomyopathy, hepatomegaly are the main clinical manifestations. Less frequent conditions are diabetes, chronic pancreatitis and renal involvement.

**Method:** A 27-year-old woman visited our hospital on November 2022 because of progressive onset of edema, dyspepsia, nausea and loss of appetite. The medical history showed that 4 years before she was diagnosed with diabetes mellitus and she has been suffering from severe muscle weakness (she was helping herself with the wheelchair) for two years. In 2017 a proctological evaluation showed an anal hypotonia from likely neuropathy. Blood chemistry tests revealed a metabolic acidosis, a decreased renal function, anaemia and nephrotic range proteinuria at the urinalysis. A bilateral pleural effusion was described at the chest radiograph and a circumferential pericardial effusion at a first echocardiogram. The ultrasound of the abdomen described a small size of the right kidney (90 mm) and an angiomyolipoma on the left kidney. Neurological examination showed a mild intellectual disability, facies with dysmorphic appearance and hypotonia of proximal and distal muscular masses of the upper limbs. Lower limbs showed a more pronounced strength deficit on the left and a hypotonia to proximal muscle masses. Electromyography showed a condition of severe sensitivity polyneuropathy: signs of chronic denervation and morphological alterations of the motor unit especially in the proximal districts of the lower limbs. Ophthalmological examination showed an advanced cataract. Cardiological evaluation through heart echo scans showed a dilated heart disease with ventricular function and dilation of the pulmonary artery. A quadriceps muscle biopsy finally revealed myogenic features consistent with neutral lipid storage disease. Fabry test came back negative. Despite several drug treatments, the patient continued to be asthenic, inapprarent

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**Abstracts**
and the oxygen therapy could not be removed because frequent episodes of desaturation. The deterioration of the patient's clinical conditions required the onset of dialysis immediately. Unfortunately, despite adequate information on the risks of possible refusal, the patient denied consent for central venous catheter placement and hence the beginning of renal replacement therapy. Sadly, the patient was lost to follow up and it was not possible to carry out other diagnostic investigations.

**Results:** Our patient developed an end-stage renal disease in the framework of a remarkable BM disease decrease before cytotoxic lipid droplets are ubiquitous organelles, we can assume that in this case, kidney involvement is due to a pathogenetic mechanism similar to that of other storage diseases such as Fabry disease (Table 1).

**Conclusion:** Here we describe a 27-year-old NLSD female patient showing late onset myopathy and difficulties in mobilization in association with severe cardiac and ocular involvement, mild intellectual disability, diabetes mellitus, type 2 and end stage renal disease. Our data expand the clinical manifestations of NLSD, providing further evidence for clinical NLSD heterogeneity and mainly, further evidence for storage diseases with renal involvement.

**Table 1: NLSD and Fabry disease, main pathogenetic and clinical features.**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Genetic mutation</th>
<th>Enzymatic defect</th>
<th>Result</th>
<th>Deposition tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLSD</td>
<td>PNPLA2 (autosomal recessive)</td>
<td>Adipose-triglyceride lipase</td>
<td>Systemic triacylglycerol deposition in cytoplasmic lipid droplets</td>
<td>Skeletal and Cardiac muscles</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Liver Eyes</td>
</tr>
<tr>
<td>FABRY</td>
<td>GLA (X-Linked)</td>
<td>α-galactosidase A</td>
<td>Systemic lysosomal accumulation of glycolipids</td>
<td>Kidney Peripheral blood</td>
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<td>Heart Eyes</td>
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<td>Peripheral nervous system</td>
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<td>Lympathic and blood vessels</td>
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<td>Lung</td>
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<td>Gastrointestinal system</td>
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#2635

**ASSOCIATION BETWEEN PLASMA LYSO-Gb3 LEVELS AND BONE MINERAL DENSITY IN PATIENTS WITH FABRY DISEASE**

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**Background and Aims:** Fabry disease is a rare X-linked genetic disorder that contributes to various clinical manifestations including cardiac hypertrophy, renal dysfunction, cerebrovascular disease, angiokeratoma, and anhidrosis. Several previous reports showed that male patients with Fabry disease had decreased bone mineral density (BMD). However, the association of BMD with clinical characteristics and biomarkers of organ damage in patients with Fabry disease has not been sufficiently studied. Therefore, we aimed to investigate their associations in patients with Fabry disease.

**Method:** Patients with Fabry disease who attended our hospital from January 2008 to June 2021 were included in this study. Patients without enough clinical and laboratory data were excluded from this study. The remaining fifteen patients were assessed in this study. We examined clinical characteristics, biomarkers including blood globotriaosylsphingosine (lyso-Gb3) levels, and BMD, and compared them between male and female patients. We measured the lumbar spine and femoral BMD by dual-energy bone X-ray absorptiometry and calculated the Z-score. Furthermore, we also examined ΔBMD, defined as the two-year change in the Z-score, for ten patients who underwent BMD measurement before and after starting ERT. Because two patients already had received ERT, two did not undergo BMD measurement, and one took an anti-osteoporotic agent, they were excluded from the analysis.

**Results:** Both lumbar spine BMD and femoral BMD decreased in male patients, while they were preserved in female patients (lumbar spine Z-score: -1.9 ± 2.0 versus 0.8 ± 0.8, p < 0.05; femoral Z-score: -1.0 ± 1.4 versus 0.6 ± 0.6, p < 0.05) among all the study patients. Lumbar spine and femoral BMD showed a significantly negative correlation with blood lyso-Gb3 levels. Moreover, blood lyso-Gb3 levels were significantly correlated with the lumbar spine BMD (r = -0.92; p < 0.01) and femoral BMD (r = -0.91; p < 0.01) in male patients. On the other hand, there was no significant correlation of blood lyso-Gb3 levels with the lumbar spine BMD (r = 0.66, p = 0.18) and femoral BMD (r = 0.41, p = 0.99) in female patients. After starting ERT, blood lyso-Gb3 levels were significantly reduced in both male and female patients. The lumbar spine ΔBMD in male patients improved whereas that in female patients remained unchanged despite no changes in kidney function and serum calcium and phosphates levels.

**Conclusion:** Our findings suggested that lumbar spine BMD and femoral BMD decreased in male patients with Fabry disease possibly due to the deposition of lyso-Gb3 in bone tissue and ERT could improve BMD in these patients.

**#2845**

**TOLVAPTAN TREATMENT FOR THREE YEARS SIGNIFICANTLY IMPROVED RENAL PROGNOSIS IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) PATIENTS**

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1 General Hospital of Athens “G. Gennimatas”, Athens, Greece and 2 Bioiatriki, Department of Magnetic Resonance, Greece

**Background and Aims:** Vasopressin receptor antagonist, tolvaptan, is the first specific treatment approved for ADPKD. Long-term real clinical results with this drug are not yet available. We present the results regarding renal function, cyst-kidney volume and renal prognosis in patients with rapidly progressive disease after three years of tolvaptan treatment.

**Method:** Forty-one ADPKD patients who remained in tolvaptan treatment, without adverse reactions for 3 years, were included in the study. Total kidney volume (TKV) was measured using Magnetic Resonance Imaging (MRI), before and after three years of treatment. The Mayo Clinic Imaging Category (MCIC) and the prediction of End Stage Renal Disease (ESRD) based on the Mayo Clinic formula (Irazabal MV et al, JASN, 2015) were also calculated for all patients, before and 3 years post treatment. Using the same formula the expected estimated-glomerular filtration rate (e-GFR) at 3 years without treatment was calculated and compared to the e-GFR found after three years of treatment. The expected TKV increment at 3 years was calculated (5.3% increment per year) and was compared to the TKV measured in the second MRI. Finally, the expected renal prognosis at the time of treatment initiation (i.e. minus 3 years at the end of the study) was compared to the prognosis calculated based on real patients’ data found after 3 years of treatment. The dose of tolvaptan was adjusted according to the urine osmolarity (< 200 mOsm/Kg). In the third year of treatment, 15, 13 and 13 patients were treated with 90/30, 60/30, and 45/15 mg/day of tolvaptan respectively. Paired t-test and Wilcoxon signed-rank test were used for statistical analysis.

**Results:** Forty-one patients (18 females, 23 males), mean (SD) age 42.5 (8.6) years old were treated with tolvaptan for 3 years. According to MCIC, 41% of the patients were classified as 1C, 44% as 1D, and 15% as 1E. Pre-treatment mean (SD) e-GFR was 61.8 (24.6) ml/min while 15% of the patients were on stage 1 of Chronic Kidney Disease, 42% on stage 2, 12% on stage 3a, 24% on stage 3b, and 7% on stage 4 (>25 ml/min). The expected mean (SD) TKV at 3 years without treatment was 2717 (1839) ml, while the measured TKV found
after 3 years of treatment was 2773.3 (2086.9) ml (p = 0.44). The expected e-GFR at 3 years without treatment was calculated at 31.1 (25.2) ml/min while the measured e-GFR after 3 years of treatment was 57.3 (30.2) ml/min (p = 0.001). Finally, while the expected mean (SD) ESRD prediction at the time of treatment initiation was 10 (6.9) years, the calculated ESRD prediction after 3 years of tolvaptan treatment was 12 (8) years (p < 0.001).

Conclusion: Tolvaptan treatment for three years slowed down the clinical course of ADPKD in terms of renal function decline and ESRD prediction, but had no impact on total kidney volume.

#4097
BASELINE CHARACTERISTICS OF THE KOREAN GENETIC COHORT OF INHERITED CYSTIC KIDNEY DISEASE
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Background and Aims: We report the baseline and genetic characteristics of the nationwide genetic cohort for Korean hereditary cystic kidney disease prior to detailed molecular analysis.

Method: We performed a 3-year prospective, multicenter cohort study at 9 hospitals from May 2019 to May 2022. Patients with more than 3 renal cysts were enrolled and classified into 3 categories: typical and atypical autosomal dominant polycystic kidney disease (ADPKD), and pediatric PKD. Clinical and genetic characteristics were compared among categories. Genetic analysis was performed by using gene panel comprised of 89 ciliopathy-related genes.

Results: A total of 798 patients were enrolled. Mean age was 42.7 ± 17.3 years, and 47.8% were male. Patients were categorized into typical ADPKD (560, 70.2%), atypical ADPKD (165, 20.7%), and pediatric PKD (73, 9.1%). Typical ADPKD group of 62 subjects with ADPKD (mean age -54.3years old, men:women 34:28, with 1A and 1B Mayo ADPKD risk classes) and a group of 37 healthy subjects, similar as sex, mean age, ADPKD diagnosis was based on familial history, clinical exam and CT or MRI scan. We excluded from the study subjects that presented cysts in other organs except the kidney, with hypertension treatment for less than 6 months; metabolic disorders (carbamoyl phosphate synthase 1 and N-acetyl glutamate synthase deficiencies, lack of ornithine transcarbamilase, hyperargininemia, phenylketonuria). Laboratory tests: serum level of arginine, enzymatic activity of arginase 2 (ARG-2) and nitric oxide synthesis (Asymmetric Dimethylarginine -ADMA, Symmetric Dimethylarginine -SDMA). ADMA and SDMA were overexpressed in ADPKD group compared with control group.

Conclusion: The measured e-GFR after 3 years of treatment was 2773.3 (2086.9) ml (p < 0.001). Pathogenic variants were found in 40% of patients (122/306). Having higher discovery rate (62.3%) compared to atypical ADPKD (57.3%) and control group (33.9%).

Table 1: The serum levels of the analysed metabolites.

<table>
<thead>
<tr>
<th>Metabolites</th>
<th>ADPKD group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arg (umols/L)</td>
<td>47.6±16.8</td>
<td>89.2±12.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Direct nitrite (umols/L)</td>
<td>10.1±2.2</td>
<td>15.3±2.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total nitrite (umols/L)</td>
<td>23.5±6.6</td>
<td>33.9±6.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nitrate (umols/L)</td>
<td>13.4±7.8</td>
<td>18.6±4.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ARG 2 (U/L)</td>
<td>10.9±4.8</td>
<td>8.2±2.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NOS2 (U/L)</td>
<td>14.8±2.9</td>
<td>12.9±1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ADMA (umols/L)</td>
<td>0.88±0.33</td>
<td>0.58±0.04</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SDMA (umols/L)</td>
<td>1.38±0.36</td>
<td>0.52±0.08</td>
<td>&lt;0.010</td>
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#4542
L-ARGININE-NITRIC OXIDE MOLECULAR PATHWAY IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE
Corina-Daniela Ene1,2, Ilina Nicolae3, Mircea Penescu1,2 and Cristina Capusa1,2
1Carol Davila Clinical Hospital of Nephrology, Nephrology, Bucharest, Romania, 2Carol Davila University of Medicine and Pharmacy, Nephrology, Bucharest, Romania and 3Victor Babes Clinical Hospital of Infectious Diseases, Research, Romania

Background and Aims: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is an inherited, complex disease, cystogenesis and phenotypic changes in this disorder being not yet fully understood. Recently, arginine, important for renal cells metabolism, was proved to play an important role in ADPKD physiopathology [1]. The inability of cells to recycle or synthesize intracellular arginine through the urea cycle is defined as arginine auxotrophy. Arginine auxotrophy in ADPKD induces cell hyperproliferation, and cysts formation [2]. We aimed to explore L-Arginine (Arg) - Nitric Oxide (NO) molecular pathway in ADPKD, a multisystemic, arginine auxotrophy disease.

Method: We developed a prospective, case control study, in Carol Davila Clinical Hospital of Nephrology, Bucharest, Romania. The study included a group of 62 subjects with ADPKD (mean age -54.3years old, men:women 34:28, with 1A and 1B Mayo ADPKD risk classes) and a group of 37 healthy subjects, similar as sex, mean age, ADPKD diagnosis was based on familial history, clinical exam and CT or MRI scan. We excluded from the study subjects that presented cysts in other organs except the kidney, with hypertension treatment for less than 6 months; metabolic disorders (carbamoyl phosphate synthase 1 and N-acetyl glutamate synthase deficiencies, lack of ornithine transcarbamilase, hyperargininemia, phenylketonuria). Laboratory tests: serum level of arginine, enzymatic activity of arginase 2 (ARG-2) and nitric oxide synthesis (Asymmetric Dimethylarginine -ADMA, Symmetric Dimethylarginine -SDMA).

Results: In ADPKD patients, the serum levels of arginine and of the stable metabolites of nitric oxide had statistically significant lower levels compared with control group (Table 1). The levels of the principal enzymes that metabolizes arginine – arginase 2 and nitric oxide inducible synthase, respectively the endogenous inhibitors of nitric oxide synthesis were statistically significant higher in ADPKD group when compared with control group (Table 1). The AR2/Arg, NOS2/Arg, Nitrite/Arg, Nitrate/Arg, ADMA/Arg and SDMA/Arg ratios were statistically significant overexpressed in ADPKD group when compared with control group.

Conclusion: ADPKD is a metabolic kidney disease, auxotrophic for arginine. The metabolic ADPKD phenotype of renal cells with low risk of progression (1A and 1B Mayo) is defined by the alteration of L-Arginine-NO molecular pathway, the significant reduction of systemic arginine, moderately increased enzymatic activities of ARG2 and NOS2, the reduction of the synthesis and bioactivity of NO. Exploring arginine reprogramming and related molecular L-Arg-NO pathways disturbances could offer more information about ADPKD physiopathology.

REFERENCES
Background and Aims: In approximately 10% of adults with chronic kidney disease, a hereditary cause can be identified. Important representatives are Alport syndrome and inherited podocytopathies, which often show the histological picture of focal segmental glomerulosclerosis (FSGS). FSGS is a histological finding of various etiologies (primary, hereditary, secondary). Especially in suspected glomerular kidney disease, kidney biopsy can provide a clue to the underlying inherited kidney disease. Biopsies were further investigated by proteomics via liquid-chromatography-mass spectrometry (LC-MS) to potentially elucidate the underlying protein defect.

Method: The cohort for this retrospective study consisted of 23 individuals with a genetically confirmed inherited nephropathy and a previously performed kidney biopsy. A systematic pathological secondary review of the 23 biopsies was carried out (genetic diagnosis unknown at secondary review). The findings of the biopsies were compared with the molecular genetic results. 9 proband and 9 control biopsies were additionally evaluated through LC-MS. Laser capture microdissection was used to extract glomeruli from the tissue samples, which were then further analyzed on alterations in protein expression secondary to the respective disease-causing variants.

Results: In the cohort, disease-causing variants were identified in the following genes: COL4A3 (n = 3), COL4A5 (n = 4), WT1 (n = 3), UMOD (n = 3), and each n = 1 for the genes INF2, DAAM2, MUC1, COQ8B, NPHS4, TRIM8, CD2AP, NPHS2, CLCN5, and PAK2. The biopsies showed predominantly segmental glomerulosclerosis and parenchymal scarring, as well as podocyte damage. Four individuals with the histological diagnosis of Alport syndrome were genetically confirmed as having X-chromosomal (n = 2; including one female carrier) and autosomal-recessive (n = 2) Alport syndrome. Proteomics showed heterogeneous results. Proband samples carried variants in COL4A3 (n = 3), COL4A5 (n = 3), ADCK4, NPHS4, and WT1 (the last three each n = 1). COL4A3 was detected in 6/9 of control samples and in 0/9 of proband samples; COL4A5 was detected in 5/9 of control samples and in 0/9 of proband samples. ADCK4, NPHS4, and WT1 could not be detected in this analysis, neither in control, nor in proband samples.

Conclusion: In this study, molecular genetic diagnostics allowed a more precise disease assignment and thus provided information on therapy, prognosis, recurrence in the transplant, possible extrarenal phenotypes, and inheritance. Histological findings can indicate an inherited disease and help to trigger genetic testing (e.g., Alport syndrome). However, genetic diagnostics can also classify cases for which there are no typical morphological criteria described or if severe scarring impairs morphological diagnosis. Numerous cases of a respective monogenic disease would have to be analyzed in order to establish common histopathological criteria, if present. This is a challenge due to the rapid discovery of new disease-associated genes and the rarity of the respective diseases. LC-MS-based proteomics from kidney biopsy samples showed to be of limited value in further characterizing changes associated with specific variants. Unlike the genome, which is consistent due to the stability of DNA, the proteome is influenced by various effects: Different stages of fibrosis depending on the time of biopsy and other factors like coexistent disease lead to varying protein intensities even in two separate samples that present identical genetic variants. The detected protein intensity patterns could not be sufficiently correlated with the genetic findings. Despite the detection of certain proteins of interest like type IV collagens, their intensity variation due to advanced tissue damage did not allow reliable conclusions on the underlying cause. Alternatively, molecular methods such as MALDI imaging could further visualize these changes.
Figure 1: Genotype-phenotype relationship in FRG patients. (A) Twenty-four-hour urinary glucose excretion (24hUG) is inversely related to RTG (\(\log(24hUG) = -0.1881 \times \text{RTG} + 2.252, R^2 = 0.7650\)). (B) In our cohort, patients with two SLC5A2 variants had lower RTG than those with only one (Mean RTG 3.9±2.1mmol/L vs 6.2±2.0mmol/L, \(p = 0.057\)). (C) Literature review showed that 24hUG corrected by body surface area of patients carrying a single SLC5A2 variant were significantly lower than those carrying two variants (7.20±9.28g/1.73m\(^2\) vs. 52.39±45.22g/1.73m\(^2\), \(p<0.0001\)). (D) Patients from the literature were divided according to the type of variant they carried: mis+in-frame (missense variants and in-frame indels), truncating (nonsense variants and frameshift variants), and splicing variants. Patients with homozygous splicing variants had significantly less 24hUG (35.8±27.10g/1.73m\(^2\)) than those with homozygous truncated (81.6±39.88g/1.73m\(^2\)) or mis+in-frame variants (82.3±40.34g/1.73m\(^2\), \(p<0.05\)). Homo = homozygous, hetero = heterozygous. (E) Patients carrying missense variants were divided according to the conservation of the involved amino acid. Patients with homozygous variants at conservative residues had more 24hUG (104.7±31.70g/1.73m\(^2\)) than those with variants involving non-conservative residues (46.3±22.38g/1.73m\(^2\), \(p = 0.0031\)). (F) Daily urinary glucose excretion (24hUG) mapped on the SLC5A2 gene structure. Each node represents one variant, and the node's height corresponds to an average of 24hUG of FRG patients carrying this variant. Nodes on the top: homozygotes; nodes on the bottom: heterozygotes. The color of the nodes represents variant types (black: missense variants; pink: in-frame indels; green: frameshift indels; blue: nonsense variants; cyan: splicing variants). Circles: 24hUG normalized by body surface area (g/1.73m\(^2\)/d); squares: 24hUG in g/d.

#3572
CLINICAL AND GENETIC CHARACTERISTICS OF CHILDREN WITH BARTTER SYNDROME: A SINGLE CENTER LONG-TERM EXPERIENCE
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Children's Hospital "P&A Kyriakou", Pediatric Nephrology, Athens, Greece

Background and Aims: Bartter syndrome is an autosomal recessive renal tubular disorder. Clinical diagnosis can be challenging due to rarity and phenotypic overlap. Little information is available on a long term follow-up in Bartter syndrome. Our aim was to describe clinical -genetic correlations as well as our experience from the long term follow up of these patients.

Method: Clinical and genetic characteristics of patients with Bartter syndrome at diagnosis and long term follow up are reported in 19 children. Genetic testing (whole exome sequencing, WES) was done in 14/19 patients. The study period was 17 years (January 1, 2006 to December 31, 2022).

Results: 16 Caucasian and 3 of gipsy origin (13 boys, 68%) were included. The median age at diagnosis was 0.52 yrs. Median follow up time was 9.8yrs (IQR 6.86-13.8). WES revealed 6 mutations in KCNJ1 genes, 5 in SLC12A1 and 3 in CLCNKB genes. 4 new mutations were identified (3 in KCNJ1 genes and 1 in SLC12A1). 18/19 children were born pre-term (including 2/3 patients with CLCNKB). Nephrocalcinosis was present in 18/19 patients (included the 3 patients with CLCNKB mutations). 4/6 patients with KCNJ1 mutations presented initially with hyperkalemia. Medical treatment in the last follow up included supplementation with potassium in 18, non-steroidal anti-inflammatory agents in 15 and gastroprotective drugs in 13, ramipril in 2. 2/19 received recombinant growth hormone. At last follow up body weight and height were within normal ranges in 16/19 (84%) patients. Hyperparathyroidism (median time of PTH 151.5 pg/ml) have 6/11
(56%) of patients with Bartter I (KCNJ1 mutation) and Bartter II (SLC12A1 mutation) and only 1/3 with Bartter III (CLCNKB mutation). 2/19 patients have proteinuria. Chronic kidney disease (CKD) occurred in 7/19 (37%) suggesting that the long term prognosis can be unfavorable (4 CKD stage II, 3 CKD stage III). Of note 2 patients with CKD had impaired renal function since diagnosis while the remaining 5 progressed gradually during followup. Conclusion: WES is useful in dealing with the phenotypic heterogeneity of Bartter syndrome. Our results emphasize the need for early diagnosis, regular followup and appropriate treatment in order to maintain normal renal function and achieve normal final height and weight.

#6060
A NOVEL CT-BASED RADIOMICS APPROACH FOR KIDNEY FUNCTION EVALUATION IN ADPKD
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Background and Aims: Clinical management of autosomal dominant polycystic kidney disease (ADPKD) might take advantage of the use of new tools to predict risk of progression towards end stage kidney disease (ESKD). The aim of this study is to develop and validate a model based on radiomic features to predict kidney function among patients with ADPKD obtained from CT scans performed for the determination of total kidney volume (TKV).

Method: We retrospectively selected a cohort of 58 patients with ADPKD who underwent CT scan from February 2020 to March 2021, including 30 patients with eGFR ≥ 60 mL/min/1.73 m² and 28 with eGFR < 60 mL/min/1.73 m² at baseline. An expert radiologist generated a region of interest (ROI) segmentation for cystic kidney compounds, obtaining 58 ROIs from which we extracted 217 radiomic features using a dedicated software. We built three different logistic regression models to predict kidney function based on different predictors: height-adjusted TKV (ht-TKV), a selected radiomic feature (F_cm_merged.clust.tend), and both. Area under the curve (AUC) of the receiver operating characteristic (ROC) and accuracy were employed to evaluate models’ performance in discriminating between the two eGFR groups. Internal 3-fold cross-validation (CV) was performed.

Results: The ht-TKV, radiomic and combined models presented respectively an AUC (95% confidence interval) of 0.79 (0.67, 0.91), 0.83 (0.72, 0.93), 0.84 (0.74, 0.94), confirmed by the CV. Mean (standard deviation) values of the accuracy over CV iterations were 0.67 (0.10), 0.77 (0.09), 0.77 (0.09) for the three models. A model combining ht-TKV with a radiomic feature based on CT images from polycystic kidneys resulted effective in the prediction of baseline kidney function in our cohort. Furthermore, a logistic regression model based on a different radiomic feature (F_cm.2.5Dmerged.info.corr.2) selected among a subcohort of 29 ADPKD patients with a clinical follow-up, predicted rapid progression with an AUC of 0.81, a sensitivity of 100% and a specificity of 53%.

Figure 1: ROC curves from Ht-TKV, radiomic and combined models.
Conclusion: This is among the first studies which aimed to investigate, in a clinical setting, radiomics potential ability in discriminating eGFR at baseline and to explore as well whether a reliable radiomic feature could be taken into account in predicting faster rapid kidney function impairment over time. Further studies should implement a model extension to predict kidney function slope in order to confirm the role of radiomics in ADPKD management.

DEVELOPMENT OF AN EXPERT MODEL FOR THE DIAGNOSIS OF INHERITED KIDNEY DISEASES

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Background and Aims: Inherited kidney diseases (IKDs) account for 10–20% of cases of Chronic Kidney Disease (CKD). Mutations in over 400 genes are known as drivers of more than 150 monogenic kidney disorders. Clinical diagnosis is often challenging as these disorders are characterized by numerous clinical features often shared by many diseases as well as very variable expression. Over the years, rare-disease databases such as OMIM and Orphanet have compiled information to facilitate diagnosis of rare diseases. Based on these, The Human Phenotype Ontology (HPO) developed a standardized directory for phenotypes with phenotype-disease associations. New phenotype-driven gene-priorization tools such as Phenomizer have been developed in the recent years using these resources, however structural inaccuracies prevent a proper uptake of these tools. To date, no specific renal disease databases have contributed significantly to improving the clinical diagnosis of rare diseases. However, these tools are nonspecific and imprecise when focusing on a specific field such as IKDs. Curation of current annotations by experts in the field will greatly improve the accuracy of these tools and facilitate clinical diagnosis of IKDs.

Conclusion: Current phenotype-based gene prioritization tools and rare disease databases have contributed significantly to improving the clinical diagnosis of rare diseases. However, these tools are nonspecific and imprecise when focusing on a specific field such as IKDs. Curation of current annotations by experts in the field will greatly improve the accuracy of these tools and facilitate clinical diagnosis of IKDs.

CLINICAL EXOME SEQUENCING AS A TOOL FOR GENETIC DIAGNOSIS OF ALPORT SYNDROME AND THIN BASEMENT MEMBRANE DISEASE

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Background and Aims: Alport syndrome (AS) is an inherited nephropathy caused by pathogenic variants in COL4A3 (autosomal dominant -AD- and autosomal recessive -AR- inheritance), COL4A4 (AR) and COL4A5 (X-linked dominant –XLD). It is characterized by glomerular nephropathy with
hematuria progressing to end-stage renal disease, frequently associated with sensorineural deafness and ocular anomalies. In thin basement membrane disease (TBMD) most patients are asymptomatic and are incidentally noted to have microhematuria, mild proteinuria, and occasionally gross hematuria, with normal renal function. This condition is caused by pathogenic variants in COL4A3 and COL4A4 (AD). We have systematically applied genetic testing to pediatric and adult patients with clinical features suggestive of AS (Table 1).

Method: Clinical exome sequencing (CES) was performed on a cohort of 95 patients referred to our center from 2019 to 2022. Analyses were performed on an in-silico designed panel including 523 renal genes. Whenever possible, identified variants were segregated by Sanger sequencing.

Results: We identified causative (C4/C5) variants in 43 (45.3%) patients. Among them, genetic diagnosis of AS was obtained in 25 patients (58.1%): one (4.0%) with biallelic variants in COL4A4, 13 (52.0%) with COL4A5 variants (6 females and 7 males), 5 (20.0%) with COL4A3 variants (4 heterozygous and 1 homozygous) and 6 (24.0%) cases with coexisting variants in one or more other collagen genes. In 16 (37.2%) patients, we found causative monoallelic variants compatible with TBMD: 12 (75.0%) patients with variants in COL4A4 and 4 (25.0%) in COL4A3. Lastly, in 2 cases, we found variants in COL4A1 (#120130) and MYH9 (#160775), both genes associated with other renal diseases with a clinical presentation partially overlapping with AS. In additional 16 cases (16.8%), we identified C3 variants in collagen genes. In the remaining patients, genetic testing was negative (14 patients, 14.7%) or inconclusive (22, 23.2%). Of note, we identified 6 families with digenic AS. In 4 of them - 3 with COL4A5/COL4A4 variants and one with COL4A3/COL4A4 variants – the coexistence of two variants was associated to earlier renal failure, compared to family members bearing a single variant. In contrast, in the remaining 2 families (33.3%), members with COL4A5/COL4A3 missense variants had a milder phenotype compared to male family members with the single variant COL4A5 variant. In families with digenic AS, at least one variant involved the substitution of a glycine with another amino acid in the triple helix domain, frameshift indel variants in the triple helix domain or inframe indel in the collagen IV domain non-collagenous. To better understand the impact of multiple variants on collagen structure, computational studies are currently ongoing.

Conclusion: CES is a powerful tool to clearly define the diagnosis when AS or TBMD are suspected, as witnessed by a detection rate of 43.2%. Genetic diagnosis allows to identify the causative gene offering the possibility of extending diagnosis to other family members, also in the prenatal setting. In addition, it offers the possibility to identify multiple variants in collagen genes associated with digenic AS, as well as to find variants in other genes implicated in kidney disease. Notably, the presence of digenic variants is not necessarily predictive of a worse disease outcome. For all these reasons, molecular diagnosis can be useful to improve clinical management, to calculate recurrence risk and to better define the prognosis of the patient.

REFERENCE

#6143

FAMILIAL LECITHIN: CHOLESTEROL ACYLTRANSFERASE (LCAT) DEFICIENCY AS A CAUSE OF CHRONIC KIDNEY DISEASE – A CASE REPORT
Motaz Obeidat1, Marya Obeidat2 and Mohammad Al-Shboul2

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Background and Aims: Genetic causes of chronic kidney disease are becoming more recognized. Familial lecithin: cholesterol acyltransferase (LCAT) deficiency (FLD) is a rare genetic disorder caused by loss of function mutations in LCAT gene. Patients present with abnormal lipid profile characterized with markedly reduced HDL-C, corneal opacification, anemia, and renal disease, which eventually progresses to kidney failure. Several studies reported genetic variants in LCAT gene that are associated with FLD, and others in certain apolipoprotein genes that act as risk factors for the disease. Incomplete form of FLD, caused by certain mutation, leads to fish-eye disease characterized by progressive corneal opacification. FLD was described in studies from Europe, Latin and North America, Australia and Japan. In Jordan, genetic and clinical studies in FLD patients are absent.

Method: We present a 36-year-old female who presented with nephrotic-range proteinuria, high serum creatinine, hypertension and corneal opacity. Further examination showed a severely reduced HDL level, an increased triglycerides level, anemia and mild thrombocytopenia. Patient’s laboratory values at presentation are shown in Table 1. Her blood film showed normocytic and normochromic red blood cells, anisopoikilocytosis and target cells. Light and electron microscopy examination of the kidney biopsy revealed intramembranous, subendothelial and mesangial lipid deposition and vacuolization. In addition, the patient was found to have a family history of corneal opacity and chronic kidney disease. Therefore, FLD was suspected. Whole exome sequencing was employed to identify FLD variants.

Results: The patient was found to be homozygous at 154+5delG in LCAT gene, heterozygous at 388T>C in apolipoprotein E gene (APOE) and homozygous at 1114G>C in WW domain-containing oxidoreductase gene (WWOX). The patient’s chronic kidney disease was managed supportively with low salt diet, moderate protein intake, statins, angiotensin receptor blockers and blood pressure control. After one year of follow up, her serum creatinine is 220 μmol/l and estimated proteinuria is 1.2 gm/24 hrs.

Conclusion: FLD should be suspected in patients who present with kidney disease associated with significantly low HDL cholesterol and corneal opacity. Family members should also be screened for kidney disease and genetic mutation in LCAT gene. To date, treatment is mainly supportive and enzyme replacement therapy is not yet widely available.

Table 1: Cohort description.

<table>
<thead>
<tr>
<th>Age</th>
<th>N° patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18 yo</td>
<td>21 (22.1)</td>
</tr>
<tr>
<td>≥ 18 yo</td>
<td>74 (77.9)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47 (49.0)</td>
</tr>
<tr>
<td>Female</td>
<td>48 (51.0)</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>56 (58.9)</td>
</tr>
<tr>
<td>Negative</td>
<td>39 (41.1)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>82 (83.1)</td>
</tr>
<tr>
<td>African</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (9.5)</td>
</tr>
<tr>
<td>Clinical features</td>
<td></td>
</tr>
<tr>
<td>Microhematuria</td>
<td>63 (66.3)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>45 (47.4)</td>
</tr>
<tr>
<td>Biopsy compatible with Alport syndrome</td>
<td>20 (21.1)</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>27 (28.4)</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>19 (20.0)</td>
</tr>
</tbody>
</table>
Abstracts

Background and Aims: Alport Syndrome (AS; ORPHA63) is one of the most frequent hereditary kidney diseases (HKD). Its autosomal dominant form due to COL4A3-4 heterozygous mutations is being increasingly diagnosed thanks to the generalization of genetic studies. Since there is no curative treatment for the disease, management is based on drugs that slow its progression, mainly RAAS inhibitors. The SGLT2 inhibitor Dapagliflozin has demonstrated to slow chronic kidney disease (CKD) progression by decreasing proteinuria, however very few ADAS patients were included in its clinical trial. Our aim is to analyze whether dapagliflozin is associated with a decrease in proteinuria in ADAS patients.

Method: In this prospective observational study, we analyzed 12 ADAS patients that started dapagliflozin due to proteinuria in spite of maximum tolerated RAAS inhibitor treatment and eGFR > 25 ml/min/1.73 m². We analyzed diabetes and hypertension presence (and its control), weight changes, possible adverse effects and laboratory variables before and after treatment initiation (Cr, eGFR, K, uricacid, albuminuria, proteinuria). Results: During a mean follow-up period of 7±4 months, we observed 12 patients, 5 (41.7%) male, 61±10 years old. 2 (33.3%) had type 4 diabetes, 2 (16.7%) had impaired fasting glucose (IFG), 11 had hypertension diagnosis, 1 patient had obesity (BMI 36) and other 7 were overweight (mean BMI 28±2). 9 patients had the higher dose of an RAASi, the other three couldn’t achieve it because of hypotension events. 3 patients also took an antagonist of mineralocorticoid. Only one had another diuretic prescription (furosemide 2022), in our pediatric tertiary center. Data regarding demographic variables, whether dapagliflozin is associated with a decrease in proteinuria in ADAS patients.

TABLE 1: PATIENT’S LABORATORY VALUES AT PRESENTATION.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient’s value</th>
<th>Normal range</th>
<th>Variable</th>
<th>Patient’s value</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Creatinine (µmol/l)</td>
<td>5.46</td>
<td>53-97</td>
<td>Urine protein (dipstick)</td>
<td>2+</td>
<td>negative</td>
</tr>
<tr>
<td>Serum albumin (g/l)</td>
<td>25.4</td>
<td>35-52</td>
<td>Urine RBCs/ hpf</td>
<td>15-18</td>
<td>0-2</td>
</tr>
<tr>
<td>Serum sodium (mmol/l)</td>
<td>134</td>
<td>135-145</td>
<td>Urine WBCs/ hpf</td>
<td>18-20</td>
<td>0-2</td>
</tr>
<tr>
<td>Serum potassium (mmol/l)</td>
<td>5.18</td>
<td>3.8-5.1</td>
<td>Spot urine proteins (mg/dl)</td>
<td>697</td>
<td>0-15</td>
</tr>
<tr>
<td>Serum bicarbonate (mmol/l)</td>
<td>12.7</td>
<td>22-29</td>
<td>Spot urine creatinine (µmol/l)</td>
<td>8252</td>
<td>2470-19200</td>
</tr>
<tr>
<td>Serum calcium (mmol/l)</td>
<td>2.12</td>
<td>2.15-2.5</td>
<td>Total cholesterol (mmol/l)</td>
<td>3.28</td>
<td>&lt;5.2</td>
</tr>
<tr>
<td>Serum phosphorus (mmol/l)</td>
<td>2.25</td>
<td>0.81-1.45</td>
<td>HDL cholesterol (mmol/l)</td>
<td>0.29</td>
<td>&gt;1.45</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>7.1</td>
<td>11-16</td>
<td>LDL cholesterol (mmol/l)</td>
<td>Can’t be calculated</td>
<td>&lt;3.37</td>
</tr>
<tr>
<td>WBC count/ mm³</td>
<td>3.81 × 10³</td>
<td>(3.5-11) x10³</td>
<td>Triglycerides (mmol/l)</td>
<td>5.71</td>
<td>&lt;1.8</td>
</tr>
<tr>
<td>Platelets count/ mm³</td>
<td>120.0 × 10³</td>
<td>(150-400) x10³</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Slower progression drugs are the main treatment of ADAS nowadays. Dapagliflozin has demonstrated its beneficial effects in other proteinuric CKD, but it hasn’t been well studied in ADAS. In our sample, it seems to achieve a proteinuria improvement without significant adverse effects and known bearable eGFR fall. Large studies must be considered to determine its beneficial use in a long-term basis.
Background and Aims: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common genetic cause leading to end stage renal disease (ESRD). The most striking ADPKD feature, which is the growth of renal cysts leading to nephromegaly and renal function loss, is attributed to the loss of PKD1 and PKD2 genes coding respectively for Polycystin 1 and Polycystin 2, which are proteins located on the primary cilium. ADPKD is considered a systemic disease as several extra-renal manifestations including liver cysts and hepatomegaly, valvular heart disease, aneurysms and diverticulosis can be associated to it. Because of the remarkable renal and hepatic involvement, patients affected by organomegaly may suffer from pressure-related conditions like malnutrition. Nutritional and hydration status can be assessed through Bioelectrical Impedance Analysis (BIA), used both in the healthy population and in patients affected by chronic kidney disease (CKD). It is nowadays still not clear whether the presence of renal and hepatic cysts may exert an influence on raw BIA measurements and consequently this is an important index for malnutrition in patients affected by chronic kidney disease (CKD) secondary to ADPKD or not. Together with other values derived from BIA evaluation, this could be used in the future in order to guide the therapeutic choice even in patients with a preserved renal function or a mildly reduced eGFR.

Conclusion: The results of our study are concordant with the only one present in the literature. Phase angle (PhA) has shown to be an important index of malnutrition both in healthy and ADPKD patients, we observed that it is independent of ADPKD and mostly correlated with age.

Method: We enrolled 132 adult patients (> 18 years of age), 71 being affected by ADPKD, 33 being affected by non-ADPKD related CKD and 28 healthy controls. Each patient accepted to undergo BIA analysis and anthropometric measurements (height, weight, BMI), which were performed on the same day. We then classified ADPKD patients according to their residual renal function degree and compared them to the corresponding non-ADPKD of the same grade of renal insufficiency.

RESULTS: We observed that in ADPKD patients showing organomegaly, in particular hepatomegaly, there is a positive correlation between this factor and BIA parameters including TBW%, ECW% and ICW%. On the other hand, no significant correlation with age and GFR was found. As far as PhA concerned, which is an indicator of malnutrition both in healthy and ADPKD patients, we observed that it is independent of ADPKD and mostly correlated with age. It has also been demonstrated that PhA significantly decreases in presence of organomegaly or when renal diameters are increased, even in subjects with a preserved or mildly reduced eGFR.

Conclusion: The results of our study are concordant with the only one present in the literature. Phase angle (PhA) has shown to be an important index for malnutrition in patients affected by chronic kidney disease (CKD) secondary to ADPKD or not. Together with other values derived from BIA evaluation, this could be used in the future in order to guide the therapeutic choice even in patients with a preserved renal function or a mildly reduced one.

#6841

IS NEPHRECTOMY ALWAYS USEFUL IN ADPKD? A CASE REPORT OF HEPATIC FIBROSIS WITH SPLENOMEGALY AND PANCYTOPENIA AS LATE CONSEQUENCE

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San Raffaele Hospital, Milano, Italy

Background and Aims: Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic kidney disease. Its main feature is the progressive enlargement of both kidneys with progressive loss of kidney function. ADPKD is the 4th leading cause of dialysis in the world. The disease has systemic involvement. Liver cysts are the most common extrarenal manifestations of ADPKD and are often incidentally found. However the liver can reach considerable size but its function is always preserved. Cysts lead to structural changes of the biliary tree and determine discomfort related to mass effect when significant liver enlargement occurs. Few cases of Budd Chiari syndrome (BCS) or of hepatic fibrosis have been reported in ADPKD patients after nephrectomy. Probably the removal of the kidneys can lead to obstruction of inferior vena cava by liver cysts.

Method: We report a case of hepatic fibrosis with splenomegaly and severe pancytopenia as a tardive complication after bilateral nephrectomy.

Case report: A 47 years old man was admitted c/o Division of Nephrology of San Raffaele Hospital in August 2018 because of a high-grade fever, general malaise, nausea and abdominal pain. The patient had a previous diagnosis of ADPKD. Genetic test indicative of PKD1 truncating mutation. He was chronically attended in the outpatient clinic of the same Division. On admission in hospital his renal function was severely impaired (crea 10 mg/dl; urea 213 mg/dl). No abnormalities at the blood count. Reactive C protein was elevated (156 mg/l nv 0-6). Urine culture was found negative. Abdominal NMR showed an important volumetric increase (compared with a NMR performed in 2014) of both kidneys with diameters of about 30 cm, several cysts with hemorrhagic and infective features and numerical and dimensional increase of the hepatic cysts; spleen was reported with normal diameters. Multiple antibiotic treatments were performed unfortunately without benefit. Therefore considering the state of end stage renal disease, the persistent infection and the severe symptoms, in September 2018 the patient underwent bilateral nephrectomy and hemodialysis was started. During the following years imaging studies aimed at the preparation for transplantation were performed. In November 2020 an abdominal NMR showed for the first time splenomegaly with a bipolar diameter of 14 cm. A NMR follow up was started. In January 2021 a further increase was reported as spleen diameter reported of 14.5 cm and a volumetric increase of hepatic cysts was shown. In September 2022 spleen reached to a diameter of 17 cm. Contextually in November 2020 patient started to present pancytopenia that had progressively been worsening with many concomitant infective and bleeding episodes. All hematologic causes were excluded. Just to explain the genesis of the splenomegaly in September 2022 a fibroscan was performed and a pathological liverstiffness was found. All hepatitis markers were negative and immunologic ones as well. Splenectomy was assumed, but patient clinical conditions so far do not allow it. Transplantation is currently contraindicated.

Conclusion: These evidences underline the necessity of scrupulous evaluation of polycystic kidneys and their anatomic relationship with the liver before nephrectomy. Nephrectomy is frequently considered in the preparation for renal transplantation. In light of these possible complications, maybe removal
of kidneys should be considered carefully in ADPKD patients with large involvement of the liver by cysts.

#6786

ADTKD DUE TO MUC-1 GENE MUTATION: A MAJOR DIAGNOSTIC CHALLENGE, NOT IDENTIFIED BY EXOME SEQUENCING

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1Nephrology operating unit, Florence University Hospital, Medicine and Surgery, University of Florence, Florence, Italy; 2Nephrology operating unit, Parma University Hospital, Medicine and Surgery, University of Parma, Parma, Italy and 3Laboratory of Genetics, University of Eastern Piedmont, Department of Health Sciences and IRCAD, Novara, Italy

Background and Aims: Autosomal dominant tubulointerstitial renal disease (ADTKD) is a rare cause of end-stage renal disease (ESKD) in adulthood. In addition to its rarity, ADTKD is probably underdiagnosed due to the very non-specific and heterogeneous clinical-laboratory-histopathological-instrumental picture and because of the diagnostic need to use specific methods of genetic investigation in order to highlight the mutations within the VNTR sequences of the MUC1 gene, not recognized by the most common exome sequencing. Mutations in the MUC1 gene, together with those in the UMOD gene, are the main mutations implicated in the pathogenesis of ADTKD.

Table 1: Genetic, clinical and laboratory characteristics of our cohort of patients with ADTKD due to MUC1 gene mutation.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients</th>
<th>Number of families</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic tests</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Exome sequencing</td>
<td>(1/10)</td>
<td></td>
</tr>
<tr>
<td>SNaPshot minisequencing (9/10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence of confirmatory genetic testing (7/17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic mutations</td>
<td>c.428dupC (9/10)</td>
<td></td>
</tr>
<tr>
<td>c.1442C&gt;G; [p.Ser481Cys]</td>
<td>(1/10)</td>
<td></td>
</tr>
<tr>
<td>Changes in urine sediment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria &gt; 1g/24h (3/13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microhematuria (0/13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-active sediment (10/13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biopsy not done (9/17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubular atrophy and interstitial fibrosis (3/4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal and segmental glomerulosclerosis (1/4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic ectasia of the tubular lumen at the cortico-medullary and/or medullary passage (2/4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thickening, un laminating or reduplication of the tubular basement membranes (2/4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative or nonspecific immunofluorescence (slight mesangial IgM/C3+) (3/3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset of CKD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 35 y (6/13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-65 y (5/13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 65 y (2/13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at ESKD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 35 y (4/9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-65 y (2/9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 65 y (3/9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ESKD: 4/13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ESKD, end-stage renal disease; CKD, chronic renal failure. In brackets the number of patients presenting the specific characteristic, out of the total number of patients for which data is available.

Figure 1: Family tree of a family followed by our center for familial nephropathy with MUC1 positive genetics.

Method: We analyzed the clinical, laboratory and histopathological characteristics of four families followed by our center with suspected diagnosis of ADTKD and detection of mutation of the MUC1 gene.

Results: Our data (Table 1) revealed a marked phenotypic variability, even within members of the same family (Fig. 1), and in particular as regards the age of disease onset and the different rate of progression towards ESKD (range 16 – 88 years). From a laboratory point of view, in 10 out of 13 patients the sediment was negative, and only in 3 patients proteinuria > 1 g/24h was highlighted. In 6/13 the onset occurred at the age of less than 35 years and among these, 4 of them presented ESKD early. In the few cases in which renal biopsy was performed (4/17), representing 0.4% of all biopsies in our centre, the most frequent finding was the presence of tubular atrophy and interstitial fibrosis (3/4), with cystic ectasia of the tubular lumen at the cortical-medullary level in half of the cases. Among the 10 patients subjected to genetic analysis, only in one case the mutation was highlighted by exome sequencing.

Conclusion: The large phenotypic variability, in particular of age at achievement of ESKD, suggests that other factors (modifier or environmental genes) could also affect disease progression. Common gene sequencing methods (e.g. exome sequencing, Sanger) have proved unable, in most cases, to identify mutations within the VNTR sequences of the MUC1 gene.

#2841

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) PATIENT CHARACTERISTICS ASSOCIATED WITH BETTER RESPONSE TO TOLVAPTAN TREATMENT

Vasiliki Gikas1, Eirini Evangelou1, Dimitra Gkalitsiou1, Paraskevi Liaveri1, Michaela Louka1, Angelos Drakopoulos4, Eirini Tigka1, Kyriaki Vasileiou1, Mihail Tsagkatakis2 and George Tsirpanlis1

1General Hospital of Athens “G. Gennimatas”, Athens, Greece and 2Bioiatriki, Department of Magnetic Resonance, Greece

Background and Aims: Tolvaptan treatment is indicated in patients with rapidly progressive ADPKD. The factors associated with a favorable mediation response are not completely analyzed. We looked into the characteristics of ADPKD patients who responded better to tolvaptan treatment after three years of treatment.

Method: Forty-one (41) patients, 18 females, 23 males, with rapidly progressive ADPKD (Mayo Clinic Imaging Category, MCIC, 1C, 1D and 1E, mean (SD) age 42.5 (8.6) years and estimated-glomerular filtration rate (eGFR) > 25 ml/min) who completed three years treatment with tolvaptan, were included in the study. Total kidney volume (TKV) was measured using Magnetic Resonance Imaging at the initiation of the study and 3 years post treatment. The expected e-GFR decline at 3 years without treatment was calculated using the Mayo Clinic formula (Irazabal MV et al., JASN, 2015) and compared to the e-GFR found after three years of tolvaptan treatment (e-GFR measured after 3 years of treatment versus expected e-GFR). Based on the same formula, the End Stage Renal Disease (ESRD) prediction was calculated, before and after 3 years of treatment (i.e. we focused on the difference between the ESRD prediction calculated prior to treatment initiation and the prediction calculated with the data measured after 3 years of treatment). The above mentioned differences in e-GFR and ESRD prediction were used as response to treatment markers and correlated with a series of patient characteristics (age, sex, age at ADPKD diagnosis, presence of hypertension (HTN) and age at HTN onset, age at ESRD of the affected parent, TKV, MCIC, etc) using univariate and multivariate statistical analysis.

Results: The median (IQR) difference between e-GFR measured after three years of tolvaptan treatment and the expected without treatment was 5.3 (-1.3, 8.7) ml/min (i.e. more than the expected at 3 years without treatment). The median (IQR) prediction of ESRD had been prolonged by 1 (0, 2) years of tolvaptan treatment and the expected without treatment was 5.3 (4.0, 6.3) years.

Abstracts
In univariate analysis, the baseline e-GFR (immediately before treatment) and the age at which the affected parent had developed ESRD were both positively associated with the e-GFR improvement and ESRD prediction prolongation (p = 0.02, 0.047, 0.01, and 0.02, respectively). In multivariate analysis, e-GFR improvement was associated with the age of the patient at treatment initiation (β = -0.9, 95%CI: -1.52 - 0.29, p = 0.006), the age of the patient at hypertension diagnosis (β = 0.88, 95%CI: 0.25 - 1.52, p = 0.008) and the age at which the affected parent had developed ESRD (β = 0.57, 95%CI: 0.16 - 0.98, p = 0.008). In addition, ESRD prediction prolongation was associated with the initial e-GFR (p = 0.001), the age at which the affected parent had developed ESRD (p = 0.013) and the MCIC (β = 1.93, 95%CI 0.46 – 3.39, p = 0.013) (i.e. greater ESRD prediction prolongation for patients at MCIC 1E than at 1C).

Conclusion: Tolvaptan treatment seems to be more efficient in younger patients with rapidly progressing ADPKD, well-preserved renal function, a less severe family history, and a shorter chronicity of hypertension.

Figure 1: The proportion and number of antihypertensive and diuretic drugs used in Polish and Japanese patients with ADPKD.
Primary hyperoxaluria type 1 (PH1) is a rare genetic disease in which hepatic oxalate overproduction can lead to kidney stones, nephrocalcinosis, kidney failure, and systemic oxalosis, a condition in which calcium oxalate is deposited in various tissues, including bone [1]. Radiological signs of bone oxalosis include findings such as dense metaphyseal bands and coarse trabeculation [2]. No scale exists to grade bone oxalosis severity using X-rays.

Method: An X-ray grading scale to evaluate systemic oxalosis in specific bones was developed based on expert opinion. Scores on individual items ranged from 0−4, except for ribs and spine, which ranged from 0−2. Higher values represent more advanced oxalosis. To validate the scale, 85 X-ray images from 5 pediatric patients with PH1 who had developed bone oxalosis were collected from charts at Shaare Zedek Medical Center and de-identified [2]. Two blinded, independent raters evaluated each X-ray twice and assigned a grade to each applicable item on the scale. Inter-rater and intra-rater reliability analyses were conducted using the weighted Cohen’s kappa with asymptotic 95% confidence intervals (CIs) of the estimate and interpreted as proposed in the literature [3].

Total weighted kappa estimates were generated by pooling all observed ratings across all items. Results: Total overall inter-rater (0.83 [95% CI: 0.79, 0.87]) and intra-rater (0.95 [0.93, 0.97]) kappas demonstrate almost perfect agreement. Overall inter-rater kappa estimates were >0.8 to 1.0 (almost perfect agreement) for the left hand/wrist, left hip, left knee (femur), and left humerus; >0.6 to 0.8 (substantial agreement) for the right hip, right knee (tibia), right humerus, spine, and ribs; and >0.4 to 0.6 (moderate agreement) for the right knee (tibia) and right knee (fibula). The overall inter-rater kappa estimate for the left knee (fibula) demonstrated poor agreement (<0.08 to −0.27, 0.10)). Overall inter-rater kappa estimates for the right hand/wrist and left tibia (tibial) were considered unreliable due to lack of variability in the data, and the standard errors were not estimable. Calculable overall intra-rater kappa estimates were >0.8 to 1.0 (almost perfect agreement) for the spine and >0.6 to 0.8 (substantial agreement) for the right knee (femur) and right knee (fibula). Most other overall intra-rater kappa estimates could not be calculated because the kappas for one or both raters lacked variability. In these instances, intra-rater kappa estimates for the first and second raters demonstrated moderate to almost perfect agreement (>0.4 to 1.0; left hand/wrist, right hip, left hip, left knee [femur], right knee [tibia], left knee [tibia], right humerus, left humerus, and ribs). For the left knee (fibula), intra-rater kappa estimates for the first and second raters were −0.14 (−0.34, 0.05) and 1.00, respectively, and for the right hand/wrist, they were 1.00 and 0.00.

Conclusion: We developed a novel X-ray–based bone oxalosis grading scale for patients with PH1. Total overall weighted kappa estimates for inter-rater and intra-rater reliability demonstrated almost perfect strength of agreement. Most individual items demonstrated reliable kappa estimates. The right and left knee (fibula) were removed from the scale due to poor reliability.

REFERENCES
**Table 1: Relationship between Kidney Volume and Depression.**

<table>
<thead>
<tr>
<th>Kidney Volume</th>
<th>Beck's Depression Inventory Result</th>
<th>Median</th>
<th>Percentile 25</th>
<th>Percentile 75</th>
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<tr>
<td>Right Kidney Volume</td>
<td>Normal</td>
<td>425.50</td>
<td>320.00</td>
<td>915.00</td>
<td>0.830</td>
</tr>
<tr>
<td></td>
<td>Minimal Depression</td>
<td>507.00</td>
<td>389.50</td>
<td>771.50</td>
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<tr>
<td></td>
<td>Mild Depression</td>
<td>716.00</td>
<td>299.00</td>
<td>931.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate Depression</td>
<td>790.00</td>
<td>790.00</td>
<td>790.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe Depression</td>
<td>378.00</td>
<td>378.00</td>
<td>378.00</td>
<td></td>
</tr>
<tr>
<td>Left Kidney Volume</td>
<td>Normal</td>
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<td>267.00</td>
<td>982.00</td>
<td>0.568</td>
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<td>476.00</td>
<td>446.00</td>
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<td>572.00</td>
<td>311.00</td>
<td>720.00</td>
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<td>Moderate Depression</td>
<td>875.00</td>
<td>875.00</td>
<td>875.00</td>
<td></td>
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<tr>
<td></td>
<td>Severe Depression</td>
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<td>216.00</td>
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<td>Total Kidney Volume</td>
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<td>Severe Depression</td>
<td>595.00</td>
<td>595.00</td>
<td>595.00</td>
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</tbody>
</table>

* Kruskal Wallis Test

**Background and Aims:** The most prevalent hereditary kidney disease is autosomal dominant polycystic kidney disease (ADPKD). Multiple cysts developing in the kidneys are a defining feature of this systemic, progressive disease. The quality of life, psychosocial load, and discomfort associated with renal volume in people with ADPKD have not been well studied. This study aimed to examine the relationship between renal volume, psychological issues brought on by pain and the burden of the disease, and deteriorating sleep quality in ADPKD patients.

**Method:** The study included sixty patients who were being treated in the nephrology clinic at the Bursa Uludag University Faculty of Medicine Hospital. The ADPKD Pain and Discomfort Scale (ADPKD-PDS), Beck Depression Inventory Questionnaire, Beck Anxiety Scale, Pittsburgh Sleep Quality Scale (PSQI), and Insomnia Severity Index (ISI) were assessed. The computed tomography ellipsoid formula was used to determine the total kidney volume, and kidney volume adjusted for body size was obtained for each patient. The eGFR values computed using the CKD-EPI algorithm and the patients’ baseline biochemical parameters were recorded.

**Results:** The mean age at diagnosis was 31±13, and the mean total kidney volume (TKV) was 1526.3±1595.90. Eight (13.3%) individuals were determined to have mild mood disorders, whereas seven (11.7%) patients had borderline clinical depression. Four individuals (6.7%) were found to have severe anxiety. It was shown that 25% of the patients had poor sleep quality. There was no statistically significant difference in kidney volume between the depression groups or between the pain and discomfort scale sub-dimensions (Table 1).

**Conclusion:** It was shown that, in accordance with the literature, the severity of depression increased as the patients’ sleep quality declined in ADPKD patients. However, there was no significant relationship between kidney volume and the degree of anxiety, depression, pain or discomfort.

#5882

**AN EXCEPTIONAL CASE OF A PATIENT WITH TWO RARE GENETIC VARIANTS OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE AND ALOPT SYNDROME**

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**Background:** Alport syndrome and autosomal dominant polycystic kidney disease (ADPKD) belong to the most prevalent monogenic causes of chronic kidney disease (CKD) and both progress to end stage renal disease (ESRD). Alport syndrome, is caused by mutations in genes encoding collagen IV protein family. Inheritance might be X-linked, autosomal recessive, autosomal dominant or digenic and several pathogenic variants have been identified. ADPKD is mostly caused by mutations in PKD1 and PKD2 genes but recently, the GANAB gene, that encodes the glucosidase II subunit, has been identified has a cause of a milder form of ADPKD. We present a case report of a patient with CKD-4, bilateral sensorineural hearing loss and multiple renal cysts where two unrelated and distinct genetic variants of both diseases were concomitantly found.

**Case report:** A 63-year-old caucasian male with medical history of arterial hypertension, hematuria and bilateral sensorineural hearing loss since his 40 years-old, with cochlear implant surgery 13 years ago was referred to the Nephrology unit due to progressive CKD, currently stage 4. His mother had ESRD of unknown etiology, in peritoneal dialysis since the age of 78 years and he has two healthy sons (aged 16 and 20 years old). Physical examination was irremarkable. Laboratorial workout showed serum creatinine of 2.7 mg/dL, ratio albumin/creatinine of 105mg/g with 11 erythrocytes in urinary sediment. Renal ultrasound showed normal sized kidneys with more than 10 cysts in each kidney, the biggest with 44mm. Genetic testing via next generation sequencing was performed revealing heterozygous mutations in COLA43 (c.4421T>G.p.(Leu1474Pro)), reported in ClinVar, and described in literature as an autosomal dominant variant present in Alport families. A mutation in the GANAB (c.2281A>G.p.(Thr761Ala)) gene, classified as variants of unknown significance in was also detected, but this mutations is not reported in gnomAD or ClinVar. The patient was referred for genetic counseling.

**Conclusion:** We describe a rare case of possible overlap of ADPKD and Alport syndrome. The COLA43 mutation is described has having a risk ≥ 20% of developing ESRD, but the association of a mild variant of ADPKD might increase exponentially this risk.
and 1E (n = 17). Those who received tolvaptan showed a lower eGFR decline from baseline compared to predicted (eGFR 66.7 ± 32.7 vs 61.5 ± 29.1, p < 0.001), while a greater benefit was observed in Class 1E (eGFR 60.1 ± 36.5 vs 52.4 ± 29.5, p = 0.003) and in patients with eGFR > 45ml/min (eGFR 79.4 ± 28.8 vs 73 ± 25.2, p = 0.001).

Conclusion: Our initial experience from long-term administration of tolvaptan in patients with ADPKD demonstrates benefit on kidney disease progression. The widespread use of tolvaptan in a larger number of patients and their long-term follow up are necessary to draw more secure conclusions.

Results: PH1 was confirmed due to Homozygous mutation AGXT c.731T>C9 [p.(Ile244Thr)]. Oxalate on cord blood was 15 umol/L (nv <10), on amniotic fluid 55 umol/L (nv 19-71), on first urine 401 umol/mmolCr (nv <300 umol/mmolCr). Blood Oxalate at 6h of life rose to 32 umol/L, Glycolate to 107 umol/L and urinary Oxalate to 573 umol/mmolCr. Serum Creatinin was normal (0.3 mg/dl). At 6 hours of life the child was treated with Glycolate Oxidase RNAi Lumasiran at the dose 6 mg/kg subcutaneously, in combination with Pyridoxin 10 mg/kg/day. Hyperhydration (240 ml/kg/day) was maintained iv for 16 days in combination with oral water and potassium citrate (500 mg in 500 ml/day) above breast feeding. Blood Oxalate was serially assessed every 48 hrs showing a peak level of 108 umol/l (nv <10) at day 6, higher than the supersaturation level of 60 umol/L, then a gradual decline (65-56-62 umol/L at 10-20-30 days respectively). Lumasiran 6 mg/kg was repeated at 30 and 60 days according to schedule, then at 3 mg/kg every month. After the second dose of Lumasiran a steeper decline of blood Oxalate was observed (31-17 umol/L at 45-60 days respectively) reaching the upper normal limit of 12 umol/L after three doses, at 80 days. Urinary Oxalate in spite of Lumasiran early start rose until a maximum of 4173 umol/mmolCr (nv for age <300 umol/mmolCr) at 13 days and gradually declined to 765 umol/mmolCr at 80 days, after three doses. Blood and urine Glycolate initially paralleled Oxalate then increased after each Lumasiran dose. Renal ultrasound normal at birth, showed only minimal hyperchogenic spots during the first 2 months, then mild bilateral hyperchogenic papillary deposits without signs of nephrocalcinosis/stones. Renal function at 3 months of life is normal (serum Creatinine 0.2 mg/dl); child growth on the higher centiles (7 kg), with no adverse events.

Conclusion: Blood and urine Oxalate serial analysis in a severe case of PH1 treated immediately after birth show that Glycolate Oxidase inhibition has a latency of at least 15 days, even when no previous deposits are present. In these days extremely high level of urine and blood Oxalate, far higher than supersaturation level, are reached, in spite of normal renal function, hyperhydration, B6 and citrate supplementation. This case confirms that familiar severe forms of PH1 should be treated immediately after birth with Lumasiran in combination with aggressive supportive therapy to avoid irreversible nephrocalcinosis and renal failure. Prenatal treatment of these cases might be considered in future.

#3589

OXALATE METABOLISM IN PRIMARY HYPEROXALURIA TYPE 1 TREATED WITH LUMASIRAN IMMEDIATELY AFTER BIRTH: STILL NOT ENOUGH

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Background and Aims: Severe primary hyperoxaluria type 1 (PH1) with rapid onset nephrocalcinosis and renal function loss in early infancy required so far combined liver and kidney transplant. RNA interfering drugs are the new challenge for these children. Here we present the first case of a newborn affected by PH1 treated with RNA-interfering Lumasiran 6 hours after birth.

Method: Diagnosis of PH1 (homozygous mutation AGXT c.731T>C9 [p.(Ile244Thr)]. Oxalate on cord blood was 15 umol/L (nv 19-71), on first urine 401 umol/mmolCr (nv <300 umol/mmolCr). Blood Oxalate at 6h of life rose to 32 umol/L, Glycolate to 107 umol/L and urinary Oxalate to 573 umol/mmolCr. Serum Creatinin was normal (0.3 mg/dl). At 6 hours of life the child was treated with Glycolate Oxidase RNAi Lumasiran at the dose 6 mg/kg subcutaneously, in combination with Pyridoxin 10 mg/kg/day. Hyperhydration (240 ml/kg/day) was maintained iv for 16 days in combination with oral water and potassium citrate (500 mg in 500 ml/day) above breast feeding. Blood Oxalate was serially assessed every 48 hrs showing a peak level of 108 umol/l (nv <10) at day 6, higher than the supersaturation level of 60 umol/L, then a gradual decline (65-56-62 umol/L at 10-20-30 days respectively). Lumasiran 6 mg/kg was repeated at 30 and 60 days according to schedule, then at 3 mg/kg every month. After the second dose of Lumasiran a steeper decline of blood Oxalate was observed (31-17 umol/L at 45-60 days respectively) reaching the upper normal limit of 12 umol/L after three doses, at 80 days. Urinary Oxalate in spite of Lumasiran early start rose until a maximum of 4173 umol/mmolCr (nv for age <300 umol/mmolCr) at 13 days and gradually declined to 765 umol/mmolCr at 80 days, after three doses. Blood and urine Glycolate initially paralleled Oxalate then increased after each Lumasiran dose. Renal ultrasound normal at birth, showed only minimal hyperchogenic spots during the first 2 months, then mild bilateral hyperchogenic papillary deposits without signs of nephrocalcinosis/stones. Renal function at 3 months of life is normal (serum Creatinine 0.2 mg/dl); child growth on the higher centiles (7 kg), with no adverse events.

Conclusion: Blood and urine Oxalate serial analysis in a severe case of PH1 treated immediately after birth show that Glycolate Oxidase inhibition has a latency of at least 15 days, even when no previous deposits are present. In these days extremely high level of urine and blood Oxalate, far higher than supersaturation level, are reached, in spite of normal renal function, hyperhydration, B6 and citrate supplementation. This case confirms that familiar severe forms of PH1 should be treated immediately after birth with Lumasiran in combination with aggressive supportive therapy to avoid irreversible nephrocalcinosis and renal failure. Prenatal treatment of these cases might be considered in future.

Abstracts

Figure 1: Blood and urine Oxalate and Glycolate.
Figure 1: Family pedigree with description of available clinical features and genetic findings. Circle – female; square – male; filled (black) – affected; CKD – chronic kidney disease; HD - hemodialysis; KT - kidney transplant; y.o. - years old; † - deceased.

Abstracts
UMOD exon 11 deletion, which was excluded in two healthy relatives (III-1, III-4), establishing the primary diagnosis of ADTKD-UMOD. It is noteworthy that the only two gross UMOD deletions associated with ADTKD affected evolutionarily conserved residues in exon 4 [1]. The presence of the SLC8A1 p.(Arg6*) allele in patients IV-1 and IV-2, who had early clinical presentations, together with its absence in patient III-5, who had a significantly later clinical onset than her older brother (III-2), suggests that it exerted a pathogenic or disease modifier role in this family, in accordance with the predicted protein truncating effect. Indeed, genome-wide linkage analysis in 5 multiplex families with ADTKD identified involvement of chromosome 2p22.1-p21; SLC8A1 was the most likely gene but no pathogenic variants could be identified; copy number variants might have been missed [2]. Unfortunately, in our family study, we could not identify any subject segregating only the SLC8A1 p.(Arg6*) allele, which would have been indispensable to demonstrate its pathogenicity.

Conclusion: Herein, we report a family with hyperuricemic nephropathy where genetic testing identified a novel, likely pathogenic UMOD variant. The mechanisms underlying the pathogenicity of exon 11 deletion require further study. Additionally, the co-segregation of an ultra-rare nonsense SLC8A1 variant in some individuals was associated with earlier onset and faster progression of CKD, suggesting once again a role for SLC8A1 in the pathogenesis of ADTKD.

REFERENCES

#6861
FABRY DISEASE: A DESCRIPTIVE STUDY OF A COHORT OF PATIENTS
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1 Torrecárdenas Hospital, Nephrology, Almería, Spain and 2 Torrecárdenas Hospital, Cardiology, Spain

Background and Aims: Fabry disease is a rare X-linked disease, caused by deficient activity of the lysosomal enzyme α-galactosidase A. Accumulation of globotriaosylsphingosine leads to organ failure and premature death. The aim of this study is to describe the population of patients with Fabry disease in our healthcare area.

Method: Descriptive observational study of patients with Fabry disease (n = 23). Demographic, clinical and treatment variables were analysed.

Results: The mean age of the patients was 47.5 years; 70% female. Symptom onset was at 18 years, being diagnosed 25 years later, similar to that described in the literature. Enzyme deficiency was observed in 61% of patients. Four types of pathogenic variants of the GLA gene were detected. The most prevalent was P205S, followed by W262X, V199G, and G80D. 48% of the patients had left ventricular hypertrophy (55% women). 48% had right bundle branch block, atrial fibrillation and sinus bradycardia. 47% (64% women) had renal involvement, defined by proteinuria. Other manifestations: hypocoagulability (17%), acropaesthesia and neuropathic pain (13%), ophthalmological (13%) and dermatological (4%). 22% were treated with ACE inhibitors/ARA II. 1 patient received isGLT2. Other complementary treatments: statins (22%), antiaggregants (13%), anticoagulants (13%), and Digoxin (1 patient). Regarding specific treatment, 43% were treated, the majority (39%) received enzyme replacement therapy with agalsidase beta (only 1 patient with agalsidase alpha), one patient received migalastat.

Conclusion: The characteristics of our patients are similar to those described in the literature. We observed a predominant general involvement in women, in contrast to other series. Cardiac involvement predominates with left ventricular hypertrophy; and renal involvement with proteinuria.

The diagnostic delay is similar to that described, emphasizing the need for early diagnosis and treatment to avoid severe complications and death.

A4 - ACID-BASE DISORDERS, NEPHROLITHIASIS & URIC ACID

Table 1: Demographic and pre and after thiazide treatment laboratory data.

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Frequency (n of patients)</th>
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<tbody>
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<td>Total cohort</td>
<td>9</td>
</tr>
<tr>
<td>F</td>
<td>4</td>
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<tr>
<td>Genetic mutation</td>
<td></td>
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<td>KLHL3</td>
<td>5</td>
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<tr>
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#6875
COMPLICATIONS AND TREATMENT OF HYPERCALCIURIA IN FAMILIAL HYPERKALAEMIC HYPERTENSION (FHH)
Viola D’ambrosio¹,², Olivia Mcknight¹, Elizabeth Wan¹, Robert Speller³, Robert Moss¹, Keith Siew² and Stephen Walsh²
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Background and Aims: Hypertension is frequently associated with hypercalciuria, nephrolithiasis and low bone mineral density. Familial Hyperkalaemic Hypertension (FHH) causes hypercalciuria, although complications of this are not reported.

Method: We examined a cohort of 9 patients with genetically confirmed FHH. Biochemical, radiological, and clinical data was obtained in patients before and after thiazide treatment. All patients gave informed consent. The study had ethics committee approval. Data were compared using paired t tests.

Results: 5 of the 9 patients were female (median age 41.7 years). The genetic diagnosis was confirmed in all patients, 5 patients had variants in KLHL3, 3 patients had variants of WNK4, and one had a variant of WNK1 (Table 1). Pre-treatment potassium was high (median 5.6 IQR 5.2-6.2 mmol/L). Pre-treatment calcium was in the normal range (2.34 IQR 2.29-2.38 mmol/L). There was significant hypercalciuria with a raised urinary calcium/creatinine ratio (0.69 IQR 0.41-1.13). However, PTH (4 IQR 3.95-4.35 pmol/L), phosphate (1.15 IQR 1.25mmol/L) and alkaline phosphatase (57 IQR 45-84 mmol/L) were all in the normal range. Thiazide treatment significantly reduced hypercalciuria (calcium/creatinine ratio 0.15 IQR 0.05-0.29 p = 0.04) as well as the serum potassium (3.9 IQR 3.5-4.4 mmol/L p = 0.0167) (Table 1). Patients also developed complications of hypercalciuria. 3 patients had kidney stones demonstrated on cross-sectional imaging (Figure 1). One of these patients (male, 30 years old) had DXA criteria for osteoporosis (T score Femoral neck -1.5, lumbar spine -2.4).

Conclusion: This is the first case series to demonstrate complications of hypercalciuria (i.e. kidney stones) in patients with FHH. We demonstrate that thiazide treatment normalises urinary calcium excretion. Thiazide treatment may have clinical utility in FHH even if hypertension or hyperkalaemia are not problematic in order to avoid the complications of hypercalciuria.

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Figure 1: Cross-sectional CTKUB showing a 2 mm calculus in the lower pole of the right kidney.

REFERENCES


#4308

EVOLUTION OF HYponatreMIA IN PATIENTS WITH CHRONIC SIADH TREATED FOR 1 YEAR WITH ORAL UREA

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Background and Aims: Hyponatremia (<135mEq/L) is the most common electrolyte disorder observed in clinical practice, associated with increased hospital admissions and mortality. One of its causes is the syndrome of inappropriate antidiuretic hormone secretion (SIADH). In chronic SIADH, urea is considered as a therapeutic possibility among other measures; however, its use is not widespread due to few studies on its efficacy.

Objects: To evaluate sodium levels in patients with chronic SIADH who received oral urea for at least 12 months.

Method: Observational, descriptive and retrospective study. Population: 13 patients with SIADH under treatment with urea for 12 months. The relationship between natremia and the rest of the clinical variables was analyzed using Chi-square, Student’s T test, and ANOVA or their corresponding non-parametric tests.

Results: Mean age: 64 years ±15. Men: 61% (n=8). Comorbidities: hypertension (50%, n=6), CKD (30.7%, n=4), diabetes (15.3%, n=2). SIADH etiology: Antiepileptics (n=4), idiopathic (n=3), intracranial pathologies (n=5) and cancer (n=1). 61% required admission for SIADH. Median of 10 ±6 months from diagnosis to start of treatment. The initial
dose was: 15 grams/day (53%, n = 7), 15 grams every 48 hours (30%, n = 4) and 15 grams every 72-96 hours (17%, n = 2). At one year, 61% of patients maintained the same dose (n = 8) and 39% of patients required an increase in the dose (n = 5) and of these 3 patients they increased to 30 grams/day. The treatment was well tolerated, only 1 patient out of 13 (7.6%) reported nausea and dysgeusia, no patient presented hypernatremia (Na >145 meq/L), hospital admissions due to SIADH, or adverse effects that led them to discontinue urea.

**Conclusion:** After a year of treatment, urea increases and maintains plasma sodium in the normal range safely in chronic SIADH. Treatment with urea is well tolerated, avoids hospitalizations, and is not associated with complications from its use.

**#4178**

**HYPERCHLOREMIC METABOLIC ACIDOSIS AFTER PLASMAPHERESIS IN A PATIENT WITH RENAL TRANSPLANT REJECTION: A CASE REPORT**

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**Background and Aims:** Plasmapheresis is an effective therapeutic intervention for several renal disorders, including renal transplant rejection. However, repeated plasmapheresis can cause various side effects and complications. We present a 61-year-old male with a medical history of type 2 diabetes, hypertension, successfully treated multiple myeloma and a post-mortem kidney transplantation 7 months ago. The patient was hospitalized because of rapid deterioration of his renal function (eGFR CKD-EPI 15 ml/min/1.73m²). Renal biopsy of the transplanted kidney confirmed the diagnosis of antibody-mediated transplant rejection. Treatment with methylprednisolone, plasmapheresis with a 40 g/L albumin solution as a replacement fluid and intravenous immunoglobulins was initiated. After 4 plasmapheresis treatments, the patient developed gastrointestinal complaints and muscle weakness. Despite the patient's use of 3 grams of oral sodium bicarbonate supplements a day, laboratory tests revealed a hyperchloremic metabolic acidosis: bicarbonate 11.7 mmol/L, chloride 111 mmol/L, sodium 138 mmol/L. Metabolic acidosis due to citrate accumulation was ruled out with a normal total-to-ionized calcium ratio. After treatment with intravenous bicarbonate supplementation, the symptoms disappeared. Analysis of the albumin plasmapheresis solution showed a chloride concentration of 132 mmol/L.

**Results:** This is the first case that describes metabolic acidosis after albumin plasmapheresis in a patient with impaired renal function. The observed hyperchloremic metabolic acidosis is most likely the result of the administration of large volumes (3.5 litres per session) of a 4% albumin solution with high chloride concentrations. We hypothesize that patients with renal impairment are more prone to develop metabolic acidosis after plasmapheresis with albumin-saline replacement fluids due to their reduced renal capacity to excrete excess acid and chloride.

**Conclusion:** Special attention should be paid to the acid-base balance during plasmapheresis in patients with impaired renal function. Future research should investigate the incidence of hyperchloremic metabolic acidosis during albumin plasmapheresis in different eGFR categories.
EFFECTS OF URIC ACID-LOWERING THERAPY ON RENAL OUTCOMES IN CKD PATIENTS WITH ASYMPTOMATIC HYPERURICEMIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: It is well known that hyperuricemia and gout play an important role in the adverse cardiovascular and renal events both in patients with and without renal disease. However, the effect of uric acid-lowering therapy (ULT) on renal outcomes of CKD patients with asymptomatic hyperuricemia remains controversial. Therefore, our study summarized reliable results draw from published randomized controlled trials (RCTs) to evaluate the effects of ULT on renal and cardiovascular outcomes in CKD patients with asymptomatic hyperuricemia.

Method: Pubmed, EMBASE, China National Knowledge Internet (CNKI) and the Cochrane Library were searched systematically for trials up to October 2021. RCTs assessing the effects of uric acid-lowering agents on renal and/or cardiovascular outcomes in CKD patients with asymptomatic hyperuricemia were included. Both the fixed-effect and the random-effect models were used.

Results: A total of 17 RCTs (one trial divided patients into two groups according to CKD stages), including CKD patients with asymptomatic hyperuricemia were included in this meta-analysis. Compared with placebo or no treatment group, ULT group showed a higher estimated glomerular filtration rate (eGFR) with a weighted mean difference (WMD) of 3.679 mL/min/1.73 m², 95% CI [-1.592, 5.766] (p = 0.001) and a lower serum creatinine (Scr) with a WMD of -46.131 umol/L, 95% CI [-65.643, -26.619] (p < 0.0001). Subgroup analysis demonstrated a significant benefit from ULT in patients with CKD stage 1-3 (p = 0.035), from Asian countries (p = 0.005) and those younger than 60 years (p = 0.002). At the same time, ULT was associated with lower incidence of events of doubling of Scr without dialysis (relative risk (RR) 0.314 [0.203, 0.485] (p < 0.0001)). However, no difference was found for all-cause mortality, incidence of AKI, progression to end-stage kidney disease (ESKD), and cardiovascular events. In addition, ULT with allopurinol was associated with lower cardiovascular events (RR 0.678 [0.473, 0.971] (p = 0.034)).

Conclusion: ULT could slow down the progression of renal impairment in CKD patients complicated with asymptomatic hyperuricemia, especially for patients under 60 years old, early CKD stage(1-3) and the Asian descent.

Figure 1: Forest plot for the effect of uric acid-lowering therapy (ULT) on the change in estimated glomerular filtration rate (eGFR).
THE ASSOCIATION BETWEEN THE LEVELS OF URIC ACID AND RENAL OUTCOMES IN EARLY CKD PATIENTS: A MULTI-CENTER REAL-WORLD DATA ANALYSIS

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Background and Aims: It is well known that serum uric acid (SUA) plays an important role both in patients with and without chronic kidney disease (CKD). However, the effect of SUA on renal outcomes of CKD patients, especially with asymptomatic hyperuricemia, remains controversial. Therefore, our study explores the relationship between SUA and adverse events in early CKD (stage 1-3) patients in a real-world setting.

Method: This multi-center real-world study analyzed the data from Chinese Renal Data System (CRDS). Eligible CKD patients (eGFR) (estimated glomerular filtration rate $\geq$ 30 mL/min/1.73 m$^2$) were enrolled. The primary endpoint is the decline of renal function defined as at least 40% decrease in eGFR. The secondary endpoints include onset of composite cardiovascular events and all-cause mortality. A multivariable cox regression model was used and the associations between levels of mean SUA and all endpoints were evaluated on a continuous scale with restricted cubic spline (RCS) curves based on Cox proportional hazards models. Kaplan-Meier survival curves were used to illustrate the ability of SUA to predict the end points.

Results: 25,202 adults (mean [SD] age, 52.59 [17.90] years, 8,212 male [46.1%], 9,604 female [53.9%]) were included in this study. During a median follow-up period of 2.61 years, 3,451 (15.9%) at least 40% decreased in eGFR. After adjustment for confounders, higher uric acid concentrations were independently associated with the higher risk for the decline of renal function [Per SD increment adjusted hazard ratio [aHR]: 1.41, 95%CI 1.36-1.47]; composite cardiovascular events [Per SD increment [aHR]: 1.04, 95%CI 1.01-1.07], all-cause mortality [Per SD increment [aHR]:1.32, 95%CI 1.14-1.54]. RCS curves showed that HRs for renal function progression, all-cause mortality and composite cardiovascular events increased significantly with the increase of SUA concentration in CKD patients. Results were consistent in stratified analyses. The KM curves suggested that patients with asymptomatic hyperuricemia had a substantially worse survival rate for renal function.

Conclusion: SUA is an independent risk factor for the decline of renal function, cardiovascular events and all-cause mortality in early CKD patients (stage 1-3). Treatment of asymptomatic hyperuricemia may be a potential avenue to improve outcomes in CKD patients.
Figure 1: Association between serum uric acid (SUA) concentrations and the primary endpoint (at least 40% decline in eGFR) using a restricted cubic spline (RCS) regression model. Multivariable adjusted HRs (blue solid lines) and 95% CIs (light blue shadow).

Figure 2: Kaplan-Meier curves showing survival of the primary endpoint (at least 40% decline in eGFR) for patients grouped by the level of SUA (asymptomatic hyperuricemia defined that SUA > 7.0 mg/dl (416.4 μmol/L) in men and > 6.0 mg/dl (356.9 μmol/L) in women with no prior gout flares).
Abstracts

#3594

CHANGES IN ALBUMINURIA AND KIDNEY FUNCTION AFTER 8 WEEK HIGH-INTENSITY INTERVAL TRAINING PROGRAM IN 2ND AND 3RD TRIMESTER OF PHYSIOLOGICAL PREGNANCY

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¹Medical University of Gdańsk, Department of Occupational Medicine, Gdańsk, Poland and ²University of Physical Education and Sport-AWFIS, Department of Physical Culture, Gdańsk, Poland

Background and Aims: Physical exercise is the best prophylaxis of many disorders and should be continued during uncomplicated pregnancy. Several studies suggested that most pregnant women had no contraindications to perform intensive exercises. In recently published studies the beneficial effect of high-intensity interval training (HIIT) on both mental health and reduction of excessive weight gain during pregnancy has been demonstrated. The knowledge regarding kidney function after exercise in pregnancy is very scarce and only few studies concerning this topic were published. The aim of this study was to estimate changes in markers of kidney function in healthy pregnant exercising women. Changes after single intensive exercise and after 8 week training program were analyzed.

Method: The group of 36 women in 2nd and 3rd trimester of pregnancy were recruited to the study. At the beginning of the study all participants had normal kidney function (serum creatinine level below 0.6 mg/dl) and albuminuria (uACR below 30 mg/g) in rest. 19 women participated in 8-week HIIT program and 17 women in 8-week educational program (EDU group). Before and after 8 week training and education programs a progressive maximal exercise test on cyclometer was performed. Several biochemical measurements were performed.

Results: Women from both groups revealed mild changes concerning kidney function in rest, typical for physiological pregnancy (e.g. low sodium, creatinine and uric acid levels). After progressive maximal exercise test some unexpected findings were found: the fractional excretion of urea and uric acid increased (FeUrea from 41.25 to 50.05%; FeUA from 7.18 to 8.04%) and serum uric acid decreased significantly (sUA from 3.35 to 3.28mg/dL). Other changes after short exercise were typical: significant increase of uACR (from 5.12 to 21.65 mg/dL), among others. The 8-week HIIT training program did not change kidney function in rest. In both groups a significant increase of eCrCl and sUA were observed. The interesting observation was that uACR increased significantly only in EDU group.

Conclusion: Changes in kidney function after short intensive exercise in pregnancy were typical for healthy subjects, but there was no negative impact on markers of renal hyperperfusion. It was probably related to increased renal blood flow occurring in healthy pregnancy. The supervised 8-week HIIT training program had no negative impact on kidney function. The possible positive impact of this training on albuminuria was suggested.

#3069

CIRCULATING SCLEROSTIN AFFECTS URINARY CALCIUM EXCRETION AMONG STONE FORMERS

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¹Federal University of São Paulo, Nephrology, São Paulo, Brazil, ²University Medical Center Groningen, Groningen, Netherlands and ³Federal University of São Paulo, Brazil

Background and Aims: Sclerostin plays an important role in bone metabolism and adipose tissue. Experimental studies suggest that sclerostin also influences urinary calcium excretion (Uca), but this relationship has not been addressed in humans. We aimed to study the association of Uca levels with serum sclerostin, bone mineral density (BMD) and body composition among stone-formers (SF).

Method: We retrieved data from patient records, including clinical characteristics, nutritional, biochemistry and hormonal data as well as BMD and body composition determined by dual energy X-ray absorptiometry. Serum sclerostin levels were measured using ELISA kits. Determinants of Uca were studied using multivariate linear regression.

Results: A total of 107 SF (35.8 ± 9.3 years, 54% male) with eGFR of 99.8 ± 14.5 mL/min/1.73 were included. The subjects were divided by sex and clustered into tertiles according to Uca as shown in Table 1. In men the highest Uca tertile had higher body mass index (BMI) and serum sclerostin levels, were more likely to have hypertension and metabolic syndrome, had lower lean mass, a trend towards higher fat mass (p = 0.06), and no statistical differences in BMD. Women in the highest Uca tertile had higher BMI and a trend towards higher serum sclerostin levels (p = 0.06), were more likely to have hypertension and metabolic syndrome, with no differences in BMD. Sclerostin was positively correlated with fat mass (r = 0.38, p = 0.004) and inversely correlated with lean mass (r = −0.32, p = 0.01) among men, but not among women. To further adjust for the influence of weight load on BMD for both sexes, the latter was also expressed as a ratio per BMI (BMD/BMI). Although lumbar spine BMD/BMI was inversely associated with Uca (β = -0.26, p = 0.01) in univariate analysis, it lost significance in the multivariate model (Table 2). Hypertension, metabolic syndrome and serum sclerostin were independent determinants of Uca (Table 2).

Conclusion: Present findings disclosed that serum sclerostin, hypertension and metabolic syndrome were independent determinants of urinary calcium in stone formers. These data suggest that in addition to the hormones traditionally thought to alter calcium reabsorption in the kidney, sclerostin may play a significant additional role, warranting further intervention studies in order to test potential medication strategies to reduce calciuria in this population.
Table 1. Clinical, biochemistry and BMD data of SF clustered into tertiles according to urinary calcium.

<table>
<thead>
<tr>
<th>Urinary Calcium (mg/24h)</th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
<th></th>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T1</td>
<td>T2</td>
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<tr>
<td>(≤180.0)</td>
<td>155.9 ± 29.6</td>
<td>236.9 ± 31.1</td>
<td>363.4 ± 80.0</td>
<td>115.6 ± 26.8</td>
<td>217.6 ± 44.0</td>
<td>341.6 ± 58.2</td>
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<tr>
<td>(180.1 – 283.1)</td>
<td>38.3 ± 9.8</td>
<td>38.0 ± 10.3</td>
<td>31.6 ± 9.3</td>
<td>33.8 ± 8.3</td>
<td>37.4 ± 9.2</td>
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<tr>
<td>(≥283.1)</td>
<td>26.3 ± 4.8</td>
<td>26.6 ± 3.8</td>
<td>29.4 ± 4.3*</td>
<td>24.6 ± 2.5</td>
<td>26.4 ± 5.1</td>
<td>27.8 ± 5.3*</td>
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<tr>
<td>(≥150)</td>
<td>23.4 ± 7.3</td>
<td>22.6 ± 6.8</td>
<td>25.2 ± 5.4*</td>
<td>33.7 ± 6.4</td>
<td>33.8 ± 7.4</td>
<td>36.0 ± 4.8</td>
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<tr>
<td>(≥289.1)</td>
<td>73.7 ± 6.7</td>
<td>74.6 ± 6.9</td>
<td>71.8 ± 5.0*</td>
<td>63.7 ± 6.9</td>
<td>63.5 ± 7.3</td>
<td>61.4 ± 4.8</td>
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<tr>
<td>Bone Mineral Density (BMD)</td>
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<tr>
<td>Lumbar spine BMD (g/cm²)</td>
<td>0.99 ± 0.13</td>
<td>0.94 ± 0.08</td>
<td>0.94 ± 0.17</td>
<td>0.98 ± 0.03</td>
<td>0.94 ± 0.02</td>
<td>1.04 ± 0.04</td>
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<tr>
<td>Femoral neck BMD (g/cm²)</td>
<td>0.83 ± 0.16</td>
<td>0.82 ± 0.11</td>
<td>0.93 ± 0.18</td>
<td>0.83 ± 0.04</td>
<td>0.82 ± 0.03</td>
<td>0.93 ± 0.04</td>
<td></td>
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<tr>
<td>Radius BMD (g/cm²)</td>
<td>0.77 ± 0.07</td>
<td>0.76 ± 0.06</td>
<td>0.79 ± 0.07</td>
<td>0.77 ± 0.02</td>
<td>0.72 ± 0.01</td>
<td>0.79 ± 0.02</td>
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<tr>
<td>Serum parameters</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Sclerostin (pmol/L)</td>
<td>21.4 (18.3 – 26.7)</td>
<td>28.8 (19.0 – 40.9)*</td>
<td>30.9 (25.4 – 37.1)*</td>
<td>19.8 (11.0 – 23.9)</td>
<td>20.5 (17.5 – 23.0)</td>
<td>25.9 (17.5 – 29.4)*</td>
<td></td>
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<tr>
<td>I-25 Vitamin D, pg/mL</td>
<td>30.7 (17.3 – 39.5)</td>
<td>22.0 (16.6 – 50.8)</td>
<td>26.4 (18.0 – 34.6)</td>
<td>20.9 (17.8 – 27.2)</td>
<td>20.4 (15.1 – 33.0)</td>
<td>28.6 (21.1 – 60.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTH, pg/ml</td>
<td>53.0 (40.0 – 67.0)</td>
<td>52.0 (37.5 – 64.0)</td>
<td>59.0 (42.3 – 76.5)</td>
<td>50.0 (45.0 – 60.0)</td>
<td>44.0 (41.0 – 65.5)</td>
<td>52.5 (35.5 – 65.0)</td>
<td></td>
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</tr>
</tbody>
</table>

*p vs T1 p<0.05; *p vs T2 p<0.05; *p vs T3 p<0.06. Abbreviations: BMI, body mass index; PTH, parathyroid hormone.

Table 2. Potential determinants of urinary calcium (UCa).

<table>
<thead>
<tr>
<th>Potential determinants</th>
<th>Total</th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>St. β</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p</td>
</tr>
<tr>
<td>Age, years</td>
<td>0.25</td>
<td>0.01</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension, yes</td>
<td>0.31</td>
<td>0.01</td>
<td>0.30</td>
</tr>
<tr>
<td>Metabolic syndrome, yes</td>
<td>0.37</td>
<td>&lt;0.01</td>
<td>0.22</td>
</tr>
<tr>
<td>Sodium chloride intake, g/day</td>
<td>0.33</td>
<td>&lt;0.01</td>
<td>-</td>
</tr>
<tr>
<td>Calcium intake, mg/day</td>
<td>-0.24</td>
<td>0.04</td>
<td>-</td>
</tr>
<tr>
<td>Serum sclerostin, pmol/L</td>
<td>0.31</td>
<td>&lt;0.01</td>
<td>0.22</td>
</tr>
<tr>
<td>Lumbar spine BMD/BMI</td>
<td>-0.26</td>
<td>0.01</td>
<td>-</td>
</tr>
<tr>
<td>Total femur BMD/BMI</td>
<td>-0.18</td>
<td>0.06</td>
<td>-</td>
</tr>
</tbody>
</table>

Linear regression analysis with serum sclerostin as dependent variable. *Run backwards, variables with p<0.10 in univariate analysis included. Abbreviations: St. β, standardized beta; BMD/BMI, bone mineral density/body mass index ratio.
UNEXPLAINED METABOLIC ACIDOSIS - A DIAGNOSTIC DILEMMA
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Paras HMRI, Nephrology, Patna, India

Background and Aims: Metabolic Acidosis is a common condition for which nephrology consult is sought. Most often the etiology is quite obvious like renal failure, diabetic ketoacidosis, lactic acidosis etc. We describe a case of high anion gap metabolic acidosis, unresponsive to medical management requiring hemodialysis, where finding the etiology became a diagnostic challenge because of medical and social reasons prevailing in this eastern part of India.

Method: A 55 year old obese gentleman came to emergency department at 3 am with complaints of restlessness, pain abdomen and chest discomfort for last 4-6 hours. On clinical examination he had tachycardia with normal blood pressure and oxygen saturation. His sensorium was normal and systemic examination did not reveal any major abnormality. A possibility of acute cardiac event was considered but his ECG showed sinus tachycardia, echocardiography did not show any wall motion abnormality and Troponin I was less than 0.01 ng/mL. His blood gases showed an uncompensated metabolic acidosis with an anion gap of 21 (pH 7.19 / pCO2 44 / HCO3 15). The laboratory parameters showed a serum creatinine of 0.9 mg/dL, random blood sugar of 130 mg/dL. Any history of poisoning or drug overdose was denied by patient’s attendants. Pending further workup patient was admitted in intensive care unit and correction of metabolic acidosis was started with intravenous sodium bicarbonate.

Results: The metabolic acidosis initially improved with medical management but within next 6 hours patient again had severe metabolic acidosis. Meanwhile patient’s sensorium worsened and he had an episode of seizure. Patient was intubated and mechanical ventilation started. Within 30 minutes patient had status epilepticus which ultimately required intravenous thiopentone. Hemodialysis was started for correction of metabolic acidosis. Patient’s history was re-evaluated. On persistent questioning his attendants admitted that patient had consumed alcohol 4-5 hours before the symptoms started. It is important to mention here that consumption of alcohol is a punishable offence in Bihar which a state in eastern part of India. Despite alcohol being completely banned in this part of country illicit alcohol is smuggled and consumed by some. Illicit alcohol is prone to be adulterated and sub-standard. It was because of this fact that patient’s attendants suppressed the facts. Also alcohol consumption is a valid ground for rejection of medical insurance claims because of obvious reasons. After obtaining the complete history a possibility of consumption of alcohol adulterated with methyl alcohol was very likely. Serum methyl alcohol estimation was not available at our institute and patient had already received hemodialysis hence it was not done. With patient already having seizures MRI (Magnetic Resonance Imaging) of brain was done. MRI brain revealed altered hyperintense signal with cytotoxic edema in bilateral basal ganglia predominantly putamen. Subcortical white matter in bilateral cerebral hemisphere and bilateral optic nerve head showed restriction on diffusion weighted imaging. These typical features on MRI were highly suggestive of methanol toxicity. These MRI features along with the clinical scenario and history of illicit alcohol intake helped us reach the diagnosis of methanol toxicity. Patient was managed with hemodialysis sessions to remove methanol from blood until he improved clinically.

Conclusion: The etiology of the high anion gap metabolic acidosis turned out to be methanol toxicity. Typical MRI brain findings helped confirm the diagnosis. Our case highlights the importance of obtaining the correct medical history and how social and medicolegal issues sometimes become a hindrance to obtaining the same.
Conclusion: In familial nephrocalcinosis/lithiasis/hyperparathyroidism genetic counselling and screening defines individualized treatment and may prevent extra renal disease manifestations.

REFERENCE


#5727
THE BURDEN OF SYMPTOMS AND PROCEDURES IN PATIENTS WITH RECURRENT KIDNEY STONES – A REPORT FROM A STONE CLINIC
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Background and Aims: Kidney stones (KS) are increasing in prevalence and becoming a major public health problem. The extent of the disease has been described as the stone burden, a measurement based on the size and number of stones. However, the quality of life of these patients is not affected by these parameters per se, but rather by the frequency and intensity of symptoms and the need for surgical procedures. The current data on this subject is very limited. The aim of our study was to record the frequency of symptoms and surgical procedures in patients with recurrent KS and to evaluate possible associations with basic clinical data and common comorbidities.

Method: We report a retrospective study on 181 consecutive patients with recurrent KS who were examined at the University Medical Centre Ljubljana stone clinic for the first time during the period of 2018 – 2022. We performed a standardized questionnaire to record common KS symptoms, procedures, basic clinical data, and comorbidities. Events were defined as number of severe lumbar pain (SLP) events per year (8-10/10 on the visual analog scale – VAS) and number of surgical procedures (SP) for stone removal per year. Moderate lumbar pain (MLP) events (VAS 4-7/10) and passing of stones were quantified on a scale from 0-4. Due to the wide variety of frequencies the associations were analyzed with Chi-Square test using terciles when possible or with presence and absence of symptoms. We considered p values < 0.05 as statistically significant.

Results: Mean age was 51.1 (SD 14.5) years, with 51.8% females. Arterial hypertension (AH) was present in 29.8% of patients, diabetes mellitus in 6.6%, and a family history of KS in 30%. The median frequency of SLP and SP was 0.68 (IQR 0.01-1) events/year and 0.08 (IQR 0.0-0.33) procedures/year, respectively; while 26.7% and 12.8% of patients had at least one SLP event or SP per year, respectively. When comparing terciles of frequency of SLP we found an association with more common SLP events in patients with a positive family history of KS, with 40.7% with and 21.6% of patients without a family history of KS, with 40.7% with and 21.6% of patients without a family history of KS, respectively (p = 0.033). When comparing terciles of frequency of procedures we only found a trend towards more common procedures in patients with AH (p = 0.062). The frequency of MLP was as follows – 42.6% had it less than once per year, 11.6% had it once or twice per year, 11% three to five times per year, 12.9% every month, and 21.9% on a weekly basis. We found no statistically significant association between MLP and basic clinical data or comorbidities only a trend towards more frequent episodes in patients with AH (p = 0.096).

In regards to the passing of KS we found the following frequencies – 72.4% had episodes less than once per year, 14.9% once or twice per year, 5.3% three to five times per year, 3.9% every month, and 3.3% on a weekly basis. There was statistically significant difference between passing of KS and sex, with 34.5% of males and 21.3% of females passing KS at least once per year, respectively (p = 0.047). Additionally, there was a significant difference between passing of KS and family history of KS, with 40.7% with and 21.6% of patients without a history of KS passing KS at least once per year, respectively (p = 0.008).

Conclusion: Our study showed that symptoms and surgical procedures were common in patients with recurrent KS referred to our clinic. Half of the patients had severe lumbar pain at least every three years, and a quarter had severe lumbar pain and passed KS at least once per year. About a third of patients had moderate lumbar pain at least once per month. Patients with a family history of KS developed stones earlier in life and had more common severe lumbar pain and passed KS more frequently. These issues should be analyzed in greater detail, with symptom scores that would define the burden of KS in a more objective manner and help in assessing the effectiveness of KS therapies.

#460
SEDIMENT IN CLEAR AND CLOUDY URINE: CAN INTERMITTENT CATHETERS DRAIN IT?
Sotiria Athanasiadou1, Lene Nielsen2, Christian Nielsen2, Betina Sulvdart2 and Per Bagi2
1 Coloplast A/S, Medical Affairs, Humlebæk, Denmark and 2 Coloplast A/S, Pre-clinical Department, Humlebæk, Denmark and 3 Righospitalet, Urology, Copenhagen, Denmark

Background and Aims: This study characterised the types and size of sediment in clear and cloudy urine and subsequently investigated the ability of conventional eyefull intermittent catheters and a novel Micro-hole Zone catheter to drain them.

Method: Clear urine was collected from three clinical studies where subjects drained with the conventional eyefull catheter and two prototypes of the Micro-hole Zone catheter. The studies included 60 subjects, equally distributed between male and female, healthy volunteers and intermittent catheterisation users. The sediment in the samples was analysed via automated microscopy (oCelloscope). Cloudy urine was collected from patients during their visits at the Urology Department of Righospitalet, Denmark. The samples were collected after spontaneous voiding, or via a conventional eyefull catheter and were analysed with the oCelloscope. An in vitro drainage test with the two catheters was subsequently performed.

Results: The analysis of clear urine (n = 180) showed most sediment to be smaller than 50 μm, with the largest sediment up to 200 μm (2.05 to 195.76 μm). The sediment included primarily crystals, cells, and bacteria, in line with published literature. Cloudy urine was divided into two categories, based on the presence of large particles visible to the naked eye. The samples without visible particles (n = 4) contained sediment with a mean size 12.81±0.038 μm (2.75 to 131.71 μm). The sediment identity corresponded to the sediment in clear urine, but the quantity was higher. Visible particles could not be analysed in the oCelloscope due to lack of light diffraction. These particles were soft and in various shapes and sizes. The Micro-hole Zone catheter drained sediment of larger size in clear urine compared to the conventional eyefull catheter. Both catheters drained cloudy urine efficiently but had challenges draining samples with visible particles (n = 20); the Micro-hole Zone catheter drained 12 samples, either directly or after light wiggling, while the conventional eyefull catheter drained 18 of the samples.

Conclusion: The analysis showed that the type of sediment does not differ between clear and cloudy urine without visible particles, but it is rather the abundance of sediment that induces the non-transparent appearance. The sediment was smaller than the size of the micro-holes (400 μm), therefore the novel catheter could efficiently drain urine and sediment and even larger size sediment. The latter could be explained by the design of the Micro-hole Zone, that allows urine and sediment to be drained continuously through a larger area, starting below the catheter tip, and extending to the bottom of the bladder lumen, acting on the SGLT2 proteins in the renal proximal convoluted tubules, Sodium-glucose co-transporter-2 (SGLT2) inhibitors are a class of antihyperglycemic agents that recently revolutionized the paradigm of chronic kidney disease. It exerts its effect by preventing the reabsorption of filtered glucose from the tubular lumen, acting on the SGLT2 proteins in the renal proximal convoluted tubules, and thus promoting a greater urinary glucose excretion. The authors described SEVERE HYPERCHLOREMIC METABOLIC ACIDOSIS WITH SGLT-2 INHIBITORS IN PATIENTS WITH URINARY DIVERSION
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Background and Aims: Urinary diversion after cystectomy using autologous intestinal segments has been the gold standard treatment of benign and malignant diseases of urinary tract. The most frequent metabolic abnormalities is hyperchloremic metabolic acidosis, due to ammonium absorption alongside chloride gain and bicarbonate excretion in the bowel conduit. Sodium-glucose co-transporter-2 (SGLT2) inhibitors are a class of antihyperglycemic agents that recently revolutionized the paradigm of chronic kidney disease. It exerts its effect by preventing the reabsorption of filtered glucose from the tubular lumen, acting on the SGLT2 proteins in the renal proximal convoluted tubules, and thus promoting a greater urinary glucose excretion. The authors described

Abstracts
GLOMERULAR & TUBULO-INTERSTITIAL DISEASES

B1 - BASIC SCIENCE, EXPERIMENTAL & RENAL PATHOLOGY

#3979

DIGITAL SPATIAL PROFILING CAN BE USED TO STUDY GLOMERULAR ENDOTHELIAL CELLS IN IGA NEPHROPATHY

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Background and Aims: IgA nephropathy (IgAN) is the most common primary glomerular disease worldwide; approximately 30% of cases progress to kidney failure 10-20 years from diagnosis. Five histopathological kidney lesions independently predict a poor prognosis in IgAN (MEST-C score) [1]. Published case series highlight the ‘endocapillary hypercellularity’ (E1) lesion as potentially reversible with systemic immunosuppression, improving clinical outcomes [2]. Delineating differences in the transcriptomes of glomerular endothelial cells (GEnCs) associated with and without E1 (E0) may highlight avenues for safer therapeutic strategies, given the overt risks associated with systemic immunosuppression in IgAN. GEnC transcriptomes have never been profiled in diseased kidneys before. Here we used digital spatial profiling (DSP) to achieve this.

Method: DSP was performed on a Nanostring GeoMx platform. Single 5μm sections were collected from four formalin fixed paraffin embedded (FFPE) kidney biopsies with E1 and five with E0. Following deparaffinization and antigen retrieval, the tissue was incubated with a whole transcriptome atlas probe set. GEnCs were stained for CD31 (red) and macrophages (which associate with E1[3]) with CD68 (yellow) with conjugated antibodies. Glomeruli were selected as regions of interests (ROIs), and a custom JavaScript function was used to mask over GEnCs and macrophages (segmentation), which were selected as areas of illumination (AOIs) (Fig 1). Photocleaved nucleotide barcodes were sequenced using an Illumina sequencer. Single cell enrichment was assessed using the SpatialDecon algorithm, differential gene expression was explored using a linear mixed effects model, and pathway analysis was performed using Reactome.

Results: The custom written JavaScript function allowed good segmentation on GEnCs and macrophages (Fig 1). Single cell deconvolution performed using the human kidney cell atlas as a reference showed significant enrichment of GEnCs relative to neighbouring cell types (Fig 2). Exploration of differential gene expressions using a linear mixed effects model found an up-regulation of TRIM23, IL27RA, TMEM139, P14K2B and PSMD9, after P value adjustment, among GEnCs associated with macrophages in glomerular capillary loops compared to those in the absence of macrophages (Fig 3). Pathway analysis based on differential gene expression performed using Reactome revealed that the complement cascade and regulators of the complement cascade were enhanced in GEnCs associated with macrophages (Fig 4).

Conclusion: This pilot study found DSP on the GeoMx to be effective at enriching GEnC transcript signals from neighbouring cell types in FFPE tissue. This preliminary data also shows that GEnCs associated with macrophages may display a more inflammatory phenotype, which may be related to up-regulation in complement activity and may account for the progressive phenotype associated with E1 in IgAN. With several trials investigating complement system targeting therapeutics in IgAN, validation of these findings might highlight a cohort of patients with IgAN most likely to benefit from treatment.

REFERENCES


**Background and Aims:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by immune-complex deposits and inflammatory cell infiltrations in multiple organs, and approximately half of lupus patients have nephritis. Lymphangiogenesis is the proliferation of pre-existing lymphatic vessels (LVs), which regulate tissue fluid homeostasis and immune cell trafficking, responding to the tissue environment. In this study, we evaluated the therapeutic effect of SAR131672, a selective VEGFR3 inhibitor, on the murine lupus nephritis model by regulating inflammation and lymphangiogenesis.

**Method:** First, we reviewed medical records for the biopsy-proven lupus nephritis and performed an immunohistochemistry study for D2-40. For
animal experiments, seven to eight-week-old male BALB/c mice were used. The back area’s skin was shaved and treated topically three times per week, with 100 μg of resiquimod in 100 μl of acetone for eight weeks and concomitantly treatment of VEGFR3 inhibitor, SAR 131672 by oral gavage. We evaluated renal histology and immunofluorescent study for inflammatory cells and lymphatic vessels. We also evaluated inflammatory cytokines and chemokines, lymphangiogenic factors by qRT-PCR.

Results: In a human study, we found that the higher lupus activity index, the more D2-40(+) lymphatic vessels are expressed in the tubulointerstitial areas. In an animal study, eight weeks of topical treatment of resiquimod to BALb/c mice induces lupus-like symptoms such as weight loss, splenomegaly, and glomerular immune complexes deposits such as IgG, IgM, and C3 in immunofluorescent staining. Histologically, glomerular mesangial cell proliferation and increased inflammatory cells in tubulointerstitial areas were noted in the H&E stain. Inhibition of VEGFR3 by oral SAR131672 treatment decreases glomerular and tubulointerstitial inflammation and decreases LYVE-1(+) lymphatic vessels. The pro-inflammatory cytokines and chemokines such as ICAM-1, VCAM-1, MCP-1, CCL19, CCL21, CCR7, CXCL13, and BAFF mRNA levels were increased compared with the vehicle-treated group. Treatment SAR131672 decreases pro-inflammatory cytokines and chemokine.

Conclusions: Inhibition of VEGFR3 by SAR131672 decreases the resiquimod-induced lupus nephritis model by regulating inflammation and lymphangiogenesis.

Conclusion: Analysis of patient-specific podocytes is possible ex vivo via direct derivation from patient-derived fibroblasts by episomal reprogramming, into hiPSC-derived podocytes, with the potential to study alterations of disease-specific mutations regarding phenotypical and functional behavior in a personalized manner. The use of hiPSCs bypasses the limitation of restricted podocyte cell number and has the advantage of maintaining the patients’ genetic background at podocyte cell level. This enables future large-scale experiments regarding intercell-cell communication and interaction in glomerular and interstitial三维 structural co-cultures or via treatment with therapeutic substances or stress factors.

Abstracts

#5158 AUTOSOMAL DOMINANT TUBULAR KIDNEY DISEASE: FROM PHENOTYPE TO GENOTYPE

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Background and Aims: Autosomal dominant tubulointerstitial kidney disease (ADTKD) represent a recently described group of kidney diseases, characterized by chronic interstitial nephritis (CIN), in most cases hereditary, with an autosomal dominant inheritance pattern, subclassified according to its genetic cause, when identified. Mutations in UMOD, MUC1, REN and PKD1 genes have been implicated in their pathogenesis. Recent molecular diagnostic technologies, such as Next-Generation Sequencing (NGS), and particularly the use of restriction and Snapshot method for the detection of a cytokine insertion on the coding variable-number tandem repeat (VNTR) sequence in the MUC1 gene encoding mucin 1, have allowed the nephrologists to diagnose renal diseases of previously unknown cause, with a real prevalence probably underestimated. We present the cohort of patients identified with ADTKD in the Nephrogenetics’ clinic from the Nephrology department of our hospital from 2015 to 2022.

Method: Patients with chronic kidney disease (CKD) of unknown etiology and renal phenotype suggesting CIN (bland urinary analysis, hyperuricemia and/or anemia unrelated to the degree of CKD, hypo/hypercalcaemia, acidemia, urinary protein concentration defects, absent hypertension, renal cysts), especially with a family history of similar CKD, were referred for the Nephrogenetics’ clinic and ADTKD was investigated. In these cases, we performed a genetic study of ADTKD by the following steps: 1) UMOD, REN, HNF1B mutations studied through NGS; 2) if negative, search for the insertion of a single cytokine of the repeat unit comprising the extremely long (~1.5-5 kb), GC-rich (>80%) coding variable-number tandem repeat (VNTR) sequence in the MUC1 gene encoding mucin 1 (see Kirby et al Nat Genet. 2013). It is used a restriction and Snapshot method. 3) if negative, search for HNF1B Large deletion, detected by MLPA (kit P241-D2, MRC-Holland). Pre-genetic counselling was performed by the nephrologist, and post-genetic counselling was performed by the nephrologist and geneticist, namely to proceed with family screening of potentially affected family members when a pathogenic mutation was identified or when segregation studies were necessary.

Results: 31 families were studied and a confirmed genetic diagnosis was obtained in 11 (35%), allowing the identification of 30 patients with ADTKD; the mutations identified were in MUC1 in 4 families (13 patients), UMOD in 4 families (11 patients), HNF1B (2 families, 5 patients) and REN: 1 patient with a phenotype compatible with ADTKD but with a genotype compatible with renal tubular dysgenesis (two mutations in REN gene from each of the parents). One patient with HNF1B deletion also presented with a heterozygous variant of unknown significance in PKD1 gene, and a pathogenic variant of SLC2A3, heterozygous. Three families are still under study: 2 families are being studied with segregation studies to evaluate the pathogenicity of mutations in UMOD (1 family) and HNF1B (1 family), and 1 family with a phenotype of ADTKD (3 young patients with positive family history) with negative results for mutations in ADTKD genes is in study, with a negative result in WES. The study will be pursued in a specialized laboratory to better study MUC1, but at this moment we classify this family as ADTKD-NOS. If positive results are obtained for these 3 families, the percentage of families identified using this protocol will increase to 43.3% of the families studied through this model.

Conclusion: In our cohort, a genetic diagnosis was established in 35% of the families studied. MUC1 and UMOD are the most prevalent genes implicated in ADTKD at our center, similarly to what has been reported in other cohorts of ADTKD. Given the rarity of these diseases and the fact that they require specific molecular techniques for accurate diagnosis, we believe that Nephrogenetics’ clinics with dedicated nephrologists and geneticists in close cooperation are critical for an accurate diagnosis.
Background and Aims: Hyponatremia is the most common electrolyte disturbance in clinical care. Even mild presentations are associated with poor prognosis and increased mortality, in spite of which there is a trend to minimize the importance of small variations in natremia, that have historically been dismissed as not having negative consequences despite growing evidence against it. In this regard, it has not been studied to date whether an intermittent but recurrent hyponatremia is relevant. There are clinical scenarios where this condition could occur and be overlooked, such as cirrhosis or heart failure.

Method: Different rat models have been used to study the effects of different hypotonic situations on the electrolyte balance and central nervous system: intermittent recurrent hyponatremia (intraperitoneal (i.p.) daily dose of desmopressin acetate (ddAVP) and a water dose equivalent to 2.5% of the animal's body weight in hypodipsic diet fed animals), acute on intermittent recurrent hyponatremia (i.p. water overload equivalent to 10% of the animal's body weight water overload in chow fed animals). Apparent diffusion coefficient (ADC) evaluated at 7 and 14 days after the immunization. Results: In the intermittent recurrent hyponatremia model, mild and transient hyponatremia was induced (baseline Na\textsubscript{p} 136.50 ±1.73 mM/L vs 4h post-medication 129.44 ±2.00mM/L, p < 0.001), which was recovered 24h after treatment (141.25±0.96mM/L, NS compared to baseline). However, this situation was repeated over a 7 day period. This translated into a lower ADC value in the whole brain (WB) compared to chow fed animals (25.07±1.71 vs 26.71±2.40*10^{-3}mm\textsuperscript{2}/s, p = 0.05) after this 7 day period, suggesting an increase in total brain water in this situation. There was also an increase in ADC of GM and WM (1.16mEq/L, p = 0.01) and MBP 45.20 ± 8.32 vs 28.76±7.03au, p <0.01), although no significant changes in GFAP expression in the GM (p > 0.05) after this 7 day period, suggesting an increase in total brain water in this situation. There was also an increase in GFAP expression in the gray matter (GM) compared to chow fed animals (33.22±5.25 vs 25.07±2.31au, p = 0.031), although no significant changes in MBP expression were seen. Acute on intermittent recurrent hyponatremia induced hypertonic hyponatremia (116.00±1.16mM/L, p <0.001 compared to baseline). In this situation, a progressive decrease in ADC values in the WB was seen, and it was less pronounced compared to chow fed animals (slope -0.11±0.02 vs -0.26±0.006, p = 0.014). When GM and white matter (WM) were analysed separately, they both showed a progressive increase in ADC values, more evident in the WM (slope WM 0.19±0.04, p < 0.05; slope WM 0.05±0.02, p < 0.05). The water overload increased GFAP and MBP's expression in the GM (GFAP 23.17±6.37 vs 16.83±5.17au, p = 0.001; MBP 45.20±8.32 vs 28.76±7.03au, p <0.001), but no changes were seen in the GM, similarly to what had been observed in the acute hyponatremia model.

Conclusion: Intermittent recurrent hyponatremia is a novel animal model that suggests there can be significant water retention after only a few hours of hyponatremia a day, provided this situation is repeated over time. Such water retention translates into greater brain water accumulation and astroglial activation in the GM. These animal's response to an additional water overload does not show big variations compared to what is observed in acute hyponatremia. This study highlights the importance of slight fluctuations in natremia, which, if maintained over time, can translate underlying water retention with consequences at the central nervous system level.
Myeloproliferative neoplasms (MPN) are chronic disease.

**Background and Aims:** Minimal change disease (MCD) is a podocytopathy more commonly seen in children, but it also accounts for 10%–25% of adult NS. Patients with MCD manifest with abundant albuminuria, which is related to the damage of the glomerular filtration barrier. Podocytes are major components of the glomerular filtration barrier and play a crucial role in maintaining the integrity of the glomerular filtration barrier. Alterations in podocyte actin critically affect podocyte function. Tubulin polymerization-promoting family member 3 (TPPP3) is a regulator of microtubule dynamic that has microtubule bundling activity. However, the mechanism of TPPP3 involved in podocyte apoptosis is remains unknown.

**Method:** Single-cell RNA sequencing comprehensively characterized the expression of TPPP3 in human glomeruli. We cultured human immortalized podocyte cells (HPC) in vitro, and constructed the HPC injury model. Immunofluorescence, western blot were used to determine the expression of TPPP3, α-tubulin, acetylated tubulin, phospho-YAP1, Podocyte apoptosis was determined by Annexin V APC Apoptosis Detection Kit.

**Results:** TPPP3 was specifically expressed in human glomerular podocytes, and its expression level was significantly decreased in the cases of MCD and ADR induced podocyte injury (P < 0.05). Knockdown of TPPP3 led to decreasing expression of acetylated tubulin in podocytes (P < 0.05). Phospho-YAP1 was also observed in the TPPP3 knockdown HPCs (P < 0.05). Apoptosis was increased in the TPPP3 knockdown HPCs, suggesting TPPP3 may be related to the podocytes injury and apoptosis.

**Conclusion:** TPPP3 is involved with the apoptosis of podocytes by regulates nuclear recruitment of YAP which was promoted by microtubule acetylation.

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**SPECTRUM OF GLOMERULAR AND VASCULAR KIDNEY PATHOLOGY ASSOCIATED WITH MYELOPROLIFERATIVE NEOPLASMS**

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**Background and Aims:** Myeloproliferative neoplasms (MPN) are chronic blood disorders defined by an overproduction of clonal, differentiated hematopoietic cells. A high prevalence of chronic kidney disease (CKD) is described in patients with MPN. The glomerular histological pattern of MPN-related kidney disease, MPN-related glomerulopathy (MPN-RG), may not account for the entirety of CKD risk in this population, as it appears to be rare and has mostly been reported in patients with myelofibrosis. The inflammatory and prothrombotic state of clonal blood cells has been linked to a systemic vasculopathy in MPN patients, characterized by thromboses and microvascular disease. Thus, we put forward the hypothesis that intrarenal vessel injury may occur during MPN, and that vascular necrolysis may be a common histological pattern in MPN patients presenting with kidney disease.

**Method:** We conducted an exhaustive, retrospective, multicenter study of MPN kidney biopsies in four kidney pathology units. All adult patients with a history of MPN who underwent a kidney biopsy were included. We performed a systematic histological review of glomerular and vascular compartments. MPN-RG was defined as mesangial expansion and negative glomerular immunofluorescence studies, with at least one of the following: mesangial hypercellularity, or features of chronic glomerular thrombotic microangiopathy. Hematopoietic cells were detected using anti-glycophorin C, anti-myeloperoxidase, and anti-factor VIII immunohistochemistry (IHC).

**Results:** We included 47 MPN patients who underwent a kidney biopsy, including 16 patients with chronic myeloid leukemia, 14 with polycythemia vera, 10 with essential thrombocythemia and 7 with primary myelofibrosis. 14 cases (29.8%) met our definition of MPN-RG. MPN-RG was strongly associated with myelofibrosis (primary or secondary, P = 0.021) and poorer ESRD-free survival (P = 0.007). Positive IHC for circulating cells in the glomerular capillaries was not associated with glomerular injury but was positively correlated with blood leukocyte count (P = 0.004). Thirty-three patients (75.0%) had moderate-to-severe arteriosclerosis; 39 patients (84.8%) had moderate-to-severe arteriolar hyalinosis. Multivariable models including 188 control kidney biopsies revealed an association between MPN and chronic kidney vascular damage, which was independent of established risk factors such as age, diabetes mellitus and hypertension (Table 1 and Table 2).

**Conclusion:** We demonstrate the strong association between MPN-RG and myelofibrosis and confirm its poor renal prognosis. We argue that the finding of glomerular intracapillary hematopoietic cells should not be considered in the diagnosis of MPN-RG. Most notably, our results show that MPN represent a novel, independent risk factor for vascular nephrosclerosis, and establish a new link between MPN and CKD. These findings raise new hypotheses regarding the pathophysiology of vascular nephrosclerosis in the general population.

**Table 1: Multivariable model for Banff cv lesion 2-3 versus 0-1.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
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<tr>
<td>Age, years</td>
<td>1.042</td>
<td>1.018, 1.069</td>
<td>&lt;0.001</td>
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<tr>
<td>Myeloproliferative neoplasm</td>
<td>2.427</td>
<td>1.112, 5.619</td>
<td>0.026</td>
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<tr>
<td>Diabetes mellitus</td>
<td>1.117</td>
<td>0.576, 2.188</td>
<td>0.744</td>
</tr>
<tr>
<td>Antihypertensive drugs, n</td>
<td>1.116</td>
<td>0.894, 1.397</td>
<td>0.333</td>
</tr>
<tr>
<td>Globally sclerotic glomeruli, %</td>
<td>1.016</td>
<td>1.002, 1.030</td>
<td>0.027</td>
</tr>
</tbody>
</table>

**Table 2: Multivariable model for Banff aah lesion 2-3 versus 0-1.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
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<td>0.989, 1.037</td>
<td>0.305</td>
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<tr>
<td>Myeloproliferative neoplasm</td>
<td>4.446</td>
<td>1.892, 11.81</td>
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<tr>
<td>Diabetes mellitus</td>
<td>2.040</td>
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<td>Globally sclerotic glomeruli, %</td>
<td>1.009</td>
<td>0.996, 1.024</td>
<td>0.188</td>
</tr>
</tbody>
</table>
CLINICOPATHOLOGIC CHARACTERISTICS IN RENAL THROMBOTIC MICROANGIOPATHY
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Background and Aims: Thrombotic microangiopathy (TMA) is a life-threatening condition that can be caused on the background of various mechanisms, converging to a severe endotheliopathy that often affects the kidneys. Morphologic features of TMA on kidney biopsy have not been systematically studied. We studied the diagnostic and prognostic role of a kidney biopsy in patients with TMA, either linked to a coexisting condition (i.e., secondary TMA) or not (i.e., complement-mediated [C-]TMA).

Method: Patients with TMA on kidney biopsy and an enzymatic activity of ADAMTS13 > 10% were recruited from the Limburg Renal Registry. C-TMA was defined as massive ex vivo C5b9 formation on the endothelium and/or rare variants in complement genes [1]; secondary TMA was defined as the presence of a coexisting condition and normal complement regulation. Kidney tissue sections were studied for activity and chronicity; also, C3d staining was performed.

Results: C-TMA and secondary TMA was diagnosed in 35 and 39 patients, respectively. The diagnosis TMA was based on a kidney biopsy in 52 (70%) out of 74 patients as systemic hemolysis, that is, microangiopathic hemolytic anemia (MAHA) and thrombocytopenia, was lacking. Morphologic activity, such as, glomerular thrombosis and mesangiolysis, was not associated with MAHA (p = 0.116) and/or thrombocytopenia (p = 0.380). Morphologic activity, however, was associated with C-TMA, as was lower age and higher serum creatinine. C3d staining did not differentiate C-TMA from secondary TMA. A Mayo Clinic Chronicity Score (MCCS) of ≥ 4 was associated with an increased partial- (p = 0.023) and complete renal remission rate (p = 0.030), and decreased end-stage kidney disease (p = 0.050).

Conclusions: Only a small proportion of patients with TMA on kidney biopsy initially present with systemic hemolysis, suggesting an essential role of histologic examination to prevent underdiagnosing. Glomerular thrombosis and mesangiolysis were associated with C-TMA, however there is no role for staining of C3d in differentiating C-TMA from secondary TMA. An increased MCCS indicates worse renal outcome in patients with TMA.

REFERENCE
SEX-, AGING AND DIABETES-RELATED ALTERATIONS IN GLOMERULAR DIMENSIONS AND PODOCYTE DENSITIES USING DEEP-LEARNING QUANTIFICATION

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Background and Aims: Kidney function, as well as its morphology, changes markedly with age and disorders such as diabetes. This process is associated with structural and functional alterations in cortical and juxtamedullary glomeruli. Currently, data on differences in cortical and juxtamedullary glomeruli associated with sex, age, genetic factors, and diabetes are limited. In this study, we investigated the abundance and morphometry of podocytes and glomeruli in mice of different ages and sex', and suffering from diabetes or not using a deep-learning based analysis of immuno-stained kidney sections.

Methods: Male and female non-diabetic C57BL/6J mice and diabetes type II (db/db) mice were sacrificed at different time points: 4, 10, 20, 30, 34, 40 weeks and 6, 24 weeks, respectively. Subsequently, kidneys were extracted, embedded in paraffin, cut into sections, stained, and imaged for histological analysis. We used immunohistochemistry staining with Wilms Tumor 1 (WT1) antibody to specifically stain podocyte nuclei. Both manual and deep-learning based image segmentation were performed to analyze abundance and morphometry of podocytes and glomeruli. In total, 4134 glomerular structures were detected, and morphometry of glomeruli and podocytes was extracted and analyzed by an automated algorithm.

Results: Our study aimed to investigate aging- and diabetes-related differences in cortical and juxtamedullary glomeruli with respect to podocyte abundance and loss. Using a customized deep learning algorithm, podocyte nuclei could be quantified with comparable quality as a time-tedious manual analysis, which takes approximately 1 minute per glomerulus. Extracted morphometric features showed that juxtamedullary glomeruli had a larger cross-sectional area than cortical glomeruli (Figure 1a). For both cortical and juxtamedullary glomeruli the cross-sectional area slightly increased on average with aging (Figure 1b). As expected, podocyte endowment in cortical glomeruli was lower than in juxtamedullary glomeruli with podocyte density being higher (Figure 2a, 2b). Over life-time the number of podocytes and podocyte density per glomerulus slightly decreased both in cortical and juxtamedullary glomeruli (Figure 2b, 3b). Interestingly, female cortical glomeruli were on average smaller and had a higher podocyte density compared to males (Figure 1c, 3c). However, podocyte numbers did not differ between male and female (Figure 2c). Finally, we found that 24 weeks old db/db mice presented with glomerular hypertrophy in contrast to non-diabetic C57BL/6J mice of the same age (Figure 1d). Db/db mice lost podocytes from 6 weeks to 24 weeks of age with a decreased podocyte density. Surprisingly, podocyte loss occurred to a lower extent in non-diabetic mice (Figure 2d, 3d).

Conclusion: During aging and early diabetic disease both podocyte loss and glomerular hypertrophy occur. Similar changes occurred in juxtamedullary and cortical glomeruli in both sex'. Hyperfiltration might explain the pronounced extent in glomerular area in diabetic mice and should represent an increase in filtration surface to handle diabetes-related hyperfiltration. Less podocyte loss in diabetic mice at 24 weeks age compared to C57BL/6J mice might relate to the different mouse model and still moderate podocyte stress during the early stage of diabetic kidney disease.
ROLE OF INTEGRIN, FIBRONECTIN, AND uPAR IN PODOCYTE-GLomerular Basement Membrane Interaction Under Fluid Shear Stress

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Background and Aims: Podocyte-glomerular basement membrane (GBM) interaction is the main component to maintain glomerular filtration barrier. Interestingly, the podocyte-GBM interaction is not static, but dynamic according to various podocyte conditions. Thus, we hypothesized that the podocyte-GBM interaction would be changed under stress conditions such as fluid shear stress (FSS). Here, we aim to explore the change of specific integrin (Itg αVβ3), fibronectin, and uPAR in the podocyte-GBM interaction under fluid shear stress (FSS).

Method: We used conditionally immortalized human podocyte cells which were differentiated only under specific (non-permissive) temperature (37°C). We exposed the podocytes to 200 rpm of FSS and applied various dish coating agents. We observed cell morphology and documented the protein and mRNA expressions of Itg β3, fibronectin, and uPAR under FSS.

Results: Podocyte morphology became more elongated with actin rearrangement under FSS. Protein expression of Itg β3 did not change under FSS, while activated Itg β3 increased from early phase (30 min after exposure to FSS) (Figure 1). Fibronectin (Figure 2) and uPAR (Figure 3) gradually increased under FSS. mRNA expressions of Itg β3, fibronectin, and uPAR did not change under FSS. Cell viability increased in collagen-1 coated dish compared to non-coated under FSS.

Conclusion: This study demonstrates that Itg αVβ3 is activated, fibronectin and uPAR increase under FSS. In addition, it is shown that extracellular matrix contributes to podocyte stability. The results suggest that Itg αVβ3, fibronectin and uPAR may have specific roles to maintain podocyte’s stability through the modulation of the podocyte-GBM interaction.

Figure 1: Activated Itg β3 increased from early phase (30 min after exposure to FSS).

Figure 2: Fibronectin gradually increased under FSS except for collagen-4 coated group.

Figure 3: uPAR gradually increased under FSS.
#5649
HEPARANASE OVEREXPRESSION MODIFIES PODOCYTE MOTILITY
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Background and Aims: Heparanase is an endo-ß-ß-glucuronidase that degrades heparan sulfate side chains, which are essential components of extra-cellular matrices and cell surfaces, including in the kidney filtration apparatus, the glomerulus. Upregulation of heparanase in glomerular diseases (GDs) was demonstrated in experimental models of GDs and in humans. Using transgenic mice overexpressing the human heparanase gene, we recently showed that heparanase reduced proteinuria and preserved the glomerular filtration barrier (GFB) after Adriamycin-induced injury. Furthermore, heparanase improved survival of key GFB cells, the podocytes and enhanced their autophagic flux both in vitro and in vivo. Here, we aimed to study the potential role of heparanase on podocyte locomotion and adhesion.

Methods: We utilized immortalized human podocyte cell line AB8/13 (a kind gift of Prof. Moin Saleem, Bristol, UK) as an experimental platform. Cells were infected with pLenti6/VS-DEST carrying the heparanase gene construct (H) or control empty vector (V) and were allowed to differentiate for 14 days. To induce injury, differentiated podocytes were treated with Adriamycin (0.5 ßg/mL), mimicking Adriamycin nephropathy, an established experimental model for progressive proteinuric GDs. For readouts, we used scratch assay, RT-qPCR, Western blot (WB) and immunofluorescence (IF) analyses.

Results: The in vitro scratch assay showed that differentiated (H) podocytes migrated at a slower rate compared with control (V) podocytes, both at baseline and after a 12-hour treatment with Adriamycin. Hence, we hypothesized that heparanase may alter podocyte adhesion properties. Indeed, IF staining of differentiated (H) podocytes exhibited an increase in focal contacts containing vinculin compared with control (V) cells treated with Adriamycin. Of note, we observed no differences in vinculin abundance by WB, suggesting that heparanase mediates the active form of vinculin. Moreover, among the integrins, we noticed temporal upregulation of ITGB1 transcription, as early as two hours after Adriamycin treatment, in (H) compared with control (V) podocytes (P = 0.032).

Conclusions: Collectively, our results suggest that in response to Adriamycin injury, constitutive heparanase overexpression could stabilize podocyte focal adhesions and control motility. Although further research is needed, improving the anchoring of podocytes over the basement membrane may provide an additional cellular mechanism by which heparanase conferred protection against Adriamycin toxicity.

#5104
GLOMERULAR DISEASES ASSOCIATED WITH SARS-COV2 INFECTION AND VACCINATION: A MULTICENTRIC REGIONAL RETROSPECTIVE STUDY

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Background and Aims: The SARS-CoV2 caused a pandemic disease, leading to millions of cases and fatalities worldwide. Kidney involvement is frequent and glomerular diseases (GD) have been reported in association with infection. Podocytropathies, endothelial injury with thrombotic microangiopathy are the most common histological findings in literature. From January 2021 anti SARS-CoV2 vaccination became available. Several GD has also been associated with vaccination. IgA nephropathy (IgAN) and minimal change disease (MCD) are the most common GD reported in patients who received vaccination. Our aim was to assess the histological findings in patients who presented kidney involvement after SARS-CoV2 infection and/or vaccination and to compare the frequencies of GD in these patients to those in non-Covid19 population.

Method: We conducted a retrospective study of kidney pathology in patients undergoing native kidney biopsy within 90 days of SARS-CoV2 infection and/or vaccination, between February 2020 and August 2022 in Apulia Region of Italy. We considered separately patients without history of urinary abnormalities and/or kidney dysfunction prior to infection and/or vaccination in order to detect GD which were more likely to be related to infection and/or vaccination than to pre-existent pathologies. We used a database of kidney biopsies performed in a period of 5 years (from January 2015 to February 2020) prior to the Covid19 pandemic as a control comparison cohort to examine glomerular diseases frequencies.

Results: Among the 808 biopsies: 36 (4.4%) were carried out within 90 days of SARS-CoV2 infection (Group 1) and 142 (17.6%) within 90 days of vaccination (Group2). Among them, we identified 12 patients with renal symptoms raised after COVID19 infection (Group 3) and 26 patients after vaccination (Group 4). In the Group 1 the main histological diagnosed founded were: podocytropathies (25.1%), IgAN (16.7%) and ANCA-vasculitis (13.9%). In Group 2, the most common histological diagnosis were IgAN (18.3%), podocytropathies (17%) and membranous nephropathy (MN) (10.6%). In the Group 3 we found a predominance of podocytropathies (33.3%) followed by ANCA-vasculitis and IgAN (three patients each, 25%). In the Group 4, the most frequent GD were podocytropathies (36.6%) followed by ANCA-vasculitis (19.2%) and IgAN (15.4%). Between the 1380 kidney biopsies from the 5 years pre-Covid19 period, the most frequent histological diagnosis were IgAN (18.3%), podocytropathies (18%) and MN (10.9%). Comparing Group 1 and Group 2 data with the 5 years pre-Covid19 database we found a significant increased prevalence only of ANCA vasculitis in group 1 (13.9% of patients after Covid19 infection vs 5.6% of pre-covid database (p-value: 0.03)). Comparing data from patients who had developed renal signs after Covid19 infection (group 3) and/or vaccination (group 4) with those in the 5 years database a significant higher prevalence of ANCA-related crescentic glomerulonephritis was found in both group. The 25% of patients of the Group 3 and the 19.2% of the Group 4 had a histological diagnosis of vasculitis, while these were found only in the 5.7% of patients from the pre-Covid19 database (p-value: 0.004 for Group 3 and 0.003 for Group 4). Furthermore podocytropathies in group 4 were significantly higher than pre-covid19 (36.6%vs18.3%, p = 0.02).

Conclusion: We found a higher prevalence of ANCA vasculitis and podocytropathies in patients with symptoms developed after SARS CoV2 infection/vaccination compared to diagnosis prevalence in a pre-Covid19 reference database.
#3789
SERUM AND URINARY SOLUBLE PD-1, PD-L1 AND PD-L2 AS BIOMARKERS FOR CHECKPOINT INHIBITOR RELATED ACUTE INTERSTITIAL NEPHRITIS
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Background and Aims: Acute interstitial nephritis (AIN) related to Immune Checkpoint Inhibitors (ICI) is a frequently described adverse effect, although the mechanisms are not fully understood. The gold standard for the diagnosis is kidney biopsy. Although it is invasive, it is necessary as AIN can be confused with other causes of acute kidney injury (AKI) in oncologic patients. The diagnosis of AIN has therapeutic consequences such as the need to withdraw the drug if confirmed, possibly diminishing patients’ life expectancy. Few biomarkers have been proposed for non-invasive diagnosis or the follow-up of these patients, which could be useful when the biopsy is contraindicated or not available. Our aim was to study the Immune Checkpoint pathway during the event, as well as analyse potential biomarkers directly related to the pathway.

Method: We performed an observational study. We recruited patients with incident diagnosis of AIN related to ICI in our institution from 2018 to 2022. We obtained serum and urine at the time of diagnosis after signing informed consent. We recruited n = 18 patients with the diagnosis of AIN related to ICI. For comparison, we recruited patients with non ICI-related AIN (n = 18), patients with active ANCA-vasculitis (n = 35), patients with acute tubular necrosis (ATN) (n = 22), and controls (n = 36) (patients with diagnosis of malignancy without AKI (n = 22), and healthy controls (n = 14)). We determined soluble PD-1 (sPD-1), sPD-L1 and sPD-L2 in serum and urine using a multiplex bead-based Luminex assay. Besides, we performed PD-L1 immunohistochemistry and PD-L2 immunofluorescence staining of kidney biopsies from patients with ICI-related AIN (n = 14) and compared to patients with non ICI-related AIN (n = 10).

Results: Serum sPD-1 was higher in patients with AIN compared to controls (p = 0.0004) and patients with ATN (p = 0.021). There were no differences between controls and ATN (p = 0.76). Urinary sPD-1 was lower in subjects with AKI compared to controls (control vs AIN (p = 0.019), control vs active vasculitis (p<0.0001) and control vs ATN (p = 0.0304)). Patients with ATN exhibited the lowest urinary sPD-1 levels, and there were statistically significant differences when compared to AIN (p = 0.0304). Focusing on oncologic patients, urinary sPD-1 concentration < 129.3 pg/ml had a 71.43% sensitivity and 94.12% specificity to differentiate ATN from AIN, with a likelihood ratio of 12.14. Serum and urinary sPD-L1 and sPD-L2 did not show statistically significant differences between AIN and ATN. In kidney biopsies, patients with ICI related AIN showed higher density of PD-L1 positive tubules than patients with non-ICI related AIN (p = 0.037). Proportion of patients having more than 2.64/mm² PD-L2 positive tubules was higher among patients with ICI related AIN compared to non ICI-related AIN (p = 0.034). There was a positive correlation (p = 0.009, r = 0.72) between urinary sPD-1 and the density of PD-L1 positive tubules (tubules/mm²). As for PD-L2, serum PD-L2 was higher in patients with positive tubular PD-L2 expression (p = 0.009).

Conclusion: Serum sPD-1 increases in AIN, contrary to patients with ATN and controls. Urinary sPD-1 decreases in patients with AKI. This decrease is more intense in the case of patients with ATN, thus being useful in the differentiation between ATN and AIN, especially in patients with neoplasms. Patients with ICI-related AIN exhibit higher positivity for PD-L1 and PD-L2 staining compared to other causes of AIN. Altogether, our findings suggest a role for these soluble molecules in the ICI-related AIN pathophysiology.

Figure 1: (a) ROC curve of urinary sPD-1. Concentrations less than 129.3 pg/ml differentiates ATN from AIN with 71.43% sensitivity and 94.12% specificity, likelihood ratio of 12.14. (b) Immunohistochemistry PD-L1 staining of a kidney biopsy section showing a PD-L1 positive tubule.
MASS-SPECTROMETRY ANALYSIS OF CONGOPHILIC URINE AND ITS DETERGENT RESISTANT FRACTION IN PATIENTS WITH AMYLOID AND NON-AMYLOID NEPHROPATHIES

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Background and Aims: Being a well-known intrinsic property of amyloid, congophilia was recently demonstrated in urine of patients with proteinuria of different etiology including renal amyloidosis (RA) and non-amyloid nephropathies (NANP) [1]. Urine proteins (UPs) responsible for congophilia in RA and NANP are supposed to have another property of amyloid such as resistance to ionic detergents and present in urine as detergent-resistant aggregates (DRA). In the pilot study we performed mass-spectrometry (MS) analysis of congophilic urine samples and its detergent-resistant fraction in patients with RA and NANP to investigate UPs and their specificity to the particular kidney disease.

Method: We collected first morning void urine samples from patients with RA (n = 4) and NANP (n = 4). Urine congophilia was assessed by Congo red Dot test as described previously [1]. To analyze bulk urine (BU) proteins, 30 µl of supernatant was precipitated with 80% acetone and boiled in 2% sodium dodecyl sulfate (SDS) for 30 minutes. Then 5 µg of UPs was separated in 10% polyacrylamide gel electrophoresis (PAGE) followed by Coomassie blue staining. The further centrifugation of 0.5-3 ml of urine at 300,000x g for 16h following by the treatment of precipitate with 3% sarcosyl in phosphate-buffered saline (PBS) for 10 min with subsequent washing of resistant aggregates in PBS were applied to obtain DRA. After boiling in SDS 8 µl of the sample was separated in 10% PAGE. UPs concentration in the DRA was estimated by densitometry regarding to 2 µg of bovine serum albumin. Then 6 µg of UPs was digested with trypsin, followed by purification on silicate (CDS Empore™ C18 Extraction Disks). Prepared samples of BU and DRA were analyzed by electrospray ionization tandem MS. We used MsFragger software to obtain lists of UPs for each sample. Most representative UPs in the sample were selected by the unique spectral count (USC). We considered the protein as having diagnosis-specific potential (DSP) if it was present in every sample of the particular disease group, i.e. AA, AL, NANP in BU or DRA, and was absent in any sample of another disease group.

Results: The patients had following characteristics: age 51±13 years, 3 male/5 female, eGFR = 45 (19; 95) ml/min/1.73 m²; 24h proteinuria = 6.3 (4.5; 7.9) g. In PAGE analysis, BU proteins appeared to be similar in all 8 samples with 2 major bends in 70 kDa and 50 kDa regions, corresponding to albumin and immunoglobulin (lg) heavy chains, respectively (Fig. 1A). The amount of protein in DRA was small and comprised 1.02 (0.71; 1.61) % of the total protein in the sample (4.7 (2.3; 5.1) g/l). Compared with BU PAGE analysis of DRA proteins revealed other bends with trace albumin bend, predominance of 45 kDa region bend and more apparent 30 kDa bend (lg light chains) in the majority of patients (Fig. 1B). Results of MS analysis are shown on the Figure 2. There were more DSP revealed in DRA vs BU: 14 vs 5, 46 vs 2 and 4 vs 2 UPs in samples of AL, AA and NANP, respectively. When compare by a particular disease group, there were no DSP found either in BU or DRA in RA samples. One protein (aminopeptidase N) and 3 proteins (isofrom 3 of unconventional myosin-LC, protein S100-A8, elongation factor 1-α 1) were detected as DSP in BU and DRA in AL, respectively. Alpha-1-acid glycoprotein 1 was only DSP for AA in DRA as well as serum paronoxase 1 for NANP in BU.

Conclusion: Although DRA represented a small portion of UPs, its composition significantly differed from BU and could contain more specific disease markers that makes urine detergent-resistant fraction promising for the future research. Understanding the role of DRA proteins in the pathogenesis of amyloid and non-amyloid renal disease and their diagnostic utility requires further studies.

REFERENCE


THE EFFECT OF TRPC5 AND PALLADIN EXPRESSION ON TREATMENT RESPONSE AND RECURRENT OUTCOME IN FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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Background and Aims: Focal segmental glomerulosclerosis (FSGS) is a disease that is among the primary glomerulopathies and often progresses to chronic renal failure. Despite advances in immunosuppressive therapy for the treatment of glomerular diseases, some FSGS patients are resistant to single or combination immunosuppressive regimens containing: glucocorticoids, cyclophosphamide, calcineurin inhibitors, mycophenolate mofetil (MMF), and/or rituximab. FSGS-related nephrotic syndrome, the degree of proteinuria and response to steroid therapy are the most important factors associated with long-term prognosis, independent of histological findings. Failure to respond to immunosuppressive therapy, including corticosteroids, has been evaluated as one of the most important markers of the risk of developing renal failure. Unfortunately, there is no reliable marker that can predict steroid response. One of the earliest manifestations of podocyte damage is cytoskeletal remodeling, known as deletion of foot ridges. It was recently shown that transient receptor potential channel 5 (TRPC5) plays an important role in initiating this process. However, the role of TRPC5 in disease progression is unknown. It is thought that calcium influx caused by sustained TRPC5 activation in the chronic disease setting may lead to calcium toxicity and podocyte death. It is known that the actin regulatory protein palladin, which is highly expressed here, is also highly related to podocyte function and podocyteopathies, and plays an important role in the stability of the actin cytoskeleton. The aim of our study was to define the frequency of TRPC5 and palladin renal expressions in podocytes in focal segmental glomerulosclerosis (FSGS) and its relationship with prognosis and treatment response.

Method: A total of 182 patients were enrolled for baseline clinical and histopathological features and 103 patients with a clinical follow-up for more than 2 years were evaluated for outcomes. Immunohistochemical staining was performed with TRPC5 and palladin antibodies on kidney biopsies and glomerular staining was evaluated.
Results: Baseline characteristics, and health parameters were similar between TRPC5+/TRPC5− and palladin+/palladin− groups. TRPC5 expression was observed in 69% of the patient biopsies and palladin expression in 73%. We found that TRPC5 and palladin expression was a significant predictor of FSGS severity and poor treatment response (both p<0.05). In addition, TRPC5 expression was significantly associated with the development of end-stage renal disease and ongoing proteinuria.

Conclusion: The development of proven treatments that delay the progression of FSGS is critical to patient survival. The development of new treatments is possible only by knowing the underlying pathophysiological mechanism of the disease. Podocyte loss is a critical step in the development of irreversible glomerulosclerosis, which causes chronic kidney disease. Therefore, blocking TRPC5 channel and palladin may be an effective treatment strategy, especially in treatment-resistant FSGS patients with positive staining on biopsy. Our study is the first in the literature to show these two antigens in kidney tissue for MCTO patients.

Figure 1: FSGS patients treatment response rates according to TRPC5 and Palladin expressions in kidney biopsy.

#3939 EFFECTIVENESS OF IMATINIB FOR MCTO NEPHROPATHY
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Background and Aims: MAFB is a podocyte-specific transcription factor. Point mutations in the MAFB transactivation domain in humans result in multicentric carpometacarpal-tarsal osteolysis (MCTO). MCTO patients show focal segmental glomerulosclerosis (FSGS) due to podocyte damage, known as MCTO nephropathy. Effective treatment for MCTO has not been found. Imatinib is a tyrosine kinase inhibitor (TKI), which inhibits PI3K-Akt pathway, and is in long-term use for the treatment of chronic myeloid leukemia.

Method: In order to develop a new treatment for MCTO, we generated disease model mice using the CRISPR-Cas9 system. These animals have the same genetic mutation as human MCTO patients. Albuminuria was evaluated at 4 weeks of age, and renal histological analysis was performed at 26 weeks of age. In addition, RNA-seq for isolated glomeruli of 10-week-old MCTO mice and wild-type animal was performed for genetic and pathway analysis.

Results: MCTO mice exhibited growth retardation, and presented albuminuria from 4 weeks of age. Foot process effacement and FSGS-like renal histological changes were shown. Nephropathy symptoms were similar to that of human MCTO patients. Interestingly, the upregulated genes in RNA-seq analysis were a group of receptor genes associated with PI3K-Akt signaling, including lpar1 and csfr1. Transcerebral administration of imatinib, a PI3K-Akt pathway inhibitor, treatment for 5 consecutive weeks decreased albuminuria and ameliorated histological renal damage. RNA-seq of isolated glomeruli of MCTO mice after imatinib treatment showed decreased expression of genes associated with TGFβ-related signaling pathways compared to the non-treated group. Recently, enhanced PI3K-Akt signaling in podocytes has been linked to several renal diseases associated with podocyte injury. In addition, lpar1 inhibition in glomeruli is known to suppress TGFβ. Imatinib suppressed PI3K-Akt signaling, which is enhanced in podocytes of MCTO mice. This may have shown a podocyte-protective effect by suppressing fibrosis-related genes such as TGFβ. Imatinib is classified as a TKI, but frequency of podocyte toxicity is lower than other TKIs.

Conclusion: The podocyte injury mechanism of MCTO nephropathy is associated with enhanced PI3K-Akt signaling in podocytes. Imatinib inhibits this pathway and suppresses TGFβ. Imatinib may become a therapeutic agent for MCTO nephropathy.

#5466 CSF-1R SYSTEM ACTIVATES PARIELT EPITHELIAL CELLS LEADING TO FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)
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Background and Aims: Focal segmental glomerulosclerosis (FSGS) is the most common glomerular cause leading to end-stage kidney disease. Actual treatment of primary FSGS by immunosuppressive agents presents inconsistent results. Thus, new innovative strategies different from those used to date by taking into consideration podocyte renewal and maintenance or even strategies complementary to immunosuppression are needed. In FSGS, parietal epithelial cells (PECs) switch to an activated phenotype (aPECs) in response to podocyte damage promoting glomerulosclerosis. Colony-stimulating factor (CSF-1) is a hematopoietic growth factor that acts via its specific receptor, the tyrosine kinase receptor CSF-1R. CSF-1 has been detected in sera and renal biopsies from patients with different renal complications, including FSGS, attributing their role and presence to macrophage but not to glomerular cells. The potential cellular and molecular mechanisms involved are also unknown. In this work, we evaluated the implication of CSF-1/CSF-1R axis in the pathogenesis of FSGS and its potential as new pharmacological target point by using specific CSF-1R inhibitors. Specifically, we focused on the modulation of PECs activation by de novo production of CD44 and the preservation of podocyte loss.

Method: We evaluated the role of the CSF-1/CSF-1R axis as a driver of glomerular damage in FSGS in adriamycin-induced nephropathy (ADR) in mice, the main experimental model to study human FSGS. To this end, we treated or not ADR-animals with CSF-1R specific inhibitors, GW2580 or Ki20227 (n = 5-7 group). We determined the expression and localization of CSF-1R in the glomerulus in tissue by triple immunofluorescence (WT-1, SSChCs and CSF-1R) and their relevance in glomerulosclerosis (PAS and pro-fibrotic genes). The determination of de novo CD44 formation and its correlation with ERK1/2 pathway by immunohistochemistry (IH). We detected podocyte in the glomerulus by WT-1 IH and the localization of aPESCs in the glomerular tuft by Claudin-1 and SSChCs markers. Finally, we used
isolated human kidney progenitor cells with and without CSF-1 treatment (n = 6/group) to identify potential key interactors of CSF-1 by RNAseq. We validated genes of interest in the FSGS experimental model. 

Results: We observed a constitutively expression of CSF-1R in the glomerulus of control mice that significantly increased in ADR-treated mice, specifically in podocytes (WT1) and pECs (SSeCks), confirmed with mRNA expression. ADR-treated mice showed important events of sclerotic glomerulus and profibrotic genes as collagen that was significantly reversed by the treatment with CSF-1R inhibitors (p < 0.001). Results reflected a CSF-1R inhibitor-dependent renal function recovery with the use of the inhibitors with a reduction of proteinuria and an increase of glomerular filtration rate (p < 0.001). We found a positive CD44 staining both in Bowman’s capsule and inner the tuff of ADR-treated mice, accompanied by an increase of ERK1/2 activation. CSF-1R inhibitors significantly reduced the percentage of glomeruli with de novo CD44 production. Remarkably, podocyte depletion was also preserved with very similar levels to non-treated animals (p < 0.001). For RNAseq results, 227 differentially expressed genes (considering a criterion of a probability of differential expression >0.9 and a [M] > 1) were subjected to enrichment analysis. The top significant gene ontology terms were mainly involved with interferon-induced genes. Genes involved in this pathway were validated in the FSGS model, showing an increase in mice treated with ADR compared to controls and alleviated with CSF-1R inhibitors (p < 0.001). 

Conclusion: In this study we propose a novel therapeutic strategy for FSGS-associated pathology based on the inhibition of CSF1-R activity having an impact on reducing aPECs, glomerulosclerosis, proteinuria, improving renal function and preserving the podocyte-progenitor phenotype, thus, in podocyte preservation against damage.

#6669

ANALYSIS OF KIDNEY BIOPSIES AND URINE SEDIMENT USING SCANNING ELECTRON MICROSCOPY (SEM) AND ATOMIC FORCE MICROSCOPY (AFM)

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Background and Aims: The classification of renal diseases is dependent on the evaluation of kidney biopsies using light microscopy techniques. Ultrastructural details (e.g. podocyte foot processes, amyloid fibrils, Fabri’s intracellular inclusions) need transmission electron microscopy (TEM) which has high costs, requires specialized personnel and is time consuming. Therefore, alternative techniques are highly desirable. Here we report our experience with scanning electron microscopy (SEM) and atomic force microscopy (AFM).

Method: Paraffin-embedded kidney sections (3 μm thick) were examined after dewaxing and Jones-methenamine methane staining for type IV collagen fibers. Dried urine sediments were prepared using standard methods for urine cytological analysis. Analysis was then performed using atomic force microscopy (nGauge system) on dried specimens and with Scanning Electron Microscopy (Zeiss) after gold-sputtering of the surface. Reference images were obtained by standard microscopy.

Results: The combination of SEM and thin paraffin sections allows the observation of ultrastructural details in kidney biopsies with a very simple and fast preparation. AFM is even faster than SEM, as it does not require any preparation of the surface of the sample. An important advantage of SEM is the possibility to view the sample at low magnification, which makes it easier to identify the location of the glomeruli. It is thus possible to switch from small magnifications (100x) to very extreme magnifications (100000x). Notably, the interpretation of the images requires knowledge of the artifacts induced by paraffin inclusion. Specifically, structures and cells containing lipids (for example foamy cells) appear empty. Chromatin is also condensed in the nuclei around the periphery of the nucleus and in spike structures whith large empty areas. The recognition of nuclei in SEM and AFM is important for the subsequent interpretation of the images. Podocyte pedicles fusion can be identified relatively easily in SEM and in AFM. Both techniques add relevant ultrastructural details of urine sediment cells, from epithelial cells to isolated tubular cells. Also, casts show many ultrastructural features which are not evident in classical optical microscopy. It is also possible to measure the thickness of the basement membrane with great precision both in SEM and with AFM. The major limitation of this approach is the limited experience of pathologists with these methods and the absence of an atlas of normal and pathological kidney.

Conclusion: Considering the affordable costs of SEM and AFM instruments and the simple preparation of samples for their analysis, these should be considered a valid alternative to TEM. SEM and AFM are alternative methods, simple and relatively cheap and very fast to obtain ultrastructural details of renal biopsies. We thank ANED and AST for the great support given to research.
AUTOMATIC SEGMENTATION OF GLOMERULAR SUBSTRUCTURES BY DEEP LEARNING
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Background and Aims: Electron microscopy (EM) complements light microscopy (LM) evaluation of the kidney biopsy. Foot process effacement, as assessed by EM, helps in diagnosing podocytopathies. However, human interpretation of EM images is time-intensive and often subjective. In this pilot, we investigate how deep learning techniques can help in adequate segmentation of the glomerular basement membranes (GBM) and podocytes in EM images. The ultimate goal would be to design an automatic tool for reliable and fast assessment of foot process effacement.

Method: Podocytes and glomerular basement membranes (GBM) of 10 patients, 5 with podocyte disease and 5 without glomerular changes (where biopsy showed tubulointerstitial pathology on LM) were annotated with a combination of manual annotation and thresholding for providing ground truth. After data preprocessing including splitting, flipping, rotating and tiling, a modified U-net architecture was applied ("baseline model"). This baseline model was compared to a combination of U-net and a self-supervised contrastive learning approach with pretraining on 100 additional images (SimCLR framework, "fine-tuned model"). Segmentation performance was measured by IoU score.

Results: Segmentation of the glomerular basement membrane was best achieved by the baseline model and resulted in an IoU score of 0.711±0.089 compared to a IoU score of 0.675±0.093 in the fine-tuned model. Segmentation of the podocytes was most successful in the fine-tuned model, with a IoU score of 0.609±0.118 compared to a IoU score of 0.591±0.118 in the baseline model.

Conclusion: This study pioneers in segmenting glomerular substructures on EM images by means of a modified U-net architecture. The next step is training and validation in larger datasets. Data annotation remains a challenge. Inclusion of more images is expected to greatly improve the performance of the model.

Guideline 1500-3600 characters

Figure 1: Example of image and corresponding masks where the finetuned model performs better than the baseline model (higher podocyte IoU scores, similar GBM IoU score).
SLC34A2 EXACERBATES TUBULAR INTERSTITIAL FIBROSIS VIA INDUCTION OF APOPTOSIS AND CELL CYCLE ARREST IN S PHASE

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Background and Aims: Chronic kidney disease (CKD) is an urgent public health issue in the world. However, effective treatments for intervention of CKD remain undefined. Phosphate (Pi) is an essential element for synthesis of DNA, RNA, ATP, phospholipid membranes, and for regulation of phosphor- ylation/dephosphorylation, cellular signaling and metabolic pathways. Solute carrier family 34 (SLC34) is responsible for Pi absorption in the small intestine. The role of SLC34 in progression of CKD is still unknown.

Method: A membrane protein, solute carrier family 34 member 2 (SLC34A2), was discovered by using big data mining from the National Center for Biotechnology Information (NCBI). SLC34A2 was overexpressed in human proximal tubular cells, HK-2, by Lipofectamine 3000. RNA sequencing was carried out to uncover SLC34A2-mediated signaling pathways by using Illumina platform. Apoptosis was evaluated by Annexin V-PI staining and TUNEL assay in cells and mouse kidneys, respectively. Cell cycle was measured by flow cytometry. Unilateral ureteral obstruction (UUO) and bilateral renal ischemia-reperfusion injury (bIRI) were employed to generate CKD mouse models.

Results: By using big data mining from the NCBI, we identified a membrane protein, SLC34A2, was upregulated in various types of nephropathies including diabetic nephropathy, focal segmental glomerulosclerosis, minimal change disease, ANCA-associated vasculitis. Overexpression of SLC34A2 suppressed viability of HK-2 cells. RNA sequencing revealed that apoptosis and cell cycle are high scored pathways modulated by SLC34A2. The results were further verified in HK-2 cells. Ectopic SLC34A2 promoted apoptosis via downregulation of BCL-2. Moreover, SLC34A2 induced cell cycle arrest in S phase via downregulation of CDK2. CKD mouse models of UUO and bIRI were carried out to confirm in vitro findings. In mice kidneys, the expression of Slc34a2 in UUO and bIRI groups was superior to that in sham groups. Enriched Bax and TUNEL-positive cells were observed in the fibrotic kidneys of mice. Moreover, increased expression of p21 and downregulated Cyclin A2 in the fibrotic kidneys further confirmed that Slc34a2 induced cell cycle arrest in S phase.

Conclusion: Slc34a2 induced apoptosis and halted cell cycle in S phase, resulting in subsequent tubulointerstitial fibrosis in mice. Our results suggest that targeting SLC34A2 might be a promising strategy for intervention of CKD.

Figure 1:

SINGLE-CELL RNA SEQUENCING REVEALS THE MOLECULAR CHARACTERISTIC OF IGA-MCD

Junli Wan, Liping Peng, Qilin Chen, Huimin Jiang, Xiaojian Feng and Qiu Li

P.R. China

Background and Aims: IgA nephropathy (IgAN) is the most common primary glomerular disease in children and adolescents worldwide, and is one of the major causes of end-stage renal disease in China. Minimal change disease (MCD) is the most common pathological type of nephrotic syndrome in children. In some rare cases, the renal pathology of these patient has IgA deposits in the mesangial regions and diffuse fusion of podocyte foot process, which is called IgA-MCD. Previous studies have analyzed the characteristics of IgA-MCD from the aspects of clinical manifestations, pathological features, therapeutic response and prognosis, but the molecular mechanism of its occurrence and development has not been clarified. For the first time, single-cell transcriptome sequencing technology was used to compare IgA-MCD, IgAN and MCD, in order to describe the unique molecular characteristics of IgA-MCD and elucidate the molecular mechanism related to clinical manifestations. It lays the foundation for formulating more appropriate treatment plan and improving prognosis.

Method: Renal fine-needle puncture tissues were collected from 3 children with IgAN, 4 children with MCD, and 1 child with IgA-MCD in Children's Hospital of Chongqing Medical University, and adjacent normal tissues were collected from 1 child with renal tumor as control group. Children in the three disease groups had clinical manifestations of nephrotic syndrome, and nephrotic-level proteinuria at the time of sampling. High-throughput, unbiased single-cell transcriptome sequencing was performed on the above renal tissue samples, and the sequencing results were systematically compared and analyzed.

Results: By analyzing single-cell sequencing data, we systematically described single-cell transcriptome cell maps of renal tissues form children with nephrotic-level albuminuria with different pathologic types (IgAN, MCD, IgA-MCD). Twelve cell types, such as mesenchymal cells and podocytes, were defined by classical marker genes. By comparing the constituent ratio of renal cells and PC analysis of cell subsets in the control group and the three disease groups, it was found that IgA-MCD was closer to MCD. By comparing the differential genes of the three disease groups with those of the control group, we found that the number of differential genes in IgAN's podocytes was significantly higher than that in the other two groups. Compared with the control group, HMGCS2 was significantly up-regulated in IgA-MCD, and cellular energy metabolism was enhanced. Through pairwise comparison among the three disease groups, it was found that there was no significant difference in genes in podocytes between IgA-MCD and MCD. Compared with IgAN, CXCL12 gene expression in IgA-MCD is significantly up-regulated, and CXCL12 can recruit immune cells and lead to cell damage.

Conclusion: The overall transcription profile of IgA-MCD is more similar to that of MCD. CXCL12 was specifically highly expressed in the podocytes of IgA-MCD, which may be used as a marker molecule for functional changes of IgA-MCD podocyte. IgA-MCD mesenchymal cells were significantly different from those in the other two disease groups. The significant up-regulation of CD81 may be a molecular signal that leads to the activation, proliferation, and secretion of more extracellular matrix of IgAN-MCD glomerular mesenchymal cells. We analyzed the associations and differences among IgAN, MCD and IgA-MCD at the single-cell transcriptome level, which provided a new perspective and insight for the follow-up study of the pathogenesis of the diseases.
We designed a pilot study in paraffin-embedded kidney tissue (FFPE) from LN patients to evaluate differences between gene expression at diagnosis (kidney biopsy diagnosis) and 2 years after achieve a complete renal response (protocol kidney biopsy). We evaluated if transcriptome analysis results could be verified through immunofluorescence staining (IF) in kidney biopsies (diagnosis biopsy vs protocol biopsy).

Method: We included diagnosis and protocol biopsies from 16 LN patients with class III and/or IV. All patients received prednisone (0.5 mg/kg) plus mycophenolic acid. Complete renal remission was defined as normal renal function, uPCR < 300 mg/gr and inactive urine sediment. RNA-Seq (RNA-Seq) was performed in FFPE, Human MSigDB Collections were used for gene enrichment analysis and Gene sets derived from the Biological Process (RNA-Seq) was performed in FFPE, Human MSigDB Collections were used for gene enrichment analysis and Gene sets derived from the Biological Process

Results: 16 LN patients were included, Class III (43.8%), Class IV (43.8%) and Mixed Class (12.5%). 100% patients were women and Caucasian with mean age 40.9±7.1 years. RNA-Seq showed 2 overexpressed groups of genes (GO) in diagnosis biopsies, expression of this GO was not detected in protocol biopsies: GO-Complement_activation (NES 2.26, p = 4.2E-0.5): Properdin, Ficolin, C3, Factor B, C3AR1, C4 y CDC59.

GO-Humoral_Immune_Response_Mediated_Circulating_Immunoglobulin (NES 2.10, p = 7.6E-0.6): IgG1, IgG2, IgA, chemokine receptors 2 y 7 and receptor 13 TNF.

Results were verified using IF staining in kidney biopsies, in protocol biopsies were observed a significant reduction in C1q and C3 complement proteins staining: C1q (78% vs 22.2%, p = 0.006), C3 (73.3% vs 27.8%, p = 0.005); results in immunoglobulins staining also agree with transcriptome analysis results, so that we observed significant reduction in IgA and IgG: IgG (69% vs 36.4%, p = 0.009) and IgA (83.3% vs 16.7%, p = 0.02) while IgM staining not showed differences between diagnosis biopsy and protocol biopsy (43.8% vs 45.5%).

Conclusion: Transcriptome analysis in kidney tissue from LN patients, identified complement proteins and humoral mediators overexpressed at LN diagnosis and infraexpressed at complete renal remission; the results could help nephrologist to investigate the role of these protein as LN biomarkers.

#5492

TRANSCRIPTOME ANALYSIS IN LUPUS NEPHRITIS: DIFFERENCES IN GENE EXPRESSION BETWEEN DIAGNOSIS AND RENAL REMISSION IN KIDNEY TISSUE

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Background and Aims: Transcriptome analysis in kidney tissue from lupus nephritis patients (LN) provide useful information about gene expression. We designed a pilot study in paraffin-embedded kidney tissue (FFPE) from LN patients to evaluate differences between gene expression at diagnosis (kidney biopsy diagnosis) and 2 years after achieve a complete renal response (protocol kidney biopsy). We evaluated if transcriptome analysis results could be verified through immunofluorescence staining (IF) in kidney biopsies (diagnosis biopsy vs protocol biopsy).

Method: We included diagnosis and protocol biopsies from 16 LN patients with class III and/or IV. All patients received prednisone (0.5 mg/kg) plus mycophenolic acid. Complete renal remission was defined as normal renal function, uPCR < 300 mg/gr and inactive urine sediment. RNA-Seq (RNA-Seq) was performed in FFPE, Human MSigDB Collections were used for gene enrichment analysis and Gene sets derived from the Biological Process

Results: 16 LN patients were included, Class III (43.8%), Class IV (43.8%) and Mixed Class (12.5%). 100% patients were women and Caucasian with mean age 40.9±7.1 years. RNA-Seq showed 2 overexpressed groups of genes (GO) in diagnosis biopsies, expression of this GO was not detected in protocol biopsies: GO-Complement_activation (NES 2.26, p = 4.2E-0.5): Properdin, Ficolin, C3, Factor B, C3AR1, C4 y CDC59.

GO-Humoral_Immune_Response_Mediated_Circulating_Immunoglobulin (NES 2.10, p = 7.6E-0.6): IgG1, IgG2, IgA, chemokine receptors 2 y 7 and receptor 13 TNF.

Results were verified using IF staining in kidney biopsies, in protocol biopsies were observed a significant reduction in C1q and C3 complement proteins staining: C1q (78% vs 22.2%, p = 0.006), C3 (73.3% vs 27.8%, p = 0.005); results in immunoglobulins staining also agree with transcriptome analysis results, so that we observed significant reduction in IgA and IgG: IgG (69% vs 36.4%, p = 0.009) and IgA (83.3% vs 16.7%, p = 0.02) while IgM staining not showed differences between diagnosis biopsy and protocol biopsy (43.8% vs 45.5%).

Conclusion: Transcriptome analysis in kidney tissue from LN patients, identified complement proteins and humoral mediators overexpressed at LN diagnosis and infraexpressed at complete renal remission; the results could help nephrologist to investigate the role of these protein as LN biomarkers.

#6541

GLOMERULONEPHRITIS DIAGNOSIS BY MACHINE LEARNING ON PERIODIC ACID-SCHIFF (PAS) WHOLE SLIDE IMAGES

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Background and Aims: Machine learning (ML) holds great promise for improving diagnostics, prognostication and theranostics in nephropathology. So far, applications have not gone much further than segmentation of tissue compartments on whole slide images (WSIs) of paraffin sections. As a proof-of-concept study, we describe the development of a diagnostic classifier for glomerulopathies based on expert-annotated or automatically segmented glomerular transactions from periodic-acid Schiff (PAS) paraffin sections only.

Method: A total of n = 350 biopsies from 5 institutions with 12 classes of glomerulonephritis IgA nephropathy (IgAN), membranous nephaso-phy (Membranous), anti-glomerular basement membrane antibody GN (ABMGN), infection-associated GN (IAGN), ANCA-associated GN (ANCA- GN), idiopathic membranoproliferative GN (MPGN), SLE GN class IV (SLE-GN-IV), cryoglobulinemic GN (CryoGN), C3 GN (C3-GN), dense deposit disease (DDD), fibrillar GN (FibrillarGN) and proliferative GN with monoclonal immunoglobulin deposits (PGNMID) were included in the study with their respective PAS sections. Glomerular transactions were expert-annotated by a nephropathologist and automatically segmented with...
our own transformer-based segmentation model trained on 100 biopsies with thrombotic microangiopathies and a range of vascular, vasculitic and glomerular diseases closely resembling/mimicking thrombotic microangiopathies. For classification, we divided the cohort into 5 folds for internal cross-validation, performed sample size augmentation with various methods (including shifts in resolution/scale, AutoAugment and others) and trained our proprietary self-attention-based MILx architecture on an EfficientNet backbone with selection of glomerular crop batches by soft Markov chain Monte Carlo sampling in a semi-supervised fashion, with diagnostic class labels for each biopsy. We compared the performance of our proprietary architecture on both expert-annotated and automatically segmented glomerular crops with a recently published benchmark architecture (CLAM) for multiple-instance learning in histopathology.

**Results:** Automatic glomerular segmentation performance was excellent with mean AUC and sensitivity (mean average recall) over all classes at 0.904, with near perfect mean average specificity (0.994), as expected best for Membranous, worst for ABMGN. Classification performance of MILx with expert-annotated glomerular crops as inputs had a mean balanced accuracy of 0.84, with AUC metrics in descending order of 0.97 for Membranous, 0.89 for ABMGN, 0.88 for IgAN, 0.86 for Fibrillar, 0.83 for MPGN, 0.80 for ANCA-GN, 0.79 for DDD, 0.78 for PGN MID, 0.75 for IAGN, 0.73 for SLE-GN-IV and CryoGN. Performance with MILx was similar for automatically segmented glomerular crops as inputs. On this dataset, MILx outperformed CLAM with both entire WSIs as well as expert-annotated glomerular crops as inputs (mean balanced accuracy of 0.72) by a significant margin.

**Conclusion:** This proof-of-concept study indicates that nephropathology-specific architectures like our MILx can be trained for complex tasks on relatively small biopsy cohorts. We should be able to deliver an end-to-end-pipeline for this diagnostic and other tasks based on training sets with case-labels provided by trusted institutions with only minimal expert labeling or annotation required.

**PAC and HQ contributed equally to this work.**

#4825

**AUTOGRAPHY REGULATES TUBULAR CELL SENESCENCE IN DIABETIC KIDNEY DISEASE**

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**Background and Aims:** Cellular senescence commonly occurs in innate renal cells of diabetic kidney disease (DKD) and autophagy may be implicated. However, the characteristics of senescent cells in different pathological stages of DKD, and the driving force behind the cell senescence remain primarily unknown. This study aimed to examine kidney cellular senescence and its relationship to renal function in DKD and the effect of autophagy on high-glucose-induced cellular senescence.

**Method:** According to the DKD pathologic type, 46 patients diagnosed with renal biopsy were categorized into I IIa IIb III IV classes. The other four normal kidney specimens taken from patients with renal trauma were as the control group. Pathological changes in kidney tissues were detected by PAS staining, and the expressions of autophagy-related protein LC3 and senescence marker p21 were demonstrated by immunohistochemical staining. DKD rats were established by intraperitoneal injection with streptozotocin (STZ). HK-2 cells were cultured with 35mM glucose with or without autophagy inhibitor (3-methyladenine, 3-MA) and lysosomal inhibitor (chloroquine CQ). Immunohistochemistry and Western Blot were used to detect the expression of the senescence markers p53 and p21, as well as the autophagy-related proteins LC3 and p62. The electron microscopy technique was used to observe the number of autophagosomes in the DKD rats and each group of HK-2 cells.

**Results:** (1) In renal tissues of DKD patients, p21 infiltrated the interstitium and tubules, while LC3 was primarily expressed in the tubules. Both p21 and LC3 expression increased over time as the disease progressed (P < 0.05) and were directly proportional to blood creatinine and proteinuria, respectively. Additionally, p21 and LC3 expression were positively correlated. (2) Compared with the control group, the renal tissue of DKD rats displayed higher levels of p21, p53, LC3, and p62 expression (P < 0.05), higher levels of renal tubular autophagosomes, and increased co-expression of p21 and LC3 (P < 0.05). (3) HK-2 cells treated with high glucose exhibited increased expression of p21, p53, p62 and LC3, as well as the number of autophagosomes (P < 0.05). (4) 3-MA reduced p21 and p53 expression compared to the high glucose group (P < 0.05), whereas the opposite trend was observed in the CQ treatment (P < 0.05). **Conclusion:** Renal tubular cell senescence is closely associated with DKD progression. Autophagic flow may be involved in high glucose-induced renal tubular cell senescence.
Table 1: Parameters of the experimental groups of rats.

<table>
<thead>
<tr>
<th></th>
<th>BG (mmol/L)</th>
<th>KW/BW (mg/g)</th>
<th>Scr (μmol/L)</th>
<th>BUN (mmol/L)</th>
<th>Proteinuria (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td>6.16±0.16</td>
<td>3.01±0.42</td>
<td>31.57±7.47</td>
<td>6.18±1.14</td>
<td>331.46±24.39</td>
</tr>
<tr>
<td>DKD</td>
<td>31.35±3.01*</td>
<td>5.73±0.51*</td>
<td>51.38±7.64*</td>
<td>18.31±3.25*</td>
<td>409.16±23.27*</td>
</tr>
</tbody>
</table>

BG: blood glucose; KW/BW: kidney weight/body weight; Scr: serum creatinine; BUN: blood urea nitrogen. Dates are presented as mean±SD (n = 8). *P<0.05 vs NC.
Background and Aims: The transforming growth factor-β1 (TGF-β1) is a pleiotropic cytokine, with distinct roles both in fibrosis and inflammation and acts through the Smad signalling in renal injury. We sought the expression of TGF-β1/Smads signalling in ANCA associated glomerulonephritis (AAGN) and we assessed this expression in correlation with the renal injury at diagnosis as well as the renal progression.

Method: We evaluated the immunohistochemical expression of TGF-β1, phosphorylated Smad3 (pSmad3) and Smad7 semi-quantitatively and quantitatively using computerized image analysis program in different compartments of 11 renal biopsies with AAGN and the results were statistically analysed with clinicopathological parameters. We also used healthy controls and disease controls with other types of Glomerulonephritis (GN).

Results: The expression of TGF-β1, pSmad3 and Smad7 were higher in AAGN, compared to healthy controls and other types of GN. The glomerular pSmad3 presented preferable expression at mesangial and endothelial cells and its intensity was correlated with higher chronicity index [global glomerulosclerosis (p<0.001) and interstitial fibrosis (p = 0.03)] (Figure 1). We also reported that the intensity of Smad7 was correlated with higher activity index [cellular crescents (p = 0.03), and fibroid necrosis (p<0.001)] (Figure 2). TGF-β1 expressed at peritubular capillaries around the areas of tubulitis and its expression was correlated with more severe renal injury at diagnosis [higher creatinine (p = 0.019) and proteinuria (p = 0.008)]. At last follow-up (median time 5 years) we reported a significant worst renal function with higher intensity pSmad3 (p = 0.05) and TGF-β1 (p = 0.005), while the expression of Smad7 tended to be beneficial in the maintenance of eGFR (p = 0.055).

Conclusion: The TGF-β1/Smad signalling is activated in AAGN and its expression is correlated with renal injury both at diagnosis and renal progression.

Figure 1: ANCA-associated glomerulonephritis (arrows indicating the positive immunostaining) pSmad3 staining in periglomerular inflammatory cells (original magnification x200).

Figure 2: ANCA-associated glomerulonephritis (arrows indicating the positive immunostaining), Smad7 staining in interstitial inflammatory cells (original magnification x200), Snapshot from image analysis.
INHIBITION OF THE STING PATHWAY AMELIORATES EXPERIMENTAL CRESCENTIC GLOMERULONEPHRITIS
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Background and Aims: Rapidly progressive glomerulonephritis/crescentic glomerulonephritis (RPGN/cGN) may compromise renal function in the short or medium term thus evolving into acute kidney injury (AKI) or chronic kidney disease. Innate and adaptive immune responses are placed at the epicentre of cGN. However, molecular pathways involved in the activation of these responses are by far less known. Sting is an innate immune DNA-sensing involved in promoting kidney injury and fibrosis with unknown participation in RPGN/cGN.

Method: We investigated whether Sting pathway activation contributes to the development and progression of RPGN/cGN in a preclinical model of nephrotic nephritis (NTN) induced by an anti-glomerular basal membrane serum. Sting expression as well as humoral and cellular innate immune responses, histological injury and functional responses in the kidney were studied in wild-type and Sting−/− mice.

Results: Sting was found expressed at higher gene and protein levels and located in tubulointerstitial and intraglomerular and periglomerular areas and tubules in kidneys from NTN wild-type mice compared to non-diseased control animals. Sting deficiency significantly decreased NTN-induced cytokine/chemokine synthesis and hence the intrarenal transit of diseased control animals. Sting deficiency significantly decreased NTN-areas and tubules in kidneys from NTN wild-type mice compared to non- and located in tubulointerstitial and periglomerular

TUNEL-positive dead cells was also significantly reduced in Sting−/− mice. Consistent with these findings, Sting absence significantly diminished NTN-increased urea and creatinine plasma levels.

Conclusion: Sting inhibition positively impacted several well-characterized cGN-associated pathogenic events thus ameliorating the outcomes of the disease. These results identified Sting antagonism as a potential therapy to help combat cGN.

Figure 1: A and B.

#3624

RENALE HISTOPATHOLOGICAL SCORING OF AMYLOID DEPOSITS PREDICTS RENAL AND OVERALL PROGNOSIS IN LIGHT-CHAIN (AL) AMYLOIDOSIS: A MULTICENTRE STUDY
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Background and Aims: Renal involvement is common in light-chain (AL) amyloidosis (60%-80% cases). To date, renal biopsy is not recommended as a routine examination in patients with AL amyloidosis and renal involvement. However, renal histology can have an important prognostic role. Amyloid load, representing the quantification of amyloid deposits into the kidney, might be linked to both systemic disease severity and temporal exposure to amyloid deposition in different organs. We proposed an amyloid load scoring system in order to predict renal and overall survival in patients with AL amyloidosis.

Method: We retrospectively collected AL cases who underwent to renal biopsy from 17 Italian Institutions. The primary composite outcome includes time to death and time to end-stage kidney disease development. We applied an Amyloid load score characterized by a semiquantitative evaluation for amyloid deposition in glomeruli, interstitium, and vessels. Each lesion was scored from 1 to 3. The sum of damage (0–9) associated with amyloid deposition was calculated, indicating total numeric codes of renal pathologic damage.

Results: Between 2008 to 2022, we recruited 162 patients. Their median age at diagnosis was 66.5 (±10) years, serum creatinine was 1.95 (±1.92) mg/dl and proteinuria was 5.4 (±4.6) grams per 24hr. After a median follow-up of 4.1 (±3.6) years and a 6-month landmark analysis, the primary composite outcome was achieved by 46/122 (38%) patients. Seventy-eight patients (60%) experienced a hematologic response, classified as a complete response or very good partial response, while 49 (37.4%) patients obtained a renal response. Among them, 39 (80%) patients had an amyloid score ≤4 and only 4 had an amyloid score> 5. Higher values of Amyloid load score, as an expression of amyloid load linked to both disease severity and temporal exposure, were significantly associated with an increased risk of end-stage kidney disease (ESKD) (log rank 12.80, p = 0.005) (Figure 1A) and death (log rank 44.97, p<0.0001) (Figure 1B). Interestingly, 6/162 (3.7%) patients had a negative Congo red stain in renal biopsy (AL amyloidosis diagnosis through an abdominal fat pad aspiration plus monoclonal restriction at immunofluorescence staining or amyloid fibrils detected by electron microscopy). Moreover, 49/156 (31.4%) patients did not show a monotypic (kappa or lambda) immunofluorescence staining. Despite the widely accepted clinical definition of renal amyloidosis is “more than 0.5 g/24hr of non-Bence Jones proteinuria in presence of a positive fat pad aspiration”, 8/162 (4.9%) patients with a biopsy-proven renal AL amyloidosis showed less than 0.5 g/24hr of non-Bence Jones proteinuria. AL amyloidosis showed to overlap in 14/153 (9.2%) patients with other Monoclonal gammopathy of renal significance (MGGRS), such as LCD (4 cases), C3 nephropathy (4 cases), light-chain proximal tubulopathy (2 cases), light chain-related tubulointerstitial nephritis (2 cases), cast nephropathy (1 case), type 1 cryoglobulinemia (1 case).

Conclusion: Renal histopathological scoring of amyloid deposits is crucial to assess disease progression in patients with AL amyloidosis, and in particular a score ≥5 identifies patients at greater risk of evolution of renal damage and mortality. If these data were also confirmed in a larger independent cohort, they could support the use of renal biopsy as an essential prognostic (as well as diagnostic) tool to be included as a routine investigation in all patients with suspected AL amyloidosis.

Abstracts
#6891
MACHINE LEARNING NEPHROPATHY DIAGNOSTICS OF THROMBOTIC MICROANGIOPATHIES
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Background and Aims: Thrombotic microangiopathies, comprising atypical hemolytic uremic syndrome (aHUS) and other diseases, can present with a broad clinical and histopathological spectrum. On our way to an evidence-base for the nephropathological work-up of TMA, we have chosen a machine-learning approach, thus eliminating suboptimal reproducibility of descriptors for individual lesions in the three decisive compartments artery, arteriole and glomerulus with human experts. Here, we present our results for an end-to-end diagnostic system.

Method: We collected 50 random biopsies with TMA s of various etiologies (including aHUS, hypertension-associated, systemic sclerosis, anti-phospholipid antibody syndrome and others) and 50 biopsies with Mimickers (diagnostic differences of TMA), including severe hypertensive nephropathy, necrotizing arteritis/arteriolitis, cryoglobulinemic vasculitis from the three participating centers Cologne, Well-Cornell Medical Center, and Turin. Whole slide images (WSIs) from all four nephropathology stainings HE, PAS, trichrome and Jones were included in this study. We developed an instance segmentation Mask-RCNN model with a Swin Transformer (t) backbone on tissue crops detected using a lightweight variant of the U-Net segmentation architecture. For the classification model we used our own MorphSet segmentation crops entered in three separate compartment channels. Batches were chosen with Monte Carlo sampling or using our own soft Markov Chain Monte Carlo (MCMC) approach. Results of the classification model are reported with 5-fold internal cross-validation.

Results: Segmentation performance measured as mIOU, mAP, mAR, mF1, mAS for artery reached 0.565, 0.739, 0.679, 0.704, 0.995, for arteriole 0.342, 0.531, 0.488, 0.490, 0.996, for glomeruli 0.818, 0.880, 0.919, 0.986, 0.993. Classification accuracy reached 90% with no false positives for TMA. Missed cases of TMA could be Salvaged by an experienced nephropathologist on the display of decisive compartment crops, which were selected using model confidence averaged across each sampling iteration.

Conclusion: We have designed and trained architectures capable of segmenting decisive compartments and diagnosing TMA s on renal biopsy sections. This will enable automatic analysis of clinicopathological datasets with TMA in large cohorts. Our ultimate goal is to use large cohorts from collaborating institutions for weakly supervised, case-level-annotated training of diagnostic, prognostic and theranostic classifiers.

#4952
CLINICOPATHOLOGIC CORRELATIONS OF URINARY PROTEOMIC AND METABOLIC ANALYSIS IN PATIENTS WITH RENAL AA AMYLOIDOSIS AND MEMBRANOUS NEPHROPATHY
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1Hacettepe University Hospital, Internal Medicine, Ankara, Turkey, 2Hacettepe University Hospital, Nephrology, Ankara, Turkey, 3Hacettepe University Graduate School of Health Sciences, Bioinformatics, Ankara, Turkey, 4Koc University College of Sciences, Molecular Biology and Genetics, Istanbul, Turkey, 5Hacettepe University Faculty of Pharmacy, Analytical Chemistry, Ankara, Turkey, 6Hacettepe University Hospital, Pathology, Ankara, Turkey and 7Hacettepe University Hospital, Biochemistry, Ankara, Turkey

Background and Aims: AA Amyloidosis is a multisystemic amyloidosis subtype that develops on the background of various chronic inflammatory etiologies. Urinary omics studies have become a promising tool for elucidating pathophysiology and prognosis of glomerular diseases. However, no urinary omics analysis has been performed focusing on renal AA amyloidosis in literature to the best of our knowledge. Our main aim in this study is to perform a comparative urine proteomic and metabolomic analysis of recently diagnosed renal AA amyloidosis and to investigate the correlation of bioinformatic results with clinical and pathological data.

Method: Urine samples of 8 recently diagnosed AA amyloidosis (AA), 8 membranous nephropathy (MN) and 6 healthy control group patients were collected before kidney biopsy procedure. Proteomic analyzes were performed with nLC-Q-TOF MS/MS and metabolomic analyzes were performed by GC/MS in all patients. Biopsy specimens were scored according to glomerulonephrosclerosis (G), tubular atrophy (TA) and interstitial fibrosis (IF) grades by two pathologists. Raw spectroscopic data was analyzed using MaxQuant and M$^3$-DIAL programs for proteomic and metabolomic studies, respectively. Statistical analysis of the differences in molecules between study groups were performed with ANOVA and HSD-Tukey tests. Principal component (PCA) and heatmap analyzes were made in R language, while gene ontology (GO), network and functional enrichment analysis of bioinformatic results were performed with PANTHER, STRING and MetaboAnalyst databases.

Results: In comparison between AA and MN groups, median eGFR values tend to be lower in the AA group (67.6 vs 112 ml/min/1.73 m² respectively, p = 0.08). Median 24-hour urine protein levels did not show statistically significant difference (9499 vs 9512 mg/day respectively, p = 0.9). Percentage of patients with moderate/severe IF/TA was higher and G score was tend to be in AA group compared to MN group (p values 0.02 and 0.07 for IF/TA and G scores, respectively). As a result of proteomic analysis, a total of 859 proteins were determined. Statistical analysis showed 51 proteins that were significantly differ in AA group compared to the control group. GO and functional enrichment analyzes showed that statistically most significant sub-domains were mainly related with cell-cell adhesion (Figure 1 & 2). In comparative analysis between AA and MN patients, uronodulin (UMOD) was lower in the AA group than in the MN group (logFC -3.37), whereas ribonuclease 1 (RNASE1) and α-1-microglobulin/bikunin precursor protein (AMBP) were higher in the AA group (logFC 3.41 and 3.07, respectively). In Spearman correlation analyzes, significant negative correlations were demonstrated between UMOD-proteinuria (r = -0.48, p = 0.03) and between AMBP-eGFR (r = -0.69, p = 0.003) variables. Metabolomic analysis showed 9 metabolites that were significantly different between AA and other study groups. Myo-inositol and urate were higher in AA group compared to MN group, while D-mannitol and N-acetylglycaramate were higher in AA group compared to the control group. Significant positive correlation independent of GFR was detected between RNASE1 and urate (r = 0.63, p = 0.01).

Conclusion: Our study is the first urinary comparative omics analysis performed on renal AA amyloidosis patients to the best of our knowledge. We demonstrated specific protein and metabolites that distinguish AA group from the control and MN groups. Enrichment and GO analyzes between AA and the control group showed a negative enrichment in cell-cell adhesion related sub-domains, suggesting a possible increased urinary shear stress resulting in downregulation of catheders in AA amyloidosis. In comparative analysis between AA and MN groups, UMOD and AMBP proteins and myo-inositol were thought to be associated with high tubulointerstitial damage, whereas RNASE1 and urate were believed to be related with systemic inflammation and endothelial damage [1].

REFERENCE
Figure 1. The analyses were performed using STRING online software with a medium confidence level (0.4), providing the significantly enriched GO terms and Reactome pathways. The vertical axis displays the significantly enriched biological functions. The horizontal axis indicates the strength of enrichment, which is the log10 (observed/expected proteins in the network that are annotated with a term). The higher the absolute value of the strength, the stronger the impact.
EFFECT OF DIET ON THE COLLECTOR DUCT BEHAVIOUR: RELEVANCE IN PRECLINICAL DRUG DEVELOPMENT

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¹Complutense University of Madrid, School of Medicine, Madrid, Spain, ²Hospital Universitario Infanta Elena, Gastroenterology and Hepatology, Valdemoro, Spain, ³Instituto de Investigación Sanitaria Gregorio Marañón, Renal Physiopathology Laboratory, Department of Nephrology, Madrid, Spain and ⁴Gregorio Marañón General University Hospital, Internal Medicine, Madrid, Spain

Background and Aims: Drug induced syndrome of inadequate antidiuretic hormone secretion (SIADH) is a common problem in clinical practice. Early detection of this side effect at a preclinical level would improve safety and efficiency. We investigate the role of different diets in preclinical detection of SIADH.

Method: Animals were divided into two groups (n = 4 each), one receiving standard pellet based diet, and the other one a diluted hyposodic gelified liquid diet. After one week, both groups were administered daily intraperitoneal (i.p.) injections of desmopressin acetate (ddAVP; 0.4 μg/kg) and a volume of distilled water equivalent to 2.5% of body weight for 7 days. Animals were placed in metabolic cages for 24h at the end of each period to collect and analyse the urine, and a blood sample from the tail vein was obtained. Weight, water and food intake were measured on a daily basis.

Results: Differences in water and electrolyte balance are shown in Table 1. Pellet fed animals presented an increased water intake and produced a more concentrated urine compared to those on a hyposodic diet. When analysed in detail, urinary osmolality was mainly driven by ionic osmoles in pellet fed animals (42.25 ± 4.72 vs 266.30 ± 17.32 mOsm/kg, p<0.005). Of note, there seems to be an occult osmole, especially prominent in the pellet group (osmol gap 20.40 ± 3.18 vs 99.89 ± 9.81 mOsm/kg, p = 0.017). All of the above suggest there is a net retention of water, sodium and potassium in those animals fed with a conventional pellet diet. Daily administration of ddAVP/water induced a mild transient hyponatremia that was recovered 24h later in both groups; this situation was repeated over a 7 day period. Pellet fed animals did not modify water intake, diuresis, free water clearance or urinary osmolality after ddAVP/water treatment, suggesting that hyperosmolar diets significantly increase urinary osmolality fixating urinary water losses and impairing further urinary concentration. On the contrary, animals on a hyposodic diet did present antiaquaresis, as shown by an increase in water intake, a decrease in diuresis and free water clearance and an increase in urinary osmolality. Animals fed with hyposodic diet progressively lost weight, while pellet fed animals did not. However, this trend was reversed after 4 days of treatment with ddAVP/water, again suggesting a degree of water retention. It is remarkable that we have found signs of water retention despite the fact that the induced hyponatremia is mild and transient.

Conclusion: The antiaquaretic effect of ddAVP is overridden by the amount of urinary osmoles excreted when on a pellet diet, which seem to fixate the amount of water in the urine. Therefore, the use of hyposodic diets in preclinical drug development is essential when SIADH is likely to be expected, as its effects will be unnoticed if a standard diet is used.
Diacylglycerol (DAG) and triacylglycerol (TAG) that were significantly elevated compared to healthy controls and patients with hypercholesterolemia. We identified lccDAGs as unique lipids in pFSGS patients with a substantially different lipid profile than healthy controls and patients with familial hypercholesterolemia. We identified lccDAGs as unique lipids in patients with pFSGS, that were not present in controls. This is an interesting finding since the DAG-analogue 1-oleoyl-2-acetyl-sn-glycerol (OAG) is known to be able to induce podocyte injury in vitro [2]. In further research, we will focus on confirming whether lccDAGs are unique to pFSGS patients, whether it is suitable as a biomarker, and whether it plays a causal role in the disease process.

#4013
LIPIDOMIC ANALYSIS OF PFSGS PATIENTS’ SERUM TO IDENTIFY POTENTIAL CANDIDATES FOR THE CIRCULATING PERMEABILITY FACTOR(S) IN THE LIPID DOMAIN
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Radboud University Medical Center, Nijmegen, Netherlands

Background and Aims: Patients with primary focal segmental glomerulosclerosis (pFSGS) present with nephrotic syndrome. Whereas the exact pathogenesis is largely unknown, there is strong evidence that one or more circulating permeability factors in the circulation induce podocyte injury. Podocyte injury eventually leads to foot process effacement, massive proteinuria and kidney function loss. Historically, research into the cause of pFSGS has focused primarily on identifying the circulating factor in the protein domain, but reports of successful treatment with lipid apheresis suggest that it could also be a lipid compound. Here, we set out to investigate the lipidome of pFSGS patients’ serum to identify potential candidates for the circulating permeability factor(s) in the lipid domain.

Method: For this lipidomics study, we included 5 patients with pFSGS in whom serum had been collected at the time they presented at our center with active nephrotic syndrome. We compared the serum lipidome of the pFSGS patients with age matched healthy controls (n = 5), and with age matched patients with familial hypercholesterolemia (n = 5) who, like pFSGS patients, have significantly elevated lipid values. Serum was analyzed using the Shotgun Lipidomics platform by Lipotype GmbH (Dresden, Germany), as previously described [1]. The amount of lipids was normalized to the total amount of lipids present within the sample.

Results: The lipidomic profile of patients with pFSGS was markedly different from the profile of healthy controls and patients with hypercholesterolemia. We found differences in various lipid classes in pFSGS patients, including cholesterol esters (CE), lyso-phosphatidylcholine (LPC), phosphatidylethanolamine (PE), diacylglycerol (DAG) and triacylglycerol (TAG) that were significantly changes compared to both healthy controls and FH patients. Diacylglycerols (DAG) were identified as the most significantly increased lipid species in pFSGS. By analyzing the subspecies we discovered that DAGs with carbon chains greater than 38 carbon atoms in both chains combined (long carbon chain DAGs, lccDAGs) were exclusively present in patients with pFSGS.

Conclusion: Our lipidomics data show that patients with pFSGS have a substantially different lipid profile than healthy controls and patients with familial hypercholesterolemia. We identified lccDAGs as unique lipids in patients with pFSGS, that were not present in controls. This is an interesting finding since the DAG-analogue 1-oleoyl-2-acetyl-sn-glycerol (OAG) is known to be able to induce podocyte injury in vitro [2]. In further research, we will focus on confirming whether lccDAGs are unique to pFSGS patients, whether it is suitable as a biomarker, and whether it plays a causal role in the disease process.

REFERENCES

Table 1: Comparison of analytical values between both groups at baseline and after a 7 day period of daily treatment with i.p. ddAVP (dose 0.4 μg/kg) and a volume of water equivalent to 2.5% of the animal’s body weight.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Hyposodic diet</th>
<th>7 days after daily ddAVP + water 2.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pellet diet</td>
<td>Hyposodic diet</td>
<td>Pellet diet</td>
</tr>
<tr>
<td>Natremia (mEq/L)</td>
<td>140.25 ± 3.30</td>
<td>136.50 ± 1.73</td>
<td>142.50 ± 0.58</td>
</tr>
<tr>
<td>Plasma Osm (mOsm/kg)</td>
<td>302.67 ± 11.55</td>
<td>310.00 ± 10.71</td>
<td>280.00 ± 15.41</td>
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<td>Hematocrit (%)</td>
<td>40.25 ± 0.96</td>
<td>42.50 ± 2.52</td>
<td>41.25 ± 1.71</td>
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<tr>
<td>Water intake (mL/d)</td>
<td>29.25 ± 5.72</td>
<td>13.96 ± 3.33*</td>
<td>30.13 ± 0.95</td>
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<tr>
<td>Sodium intake (mEq/d)</td>
<td>1.66 ± 0.11</td>
<td>0.69 ± 0.16*</td>
<td>1.45 ± 0.09†</td>
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<tr>
<td>Potassium intake (mEq/d)</td>
<td>2.21 ± 0.14</td>
<td>0.23 ± 0.05*</td>
<td>1.92 ± 0.11*</td>
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<tr>
<td>Diuresis (mL/d)</td>
<td>13.75 ± 2.10</td>
<td>72.25 ± 11.70*</td>
<td>13.25 ± 6.24</td>
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<tr>
<td>Urinary Osm (mOsm/kg)</td>
<td>736.00 ± 145.79</td>
<td>189.25 ± 32.65*</td>
<td>614.00 ± 63.38</td>
</tr>
<tr>
<td>Sodium urinary excretion (mEq/d)</td>
<td>0.86 ± 0.15</td>
<td>1.04 ± 0.31</td>
<td>0.84 ± 0.19</td>
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<tr>
<td>Potassium urinary excretion (mEq/d)</td>
<td>0.92 ± 0.20</td>
<td>0.49 ± 0.20*</td>
<td>0.90 ± 0.26</td>
</tr>
<tr>
<td>Free water clearance (mL/d)</td>
<td>−20.30 ± 4.79</td>
<td>28.55 ± 10.95*</td>
<td>−21.61 ± 4.79</td>
</tr>
</tbody>
</table>

Results are expressed as mean±SD; n = 4 per diet. †p<0.05 compared to Baseline Pellet diet. *p<0.05 compared to Baseline Hyposodic diet. ‡p<0.05 compared to Pellet diet after 7 days of daily ddAVP/water. Osm: osmolality.
Figure 1: Lipidomic analysis of pFSGS serum. (A) Principal components analysis of measured lipid species indicates distinct lipid profiles for pFSGS and FH patients compared to controls. (B) lccDAG subspecies are only present in pFSGS patients. (C) Concentrations of different lipid species in patients with pFSGS and FH and healthy controls. Triacylglycerol (TAG) and diacylglycerol (DAG) species are increased in pFSGS patients compared to patients with FH and healthy controls. CE: Cholesterol esters, Cer: Ceramide, Chol: Cholesterol, DAG: Diacylglycerol, HexCer: Hexosylceramide, (L)PC (O-): (lyso-) Phosphatidylcholine (-ether), (L)PE (O-): (lyso-) Phosphatidyethanolamine (-ether), PI: Phosphatidylinositol, SM: Sphingomyelin, TAG: Triacylglycerol.

#5400
CLINICAL PROFILE, MICROSCOPIC FEATURES AND OUTCOMES OF PATIENTS WITH MINOR GLOMERULAR ABNORMALITIES AT NKTI: A 10-YEAR DESCRIPTIVE CROSS-SECTIONAL STUDY
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National Kidney and Transplant Institute, Adult Nephrology, Quezon City, The Philippines

Background and Aims: Minor Glomerular Abnormality (MGA) is a kidney biopsy diagnosis characterized by the presence of minor structural abnormalities which are not sufficient to be classified under the other known glomerular diseases. Although usually considered a benign renal problem, few literatures mentioned it may cause deterioration of kidney function in the long term. The objective of this study is to describe the clinical profile, microscopy findings, treatment outcome and renal survival of patients diagnosed with Minor Glomerular Abnormalities in NKTI from 2005 to 2015.

Method: This is a Retrospective, Descriptive, Cross-sectional study which included 190 patients who were diagnosed with MGA. Demographic, clinical profile, CKD classification and treatment outcomes were presented using descriptive statistics while renal survival was analysed using Fisher’s Exact Test. Based on the level of proteinuria and serum creatinine, treatment outcomes of the patients were classified as either with (1) complete response [if with reduction in proteinuria to ≤ 300 mg/day (< < 0.3 g/day) and a creatinine clearance ≥ 80 ml/min with no reduction from baseline] (2) partial response [proteinuria between 300 mg and 3 g/day OR by at least 50% from baseline level and with no deterioration in creatinine clearance], (3) relapse [patients whom (a) after a complete response to treatment (baseline proteinuria ≤ 300 mg/day), there is an increase in proteinuria to ≥ 1.0 g/day or (b) after a partial response (baseline proteinuria between 300 mg and 3 g/day), there is an increase in proteinuria to ≥ 3 g/day or increase in proteinuria by ≥ 50%, or (c) after a partial response (baseline proteinuria > 3 g/day), there is an increase in proteinuria by ≥ 50%], or (4) unsatisfactory response to treatment if complete or partial response is not met. Renal survival was assessed by classifying the renal status of the patients as either with (1) Normal or Mildly Decreased GFR [CKD 1-2] or (2) with moderately decreased kidney function to renal failure [CKD 3-5].

Results: The mean age of the MGA patients at diagnosis was 37 years old. Of the 190 subjects of this study, 53.68% were female and 73.16% has no comorbidities. Proteinuria was the most common reason for consult (66.32%), followed by hematuria (38.42%) and worsening renal function (14.21%). Most of the patients had Nephrotic Syndrome (39%) before biopsy. The top three Electron Microscopy findings were Minimal Change Disease (24.4%) Segmental Podocyte Foot Processes Effacement (True MGA) at 27.4% and Thin Basement Membrane Disease (22.6%). At one year and five years, 13.68% and 4.74% respectively have complete response to treatment while 22.10% and 13.15% respectively have either partial or unsatisfactory response to treatment. Eighty patients (86.02%) at one year and 33 patients (78.57%) at 5 years remain at CKD 1-2. When the renal survival of the True MGA and Non-MGA patients were compared using Fisher Exact Test, there was no significant difference between the two groups (p values of 0.080 at 1 year and 0.99 at 5 years).

Conclusion: Minimal Change Disease is the most common Electron Microscopy diagnosis. Majority have good renal survival, but few progressed to CKD 3-5. Survival between MGA and Non-MGA patients are similar.
## Renal biopsy indications and findings (n = 190)

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<tr>
<th>Symptom</th>
<th>Frequency (%)</th>
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<td>Proteinuria</td>
<td>58.42</td>
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<td>Edema</td>
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<tr>
<td>Microscopic hematuria</td>
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<tr>
<td>Abnormal renal function</td>
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<td>Hypertension</td>
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<td>Gross hematuria</td>
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<tr>
<th>Indication</th>
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<td>Proteinuria</td>
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<td>126</td>
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<tr>
<td>Hematuria</td>
<td>38.42</td>
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<td>Worsening of renal function without treatment</td>
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<td>27</td>
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<td>Absent or unsatisfactory response to previous treatment</td>
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<td>Relapse after initial response to treatment</td>
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### Renal Clinical Syndrome

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<td>Nephrotic Syndrome</td>
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<tr>
<td>Chronic GN</td>
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<tr>
<td>Acute glomerulonephritis</td>
<td>22.11</td>
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<tr>
<td>Rapidly progressive GN</td>
<td>7.69</td>
<td>15</td>
</tr>
<tr>
<td>Asymptomatic Urine Abnormality</td>
<td>6.84</td>
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### Diagnosis on Electron Microscopy

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<th>Diagnosis</th>
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<tr>
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<tr>
<td>Segmental podocyte foot process effacement (True MGA)</td>
<td>27.37</td>
<td>52</td>
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<tr>
<td>Thin basement membrane disease</td>
<td>22.63</td>
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<tr>
<td>Immune complex-mediated glomerulonephritis</td>
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<td>Focal segmental glomerulosclerosis</td>
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<tr>
<td>Acute Interstitial Nephritis</td>
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<td>Hypertensive Nephrosclerosis</td>
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<td>Membranous nephropathy</td>
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## Outcomes of renal biopsy patients assessed for MGA

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<th>eGFR Median (Range)</th>
<th>Baseline [n=190]</th>
<th>1 year [n=93]</th>
<th>5 years [n=42]</th>
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<tr>
<td>72.46 (3.5-172.89)</td>
<td>99.6 (7.4-155.6)</td>
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<td>1</td>
<td>72 (37.89)</td>
<td>55 (59.14)</td>
<td>23 (54.76)</td>
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<td>2</td>
<td>56 (29.47)</td>
<td>25 (26.88)</td>
<td>10 (23.81)</td>
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<td>3A</td>
<td>25 (13.16)</td>
<td>3 (3.23)</td>
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<td>3B</td>
<td>17 (8.95)</td>
<td>2 (2.15)</td>
<td>1 (2.38)</td>
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<td>4</td>
<td>10 (5.26)</td>
<td>5 (5.38)</td>
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<td>5</td>
<td>10 (5.26)</td>
<td>3 (3.23)</td>
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<td>80 (86.02)</td>
<td>33 (78.57)</td>
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<th>Outcome</th>
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<tr>
<td>Partial response</td>
<td>17 (8.95)</td>
<td>8 (4.21)</td>
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<td>Unsatisfactory response</td>
<td>25 (13.16)</td>
<td>17 (8.95)</td>
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<td>Lost to follow-up</td>
<td>122 (64.21)</td>
<td>156 (82.11)</td>
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*Patients who remain at CKD 1-2 category as per KDIGO CKD Classification.*
**#2818**

**UNIQUE SIGNATURES OF EXTRACELLULAR MATRIX REMODELING IN PATIENTS WITH LUPUS NEPHRITIS, FSGS, AND MCD: A PILOT STUDY**

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**Background and Aims:** Glomerulonephritis is one of the most common causes of chronic kidney disease (CKD). Causes of glomerular diseases include lupus nephritis (LN), focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD). The hallmark of CKD is renal fibrosis characterized by an imbalanced turnover of extracellular matrix (ECM) components and CKD is associated with increased inflammation. The aim of this study was to screen a biomarker panel based on extracellular matrix remodeling biomarkers as well as fibrotic activity and inflammation biomarkers. Additionally, to identify biomarkers that are differentially expressed in glomerular diseases compared to healthy and that are differently expressed between the different etiologies. The following biomarkers were measured in serum and/or urine samples from all 154 subjects:

- Interstitial matrix remodeling biomarkers: formation of collagen type III (PRO-C3) and VI (PRO-C6), and degradation of collagen type III (C3M).
- Basement membrane remodeling biomarkers: MMP-mediated degradation of collagen type IV (C4M, C4G, TUM), laminin (LG1M) and perlecain (LG3).
- Two biomarkers of fibrotic activity; acetylated N-terminal of α-smooth muscle actin (αSMA) and transforming growth factor β (TGF-β).
- An inflammation biomarker of calprotectin (CPa9-HNE) reflecting neutrophil activity.

**Results:** Overall, all three diseases showed the same trend of change (either no change, increase or decrease compared to healthy controls) in biomarker levels. There was a significant increase of PRO-C3, PRO-C6, TUM, LG1M, αSMA, and CPa9-HNE in serum, and a significant decrease of C3M and C4M serum in patients compared to healthy controls. Four of the biomarkers were differentially expressed between the different etiologies. In serum, C4G levels were significantly higher in LN and MCD compared to FSGS, LG1M levels were significantly higher in LN compared to MCD, and CPa9-HNE levels were significantly higher in MCD compared to LN (all, P<0.05). In urine, TUM levels were significantly higher in LN compared to FSGS and MCD (P<0.05).

**Conclusion:** The data presented in this study indicate that both biomarkers of interstitial matrix and basement membrane remodeling as well as biomarkers of fibrotic activity and inflammation reflect the changes that take place during development of glomerular diseases. Some of these markers may be able to distinguish etiologies including the hardly differentiated diseases FSGS and MCD. This needs to be tested in larger studies.

**#6323**

**RENAL CONTRAST-ENHANCED ULTRASOUND AND GLOMERULONEPHRITIS: A GOOD MARKER OF DISEASE ACTIVITY**

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**Background:** Contrast-enhanced ultrasound (CEUS) could provide a lot of information of renal blood flow. Renal blood flow is an excellent marker of inflammatory and fibrotic processes in the kidney such as glomerulonephritis. Therefore, in patients with these diseases, renal CEUS can be both a prognostic marker and an index of response to therapy. Currently in the literature there are preliminary studies showing the role of CEUS in terms of histology and outcome in the evaluation of patients with glomerulonephritis. In this pilot study we used perfusion CEUS parameters (WiR and WoR; WiAUC and WoAUC) as possible markers of renal microvascular damage. We compared the perfusion parameters with the clinical and histological findings of our patients.

**Method:** Eighteen patients with clinical and laboratory signs of glomerulonephritis were enrolled. All patients underwent ultrasound-assisted renal biopsy and B-mode ultrasound examination, color Doppler ultrasound and contrast-enhanced ultrasound. Time Intensity (TI) curves were obtained from renal CEUS. TI curves and several quantitative perfusion parameters were defined using VueBox® Quantitation Software.

**Results:** From April to October 2022, 18 patients (12 men and 6 women) with clinical and laboratory suspicion of glomerular disease were enrolled. Median age was 48.05 years, all patients underwent renal biopsy and contrast-enhanced ultrasound at basal condition. Table 1 shows patients characteristics. CKD patients were stratified into two groups according to their eGFR: group I (eGFR < 60 ml/min/1.73 m², n. = 4) and group II (eGFR ≥ 60 ml/min/1.73 m², n. = 3). Moreover, we divided patients into two groups based on the presence of nephrotic-range proteinuria (≥ 3.5 g/24h). At this time, seven patient data are suitable for analysis. The small sample size at present does not allow for statistical significance. However, in our study, the persistence of contrast agent signal during the wash-out phase was differed markedly in correlation with the degree of CKD. In particular, we observed a slower wash-in phase in the presence of vascular hyalinosis (Fig. 1).

**Conclusion:** Our experience seems to confirm that CEUS parameters can be excellent indicators both in terms of patient disease outcomes and histological data. CEUS can effectively and quantitatively demonstrate renal microvascular perfusion in patients with glomerulonephritis. Future goal is that CEUS could also be a prognostic and follow-up marker after renal biopsy in patients with glomerulonephritis.
Figure 1: Relationship between perfusion CEUS parameters and renal microvascular damage.

#3345
EFFECTS OF CONDITIONED MEDIUMS COLLECTED FROM 2D OR 3D CULTURED MSCS ON KIDNEY FUNCTIONS OF RATS WITH AUTOIMMUNE DIABETES INDUCED WITH STREPTOZOCIN
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Background and Aims: The main mechanism of therapeutic action of mesenchymal stem cells (MSCs) could be resulted from their secretome content rather than their direct differentiation into damaged cells [1, 2]. Preconditioning of MSCs with different strategies like culturing in 3 dimensional (3D) culture scaffolds could improve their therapeutic potential [1]. Based on our previous study [1] in which the concentrations of total protein and specifically VEGF and IL-4 in conditioned mediums (CMs) collected from MSCs cultured in 3D culture conditions were increased compared to one of 2D, the aim of this study is comparative analysis of effects of CMs obtained from MSCs incubated under 2D and 3D culture conditions on kidney functions of rats with autoimmune type 1 diabetes (aT1D) induced with streptozocin (STZ).

Method: Isolation and characterization of the umbilical cord MSCs and the following analysis of concentrations of total protein and paracrine factors in the 2D-CMs and 3D-CMs were performed as it was mentioned [1]. Sprague-Dawley rats were treated with 20 mg/kg STZ for 5 consecutive days to induce T1D and 12 doses of CMs were intraperitoneally introduced for 4 weeks in accordance with the timeline defined in Figure 1. Therapeutic effects of CMs were comparatively investigated by biochemical, physical, histopathological and immunohistochemical analysis.

Results: At the end of the 2nd week, urinary albumin/creatinine (u-Alb/Cr) ratio and creatinine removal rate (Crr) of diabetes were significantly aggravated compared to control group (p = 0.0001 and p = 0.13 respectively). At the end of the 7th week, u-Alb/Cr ratios of both treatment groups were significantly improved compared to one of diabetes group (p = 0.029 vs p = 0.002). There was no statistical difference among all groups for Crr values. In the post treatment period u-Alb/Cr ratio was exacerbated (p = 0.014) while Crr value was not changed compared to pre-treatment period (p = 0.713). There was no statistical change between the pre- and post-treatment values of u-Alb/Cr ratio and Crr for both treatment groups. Renal mass index of control group was lower than the ones of experimental groups, while weight percent change from pre- to post-treatment period of control group was statistically higher than the ones of experimental groups (p = 0.0001). However, there was no statistical difference for both parameters among the experimental groups (Figure 2). Histopathological evaluations showed that cortical tubular damage (CTD) was significantly ameliorated in only D-+3D-CM group compared to diabetes group (p = 0.012), while there was no statistical change in glomerular fibrosis in both treatment groups (Figure 3.1 and 3.2 respectively). Immunohistochemical analysis indicated that nephrin expression was insignificantly increased in both treatment groups compared to diabetes group (Figure 3.3). Preliminary evaluation of thicknesses of glomerular basal membrane and pedicel with transmission electron microscopy (TEM) showed no clear difference among all the groups (Figure 4).

Conclusion: CM obtained from MSCs in 3D culture conditions could partially ameliorate kidney functions of aT1D by improving CTD and expression of nephrin which is crucial for the integrity of glomerular filtration barrier.

Figure 1: Timeline of in vivo experiments.
Figure 2: Physical and biochemical analysis of rats. *P < 0.05 vs D, D+2D-CM, D+3D-CM; **P < 0.05 vs D; ***P > 0.05 vs D, D+2D-CM, D+3D-CM; ^P < 0.05 vs post-treatment C; ^^^P < 0.05 vs post-treatment-D.
Figure 3: Histopathological and immunohistochemical analysis. *P<0.05 vs C and D+3D-CM, **P<0.05 vs the other groups; ***P<0.05 vs C.
REFERENCES


B2 - GLOMERULONEPHRITIS & SYSTEMIC DISEASES (AAV, SLE, ETC.)

#2561

URINE PROTEOMICS FOR PREDICTION OF DISEASE PROGRESSION IN PATIENTS WITH IGA NEPHROPATHY

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**Background and Aims:** IgA nephropathy (IgAN) may lead to kidney failure. The urinary proteomics biomarker-based classifier (IgAN237) may predict progression at the time of kidney biopsy [1]. We now studied whether IgAN237 predicts disease progression not only at the time of biopsy but also later in the course of IgAN.

**Method:** Urine samples from 103 patients with biopsy-proven IgAN were analyzed using capillary electrophoresis-mass spectrometry at baseline (IgAN237 score-1) and 89 also at follow-up (IgAN237 score-2). Patients were grouped into ‘non-progressors’ (IgAN237 score ≤ 0.38 Units) and ‘progressors’ (IgAN237 score >0.38 Units). Historical and follow-up data included, e.g., estimated glomerular filtration rate (eGFR)-slopes, urinary albumin/creatinine ratio (UACR)-slopes and medication. Multiple logistic regression analysis, using a stepwise model, was done with progressors and non-progressors as dependent factors including explanatory variables age, sex, eGFR- and UACR-slopes.

**Results:** Median age at biopsy was 44 years (range 11-92); 63% were male. Median interval between biopsy and IgAN237 score-1 was 65 months (0-606), and between IgAN237 score-1 and score-2 was 258 days (71-531). IgAN237 score-1 and score-2 values did not differ significantly and were correlated (rho = 0.44, p < 0.001). Twenty-eight and 26% of patients were classified as progressors based on IgAN237 score-1 and score-2, respectively. The IgAN237 score inversely correlated with the chronic eGFR slopes (rho = -0.278, p = 0.02 for score-1; rho = -0.409, p = 0.002 for score-2) and with ±180days eGFR slopes (rho = -0.31, p = 0.009 and rho = -0.439, p = 0.001, respectively) (Figure 1). The ±180days eGFR-slopes were more reduced for progressors than non-progressors (median -5.98 versus -1.22 mL/min/1.73m² per year for score-1, p < 0.001; -3.02 vs 1.08 mL/min/1.73m² per year for score-2, p = 0.047) (Figure 2). The only significant variable maintained in a multiple logistic regression analysis for IgAN237 score-1 (progressor vs non-progressor) was ±180days eGFR slope (p <0.001) and for IgAN237 score-2 the UACR (p = 0.002) and age at baseline (p = 0.016).

**Conclusion:** The urinary IgAN237 classifier represents a risk stratification tool in IgAN not only at the time of biopsy but also later in the course of the disease. It may guide physicians in management and follow-up strategies in an individualized manner.
Figure 1: Correlation between IgAN237 score-1 (A) and IgAN237 score-2 (B) with ±180 days eGFR-slope (eGFR_{180days-slope}).

Figure 2: Boxplot of comparisons of progressors (IgAN237 > 0.38) vs non-progressors (IgAN237 ≤ 0.38) and ±180 days eGFR-slope (eGFR_{180days-slope}) (mL/min/1.73m² per year) in IgAN237 score-1 (A) and IgAN237 score-2 (B).

**REFERENCE**


# KiM-1: A POTENTIAL BIOMARKER OF ACUTE KIDNEY INJURY AND TUBULOINTERSTITIAL INJURY IN PATIENTS WITH ANCA-GLomerulonephritis

**Background and Aims:** Kidney injury molecule 1 (KiM-1) is a transmembrane glycoprotein expressed by proximal tubular cells, recognized as an early, sensitive, and specific urinary biomarker for kidney injury. Blood KiM-1 was recently associated with the severity of acute and chronic kidney damage but its value in ANCA-associated vasculitis with glomerulonephritis (ANCA-GN) has not been studied. Thus, we analyzed its expression at ANCA-GN diagnosis and its relationship with clinical presentation, kidney histopathology, and early outcomes.

**Method:** We assessed KiM-1 levels and other pro-inflammatory molecules (CRP, IL-6, TNF-α, MCP-1 and PTX3) at ANCA-GN diagnosis and after 6 months in patients included in the Maine-Anjou registry, which gathers data from four French Nephrology Centers diagnosed since January 2000.

**Results:** Blood KiM-1 levels were assessed in 58 patients. Levels were elevated at diagnosis and decreased after induction remission therapy. KiM-1 was associated with the severity of renal injury at diagnosis and the need for KRT. In opposition to other pro-inflammatory molecules, KiM-1 correlated with the amount of interstitial fibrosis and tubular atrophy (IF/TA) on kidney biopsy, but not with glomerular involvement. In multivariable analysis, elevated KiM-1 predicted initial eGFR (β = -19 [-31, -7.6], p = 0.002).

**Conclusion:** KiM-1 appears as a potential biomarker for acute kidney injury and for tubulointerstitial injury in ANCA-GN. Whether KiM-1 is only a surrogate marker for IF/TA or a key immune player in ANCA-GN pathogenesis remains to be determined.
A PHENOTYPIC DRIVEN RITUXIMAB MAINTENANCE APPROACH IS EFFECTIVE AND SAFE IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS
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Background and Aims: Rituximab (RTX) has emerged as the first-line treatment to maintain remission in ANCA-Associated Vasculitis (AAV). However, the ideal strategy for RTX re-dosing is still unclear [1].

Method: In this monocentric and retrospective study we evaluated the efficacy and safety of two RTX-based maintenance regimens in patients with AAV. Fixed-dose (FD) RTX dosing, consisting of at least 3 pre-emptive RTX administrations every 6 months, was preferred in patients judged to be at high relapse risk. Instead, a biomarker-guided on-demand (OD) RTX dosing strategy was preferred for patients deemed at lower risk of relapse; this consisted in RTX re-treatment only in case of B-cell repopulation or rise in ANCA titer. The single patient relapse risk was assessed according to the disease phenotype (granulomatous vs vasculitic), the ANCA specificity and the disease status (onset vs relapse). Relapses were defined as increase of disease activity requiring escalation of immunosuppression; major relapses were defined in case of life/organ-threatening manifestations.

Results: The study included 100 patients followed for a median of 24 months (IQR 20-30), 51% treated with an OD and 49% with a FD strategy. The main baseline characteristics of our cohort are shown in the Table; patients treated with a FD strategy were more often GPA, PR3-ANCA positive, with relapsing disease and ENT involvement and less frequent renal involvement. The FD group received a median of 4 (IQR 4-4) administrations of RTX for a median cumulative dose of 2 g (IQR 2-2). Only 6 (11.8%) patients in the OD group received RTX as maintenance therapy with a median of 1 (IQR 1-3) administration of RTX for a median cumulative dose of 0.75 g (IQR 0.5-1.75). Thirteen relapses occurred, 6 in the FD group and 7 in the OD one. Remission rates were comparable in the two cohorts, with respectively 87.6% and 85.9% of the patients in remission at 24 months (Figure 1 - panel A). No significant differences in remission rates across the 2 groups were observed after considering only major flares or after stratification according to clinical diagnosis (MPA/GPA) and ANCA specificity (Figure 1 - panel B to F). Ten and 20 severe infections (p = 0.383) and 3 and 1 cancer (p = 0.581) occurred respectively in the FD and OD group.

Conclusion: In our case series, a phenotypic-driven approach to RTX maintenance showed comparable efficacy and safety between fixed and on-demand dosing, despite different baseline characteristics between the two groups. These results suggest that personalizing RTX maintenance may be a feasible and safe strategy.

REFERENCE
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<th>OD (n=51)</th>
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<td>68 (55-77)</td>
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<td><strong>Male sex (n, %)</strong></td>
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<td>23 (45.1)</td>
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<td>GPA</td>
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<td><strong>ANCA specificity (n, %)</strong></td>
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<td>37 (77)</td>
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<td>3 (6.3)</td>
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*missing data for 1 patient in FD group
The CIRCRNA–MIRNA–MRNAREGULATORY NETWORK AND THE POTENTIAL ASSOCIATIONS WITH THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS
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Background and Aims: This study aimed to explore the possible role of plasma and PBMCs circular RNA (circRNA) in systemic lupus erythematosus (SLE).

Method: Total RNA was extracted from blood plasma samples obtained from 10 patients with SLE and 10 healthy controls and subjected to microarray analysis to define the profile of circRNA expression. The quantitative reverse transcription-polymerase chain reaction amplification (qRT-PCR) was conducted. The overlapped circRNA between PBMCs and plasma was performed, the interactions with microRNAs were predicted, the miRNA target mRNA was predicted, and the GEO database was used. The Gene ontology and pathway analysis was performed.

Results: 131 upregulated and 314 significantly downregulated circRNAs were identified in the plasma of patients with SLE by the Fold change criteria (≥2.0) and P<0.05. The qRT-PCR results showed that the expression of has-circRNA-102531, has-circRNA-103984, and has-circRNA-104262 was increased in plasma of SLE, and the expression of has-circRNA-102972, has-circRNA-102006, has-circRNA-104313 was decreased in plasma of SLE. 28 upregulated circRNAs and 119 downregulated circRNAs were overlapped from PBMCs and plasma, and ubiquitination was enriched. Furthermore, the circRNA-miRNA-mRNA network was constructed in SLE after analyzing dataset GSE61635 from GEO. The circRNA-miRNA-mRNA network comprises 54 circRNAs, 41 miRNAs, and 580 mRNAs. In addition, the TNF signaling pathway and the MAPK pathway were enriched from the mRNA of the miRNA target.

Conclusion: We described differentially expressed circRNAs in plasma and PBMCs, and the circRNA-miRNA-mRNA network was constructed. The network’s circRNAs could be a potential diagnostic biomarker and potentially play an important role in the pathogenesis and development of SLE.
Figure 1: The miRNA-mRNA in SLE. A 781 mRNAs were overlapped from the 6603 mRNAs (target 41 miRNAs) and 2524 mRNAs (GSE61635). B 164 mRNAs were upregulated, and 416 were downregulated, the regulation trend consistent with the circRNAs in plasma and PBMCs of SLE. C The biological process terms of GO enrichment analysis of the overlapped mRNAs. D The KEGG pathway of upregulated mRNAs includes the TNF signaling and MAPK pathways.
#2652
ANTIPROTEINURIC EFFECT OF SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS IN GLOMERULAR AND SYSTEMIC DISEASES: A REAL-WORLD CLINICAL STUDY
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¹Centro de investigación Hospital Universitario 12 de Octubre, Madrid, Spain, ²Queen Elizabeth University Hospital, United Kingdom, ³Addenbrooke’s Hospital, United Kingdom, ⁴Ludwig Maximilian University of Munich, München, Germany, ⁵University Hospital RWTH Aachen, Aachen, Germany, ⁶La Paz University Hospital, Madrid, Spain and ⁷University Hospital October 12, Madrid, Spain

Background and Aims: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) have recently begun to be used in glomerular/systemic autoimmune diseases with glomerular involvement for the treatment of proteinuria, although the information on real-world clinical settings is very scarce.

Method: Retrospective, observational, international cohort study. Adult patients with biopsy-proven glomerular diseases were included. The main outcome was the percentage reduction in 24-hour proteinuria from SGLT2i initiation to 3, 6, 9, 12 months. Secondary outcomes included percentage proteinuria reduction by type of disease and a reduction of proteinuria ≥30% from SGLT2i initiation.

Results: The study group consisted of 493 patients with a median age of 55 years. All patients were on renin-angiotensin system blockade. Geometric mean percentage change of proteinuria from baseline was –35%, –41%, –45% and –48% at 3, 6, 9 and 12 months after SGLT2i initiation, respectively. Geometric mean percentage change of eGFR was –6%, –3%, –8% and –10.5% at 3, 6, 9 and 12 months, respectively. Results were similar irrespective of the underlying disease. However, a significant correlation was found between body mass index (BMI) and percentage proteinuria reduction at last follow-up (R = –0.11; p = 0.02). By mixed-effects binomial logistic regression
model, serum albumin at the onset of SGLT2i emerged as the main predictor of a $\geq 30\%$ proteinuria reduction (odds ratio for albumin $< 3.5$ g/dl: $0.53$; $95\%$ CI $0.30$–$0.91$; $p = 0.02$). Finally, a slower eGFR decline over time was observed in patients achieving a $\geq 30\%$ proteinuria reduction: $-3.7$ versus $-5.3$ ml/min/1.73m$^2$/year ($p = 0.001$).

**Conclusion:** The use of SGLT2i was associated with a significant reduction of proteinuria, irrespective of the underlying glomerular/systemic disease. This percentage change was higher in patients with higher BMI. Higher serum albumin at SGLT2i onset is associated with higher probability of achieving a $\geq 30\%$ proteinuria reduction.
LIMITATIONS AND UNCERTAINTIES OF ASSESSING AND MANAGING OLDER PATIENTS WITH ANCA ASSOCIATED VASCULITIS

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Background and Aims: ANCA associated vasculitis (AAV) has a peak incidence in 65-74 yr olds. As a result, it affects an ageing population who are vulnerable to co-morbidities, polypharmacy and frailty. Due to the high burden of morbidity and mortality in these patients, it is increasingly recognised that individualised management is needed. Whilst current immunotherapies are effective, there remains caution in treating older patients due to the potential risks. Yet despite AAV being a condition that predominantly affects older people, few studies have looked specifically at the benefit of treating AAV in such age groups, or at frailty assessment tools to guide treatment.

Method: We aimed to evaluate treatment outcomes in older AAV patients, as well as frailty assessment tools to aid prognostication and management. A cohort study evaluating outcomes of induction immunosuppression in patients ≥75yrs was constructed from 2 centres, with subsequent meta-analysis of published data [1]. In addition, studies identifying frail patients, who may be at risk of adverse outcomes, were carried out using the quantitative tools; Hospital Frailty Risk Score (HFRS) [2] and the Clinical Frailty Scale (CFS).

Primary outcomes were mortality and end stage kidney disease (ESKD). The HFRS was calculated using hospital coding data from any hospital admissions between a patient's AAV diagnosis to 2yr follow up. Patients were categorized into low, intermediate and high HFRS groups. CFS scores at presentation were documented prospectively and then repeated a minimum of 6 weeks from diagnosis. A CFS score of ≥5 was used to categorise frailty. Differences in the scores were assessed and compared to clinical outcomes.

Results: Retrospective analysis of our AAV cohort aged ≥75 yrs demonstrated that induction immunosuppression was associated with a significant reduction in the 2yr mortality risk [HR 0.29 (95% CI 0.09–0.93)]. Following systematic review, with a study population of 290 patients, the pooled HR by meta-analysis confirmed a significant reduction in the risk of death with induction treatment [HR 0.31 (95% CI 0.16–0.57)]. Treated patients had a lower rate of ESKD, but this was not statistically significant [HR 0.71 (95% CI 0.15–3.35)]. Looking separately at frailty assessments, mortality and ESKD were assessed according to HFRS and CFS. Thirty-four patients with AAV aged ≥75 yrs were assessed using HFRS and categorised into the low (n = 18), intermediate (n = 13) and high (n = 3) HFRS groups. All patients in the high HFRS groups had ≥1 episodes of hospitalization after diagnosis of AAV. However, there was no difference in frailty at diagnosis and follow-up was 4. There was no significant interval change in CFS (P = 0.16) suggesting that patients did not become frailer. Instead, there was a tendency towards improved frailty scores at reassessment (n = 17, 43%), with some patients going from a CFS of 6 (moderately frail) to 3 (managing well). There was no significant difference in ESKD between those categorised as frail and non-frail (P = 1.0), although crude mortality was higher among those initially categorised as frail (P = 0.03).

Conclusion: Our research shows that older patients with AAV benefit from standard remission-induction therapy and those treated had favourable mortality outcomes compared to those who were not. Furthermore, frailty assessment tools do not correlate clearly with clinical outcomes. Whilst there is evidence to support the use of HFRS and CFS in a many diseases, its utility in determining frailty and potential susceptibility to adverse effects of therapy in patients with multifaceted, autoimmune inflammatory disease remains limited. Patients may present ‘frail’ as a result of significant disease burden, which has the potential to improve with appropriate treatment. We suggest that age alone and frailty at assessment should not be a limiting factor when considering treatment and prospective studies of this population are needed.

REFERENCES

SINGLE CELL RNA SEQUENCING OF CIRCULATING LEUKOCYTES FROM IGA NEPHROPATHY PATIENTS IDENTIFIES AN IMPORTANT ROLE FOR INNATE IMMUNE CELLS

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Background and Aims: IgA-nephropathy (IgAN) is a slowly progressive disease characterized by mesangial deposition of IgA1 that causes kidney injury and can eventually lead to end stage renal disease. A key factor underlying the development of IgAN is the presence of galactose-deficient IgA1 (Gd-IgA1) in the circulation. The formation of IgA and IgG antibodies against Gd-IgA1 results in the formation of immune complexes which deposit in the kidney mesangium. Production of Gd-IgA1 hints to defects in B cell regulation. However, the exact immunological dysregulation leading to the formation of Gd-IgA1, and the subsequent antibody formation against it, remains elusive.

Here we use single cell RNA sequencing (scRNA-seq) of circulating leukocytes for in depth analysis of immune cell populations in patients with active IgAN to gain a better understanding of the pathogenesis of this disease.

Method: Peripheral blood mononuclear cells were isolated for scRNA-seq from the blood of four patients with active IgAN, and four controls, matched for age and estimated glomerular filtration rate (eGFR). Cell hashing (Biolegend) of individual samples was performed before pooling samples for scRNA-seq. scRNA expression libraries were performed using the chromium X machine (10xgenomics) according to 10XGenomics single cell V2 user guide. Libraries were sequenced on an Illumina Nextseq500 and reads were mapped to GrCh38 using CellRanger. Differential gene expression analysis was performed for each immune cell type (FDR < 0.05). Reactome pathway enrichment analysis was performed on the differentially expressed genes.

Results: Identification of immune cell subtypes in IgAN patients and matched controls did not show a significant difference in cell numbers or ratios. B cells showed only minor changes in gene expression between IgAN patients and controls, and T cell populations showed changes in a limited set of genes, whereas interestingly, most differentially expressed genes were found in monocytes and NK cells (Figure 1A). Analysis of the differentially expressed genes showed enrichment for genes in interferon signaling pathways, mostly in monocytes and NK cells (Figure 1B). Gene enrichment analysis showed differential expression of type 1 IFN genes and antigen presentation genes, mainly in monocytes and NK cells.

Conclusion: Our data shows the specific endotype of circulating immune cells from patients with active IgAN. While gene expression changes in T and B cells are discrete, changes in monocytes and NK cells appear especially prominent. In these cell types, we observed an important role for interferon signaling. Further analysis of scRNA-seq data in a larger patient cohort will follow, as well as analysis of T and B cell receptor clones in IgAN patients, with which we aim to gain new insights into immune dysregulation in IgAN.
Figure 1: Monocytes and NK cells from IgAN patients show large change in gene expression. Single cell RNA sequencing of peripheral blood mononuclear cells from IgAN patients and matched controls, followed by differential gene expression analysis (FDR < 0.05; n=4) shows profound changes in gene expression of monocytes and NK cells, a limited set of genes were changed in T cells, and only minor changes were discovered in B cell gene expression (A). Pathway analysis reveals an enrichment for interferon signalling pathways, mainly in monocytes and NK cells (B).

#4663
BLOOD AND URINARY CYTOKINE PROFILES AND CLINICAL OUTCOME IN PRIMARY MEMBRANOUS NEPHROPATHY AND DIABETIC KIDNEY DISEASES
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Background and Aims: Primary membranous nephropathy (MN) is an autoimmune, immune complex-mediated primary glomerulopathy causing podocyte injury and nephrotic syndrome. The results of therapy may be suboptimal and biomarkers are needed that predict the need for immune suppression and the response to different immunosuppression regimens. Diabetic kidney disease (DKD) is the most common cause of kidney failure. It is characterized by non-immune podocyte injury that may lead to nephrotic syndrome. We evaluated the circulating and urine cytokine pattern and pathophysiologic difference between both conditions. For MN, we further aimed at identifying the biomarkers of immunosuppressive treatment response.

Method: 192 MN data-points from the STARMEN trial and 92 DKD from the biobank of IIS-FJD-UAM were included. We analyzed the blood and urine samples by HISCL (Sysmex Inc. Kobe, Japan), a chemiluminescence immunoassay that can afford a high-throughput multiplex cytokine analysis. Sixteen biomarkers were measured and evaluated for the correlation with the clinical outcome (eGFR, uPCR, 24-hour proteinuria). Also, the biomarkers’ concentration at baseline was compared with the treatment response during 6-9 months and the disease status after treatment until 24 months. The treatments evaluated STARMEN were Tacrolimus-Rituximab (TacRt) and alternating therapy with corticosteroids-cyclophosphamide. Box plot and Mann Whitney U test were used to assess subgroup differences and Spearman’s rank correlation to assess correlation between variables.

Results: Median age, baseline eGFR and proteinuria for the MN and DKD cohorts were 53 and 66 years, 74 and 52 ml/min/1.73 m2, and 8.8 and 0.2 g/24h, respectively. Five cytokine markers in blood and 5 in urine from MN and 2 in blood and 2 in urine from DKD showed a significant correlation with proteinuria (Table). Circulating TNFa had been previously related to both MN and DKD pathophysiology and we confirmed its correlation with clinical outcomes in both. CCL20 is one of blood biomarkers correlated with anti-PLA2R (rS = 0.151, p = 0.036) and proteinuria in MN but not DKD. We identified a baseline urinary Protein A whose concentration differed between responders and non-responders to TacRt.

Conclusion: MN and DKD displayed characteristic cytokine patterns. Protein A is related to the progression of chronic inflammation and B cells. Its presence in urine and the differences between TacRt responders and non-responders suggest that high inflammatory progression activities may offset the treatment response. In conclusion, protein A could be the potential prognostic marker of TacRt response. However, additional investigation is needed to confirm and evaluate the possible application to other glomerular diseases.
We identified 22 patients who developed UA and/or renal impairment within 3 months of vaccination. The study aimed to examine the patients who were hospitalized in our Unit between April 2021 and January 2023 and underwent renal biopsy. This report should not highlight the need for pharmacovigilance. However, this report shall not lead to vaccine hesitancy during this pandemic as the benefits of vaccination strongly outweigh the potential risks.

#5747
COVID VACCINATION RELATED GLOMERULOPATHIES AND INTERSTITIAL NEPHRITIS
Martina Marchisio, Stefania Lalloni, Marco Morrone, Gianluca Rabajoli, Andrea Careddu, Roberta Fenoglio, Savino Sciascia and Dario Roccatello

Torino, Italy

Introduction: To date, almost 7 billion doses of the different types of vaccine against SARS-CoV-2 have been administered worldwide. Although the severity of new cases of SARS-CoV-2 has progressively decreased, and the pressure on national health systems has declined, the development of de novo glomerular injuries has been suggested.

Methods: This study aimed to examine the patients who were hospitalized in our Unit between April 2021 and January 2023 and underwent renal biopsy for new-onset urinary abnormalities (UA) and/or renal impairment within 3 months of SARS-CoV-2 vaccination.

Results: We identified 22 patients who developed UA and/or renal insufficiency within 3 months of vaccination. Minimal change disease was the most common disease in our cohort (6 patients, 27.3%) followed by the most common disease in our cohort (6 patients, 27.3%) followed by membranous nephropathy (MN; 5 patients, 22.7%), acute tubulointerstitial nephritis (TIN; 3 patients, 13.6%). The other 5 patients had a diagnosis of ANCA-associated vasculitis (2 patients), membranoproliferative glomerulonephritis (1 patient), systemic lupus erythematosus (1 patient) and tip-variant focal segmental glomerulosclerosis (1 patient), respectively. Nine out of 22 patients (40.9%) developed acute kidney injury. Two patients with acute TIN had to start hemodialysis that was discontinued after 1 and 2 months, respectively, due to the recovery of renal function. Two of the 5 patients who had a diagnosis of MN were positive for anti-PLA2r, while all patients were negative for anti-thrombospondin. All patients underwent treatment with corticosteroids and/or immunosuppressants.

Conclusion: Although it is not possible to conclusively determine whether there is a causal relationship between SARS-CoV-2 vaccination and new-onset nephropathies, based on the appearance of UA and/or renal insufficiency shortly after vaccination, we hypothesize that the immune response to the COVID-19 vaccine may be a trigger of nephropathies. Therefore, our results highlight the need for pharmacovigilance. However, this report should not

#5353
THE IDIOPATICHYPOCRYOGLOBULINEMIA AS AN EMERGING MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
Roberta Longo, Cecilia Ceruti, Martina Marchisio, Marco Morrone, Nunziante Caruso, Annalisa Guarino, Roberta Fenoglio, Savino Sciascia and Dario Roccatello

Torino, Italy

Background and Aims: A considerable number of patients with high clinical suspicion for cryoglobulinaemia vasculitis either show negative results for the detection of cryoglobulins or show only trace amounts which cannot be characterized for composition. We aimed at establishing whether the failure to detect or the detection of trace amounts of cryoglobulin with conventional methods either identifies a peculiar subset of low level cryoglobulinaemia (from now on hypocryoglobulinaemia) or represents a separate entity.

Method: Using a modified precipitation technique in hypo-ionic medium, we prospectively identified between 2008 and 2023 237 patients (median age 60.8 years [22-97], 137 females) having <0.5% cryocrit and clinical suspicion of autoimmune disorder.

Results: 54 out of 237 patients (22.7%) had a history of HCV infection. 169 out of 237 patients (71%) had an established underlying disease, while 68 patients (28.6%) (median age 62.9 years [29-93], 35 females) did not show either laboratory markers or clinical symptoms consonant with an underlying aetiology. These 68 cases with only trace amounts of cryoglobulins were defined as having a putatively idiopathic hypocryoglobulinaemia. Nineteen of these 68 patients (27.9%) had a history of HCV infection. Twenty-four patients out of 68 (35.3%) were positive for rheumatoid factor (RF), while 25 (36.7%) patients had signs of complement consumption, and 36 (52.9%) had increased inflammatory indexes. Seven patients only had arthralgia and constitutional symptoms while 61 out of 68 (89.7%) presented with at least one of the three cardinal signs of cryoglobulinaemia vasculitis including skin lesions, peripheral nerve involvement, and glomerulonephritis. Seventy-five percent of the subjects had type III hypocryoglobulins. In patients with hypocryoglobulinaemia the histologic features of glomerulonephritis (also examined by
electron microscopy) resembled those of mixed cryoglobulinemia-associated glomerulonephritis.

**Conclusion:** In conclusion, hypocryoglobulins are often polyclonal and are mainly unrelated to HCV infection. Patients who present high clinical suspicion for vasculitis, especially glomerulonephritis and yet test negative for cryoglobulinemia detected by standard techniques, could require deeper investigation even in the absence of HCV infection, RF activity or signs of complement consumption.

**#5390**

**INTENSIFIED B CELL DEPLETION THERAPY IN ANCA-VASCULITIS WITH SEVERE RENAL IMPAIRMENT AS COMPARED TO CONVENTIONAL IMMUNOSUPPRESSION**

Giorgio Amore, Martina Marchisio, Stefania Lalloni, Roberta Longo, Giovanni Geraci, Andrea Careddu, Roberta Fenoglio, Savino Sciascia and Dario Roccioletti

Torino, Italy

**Background and Aims:** Rituximab (RTX) has shown to be an effective induction treatment for small-vessel vasculitides associated with antineutrophil cytoplasm antibodies (AAV) in both newly diagnosed and relapsing patients. However, the role of RTX in the management of the most severe cases of AAV remains to be fully elucidated. The aim of this study was to assess both safety and efficacy of an intensified B-cell depletion therapy (IBCDT) protocol, including RTX, cyclophosphamide (CYC), and methylprednisolone pulses without additional maintenance immunosuppressive therapy in a cohort of 15 AAV patients with the most severe features of AVV renal involvement (as <15 ml/min GFR and histological findings of paucimmune necrotizing glomerulonephritis with more than 50% crescents of non-sclerotic glomeruli at the renal biopsy).

**Method:** Results of the IBCDT regimen have been compared to those obtained in a control cohort of 10 patients with AAV treated with a conventional therapy regimen based on oral CYC and steroids followed by a prolonged maintenance therapy with azathioprine (AZA). Plasma exchange was equally employed in the study and the control group.

**Results:** Complete clinical remission (BVAS 0) was observed at 6 months in 14 of 15 patients treated with IBCDT (93%). All cases who achieved a complete clinical remission experienced a depletion of peripheral blood B cells at the end of therapy. Of the 10 dialysis dependent patients at onset, 6 subjects (60%) experienced a functional recovery allowing the suspension of dialysis treatment. When compared to the control group, no statistically significant difference was observed in patients treated with IBCDT in terms of overall survival, 6-month therapeutic response rate, and 6- and 12-month functional renal recovery. The cumulative total dose of CYC in the case group was on average 1 g/patient while in the control group on average 8.5 g/patient (p = 0.00008).

**Conclusion:** Despite the retrospective design and relative limited sample size, IBCDT appeared to be safe and had the same efficacy profile when compared to the conventional therapy with CYC plus AZA in the management of the most severe patients with AAV. Additionally, this avoided the need of prolonged maintenance therapy for long, and limited the exposure to CYC with consequent reduced toxicity and drug-related side effect rates.

**#3858**

**ASSESSING THE EFFECTIVENESS OF LONG-TERM BELIMUMAB THERAPY IN LUPUS NEPHRITIS: A SINGLE-CENTRE OBSERVATIONAL STUDY**

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Hospital Universitario y Politécnico La Fe, Valencia, Spain

**Background and Aims:** Lupus nephritis (LN) is a major cause of morbidity and mortality in systemic lupus erythematosus (SLE). Belimumab, a monoclonal antibody that inhibits B-cell activating factor, has demonstrated efficacy in decreasing proteinuria, prevention of flares and achieving renal response after two years. However, data on its long-term efficacy is limited. The aim of this observational study is to assess the efficacy of belimumab in biopsy-proven LN patients over the medium and long term.

**Method:** In this retrospective observational study at our centre, patients with documented history of biopsy-proven LN who received belimumab were selected for analysis. Data on renal function, proteinuria (24 hours) and haematuria were collected. Immunologic activity (Anti-double-stranded-DNA, C3 and C4) was assessed. Data were retrieved at three moments: belimumab initiation, 12 months after the start of therapy and when treatment was discontinued. When treatment had not been discontinued, last available data was used. Renal flares were identified. The observational period was adjusted to be consistent between pre- and post-belimumab treatments. Clinically relevant outcomes such as possible adverse effects or major pathologic events were actively searched in patient records. Finally, the initiation of any additional antiproteinuric treatment was reported. Data analysis was performed using IBM SPSS Statistics 21©. When sample distributions were found to be normal, a parametric T-test was performed. An analysis of outcomes for patients receiving belimumab for more than 24 months was also performed.

**Results:** Seventeen patients diagnosed of LN between 1991 and 2021 began belimumab from 2014 to 2022, ten of whom received belimumab for more than 24 months. Mean treatment duration was 41.8 months. Patient characteristics are presented in Table 1, while analytic results are summarized in Table 2. A statistically significant decrease in proteinuria stands out 12 months after starting treatment with belimumab and a decrease in anti-dsDNA antibodies. As regards the subgroup of extended follow-up, results did not differ in hypothesis contrast tests. Overall, 17 renal flares were identified prior to belimumab initiation, while 9 flares were identified following its initiation (Fisher’s Exact Test: P = 0.092). A patient was diagnosed with acute bacterial meningitis, although the relationship to the drug is unclear since the patient was also receiving other immunosuppressive medications. This event did not lead to drug withdrawal. Only one patient started an angiotensin converting enzyme inhibitor (ACEI) immediately after initiating belimumab.

**Conclusion:** Currently, the optimal treatment duration with belimumab in LN is not known. Despite a decline in median GFR, results from this cohort of patients suggest a tendency to controlling proteinuria, haematuria and immunologic activity, over the middle and long term. A remarkable yet not significant decline in renal flares was observed. Finally, no relevant changes in immunosuppressive or antiproteinuric medication were made, allowing to avoid biases for this reason.

### Table 1

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#4006

**ADDING 6-MONTH PARAMETERS FOR THE PREDICTION OF RENAL PROGNOSIS IN ANCA-ASSOCIATED GLOMERULONEPHRITIS**

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**Background and Aims:** Anti-neutrophil-cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) with kidney involvement (AAV-GN) frequently evolves to end-stage kidney disease (ESKD) despite aggressive immunosuppressive treatment. Several risk scores have been used to assess renal prognosis.

We aimed to determine whether kidney function and markers of AAV-GN activity after 6 months could improve the prediction of ESKD. **Method:** This retrospective and observational study included adult patients with AAV-GN recruited from 6 French nephrology centers (including from the Maine-Anjou AAV registry). The primary outcome was kidney survival. Analyses were conducted in the whole population and in a sub-population that did not develop ESKD early in the course of the disease. **Results:** 241 patients were included in the whole cohort, with a median follow-up of 59 months. At diagnosis, Berden classification and Renal Risk Score (RRS) were not found better than kidney function (eGFR) alone, at predicting ESKD (C-index = 0.70, 0.79, 0.82, respectively). At 6 months, 20 patients reached ESKD. In the sub-population of 221 patients, 6 months eGFR outperformed Berden classification and RRS (C-index = 0.88, 0.62, 0.69, respectively) to predict ESKD. RRS performed better when it was updated with the eGFR at 6 months instead of the baseline eGFR. While 6-months proteinuria was associated with ESKD and improved ESKD prediction, hematuria and serological remission did not. **Conclusion:** This work suggests the interest of the reassessment of the renal prognosis 6 months after AAV-GN diagnosis. Kidney function at this time remains the most reliable for predicting renal outcome. To improve the long-term prediction of ESKD, there may be a place for repeated kidney biopsy following induction treatment, in order to obtain a precise evaluation of disease activity, discuss the immunosuppressive treatment strategy and improve prognosis scores.
DEVELOPMENT AND VALIDATION OF A PREDICTIVE MORTALITY SCORE IN ANCA-ASSOCIATED VASCULITIS WITH KIDNEY INVOLVEMENT

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Background and Aims: Several scores (FFS, JVAS, MVIA, Maldini, NLR, SIRI, PIIVUT and CAR scores) have been developed to predict mortality at ANCA-Associated Vasculitis (AAV) diagnosis. The validity of these scores in AAV with kidney involvement (AAV-KI) remains uncertain. We aimed to evaluate their prognostic value in a large cohort of AAV-KI and to develop and validate a novel and more accurate mortality risk model.

Method: This multicentric retrospective study included patients newly diagnosed with ANCA-KI between January 2000 and January 2021 in 4 nephrology departments (Maine-Anjou Registry). Scores were assessed at diagnosis before any therapeutic intervention. Clinical, biological and histological characteristics at diagnosis were retrieved. A multivariate analysis was performed to determine 2 new predictive models for death. The diagnosis performance (AUROC and C-index) and accuracy (Brier score) of existing scores and the newly developed models were assessed. The RENVAS registry was used as a validation cohort.

Results: Among the 228 patients with AAV-KI included in the registry, 194 had all the data available to determine each score performance. Among all existing scores of the literature, only FFS and JVAS had overall good performances to predict death in AAV-KI. After multivariate analysis, two new models were built, and considered 4 components: age, history of diabetes or hypertension, early need for kidney replacement therapy or eGFR, and hemoglobin level at diagnosis. These models were found to perform better and to be more accurate than the existing scores. Similar results were found using an external validation cohort of 186 patients with AAV-KI.

Conclusion: These novel risk prediction models may be useful to predict the risk of death in AAV-GN patients, with better predictive value than existing scores. It remains to be established, however, whether these new models could be used to assist clinical decisions.
Background and Aims: Currently, the precise mechanism of myeloperoxidase-anti-neutrophil cytoplasmic antibody associated glomerulonephritis (MPO-ANCA-GN) remains elusive. And there is a lack of dependable biomarkers for evaluating disease activity, therapeutic resistance, and risk of relapse. We try to seek valuable biomarkers and explore the mechanism of MPO-ANCA-GN by metabolomics.

Method: Urine and plasma samples from 63 MPO-ANCA-GN, 31 lupus nephritis (LN), 15 IgA nephropathy (IgAN), and 15 minimal change disease (MCD) patients and 30 HC were collected for metabolomics analysis. The samples were analyzed using Ultra Performance Liquid Chromatography (UPLC) and Tandem mass spectrometry (MS/MS). The different groups of samples were compared using Partial Least Squares-Discriminant Analysis. A Receiver Operator Characteristic (ROC) curve was constructed to assess the performance of the metabolite model in identifying active renal vasculitis.

Results: All metabolites in urine and plasma samples including hydrophilic compounds and hydrophobic compounds were identified. Compared with the disease control (DC) and HC, we observed 79 significantly upregulated metabolites (VIP > 1, FDR < 0.05, FC > 1.5) and 32 downregulated metabolites (VIP > 1, FDR < 0.05, FC < 0.67) in the plasma samples of MPO-ANCA-GN patients. KEGG enrichment analysis suggested that these upregulated metabolites were mainly associated with phenylalanine metabolism and galactose metabolism and downregulated metabolites were mainly associated with bile secretion, steroid biosynthesis, and ovarian steroidogenesis. Compared with the DC and HC, we identified a total of 122 differential metabolites in the urine samples of MPO-ANCA-GN patients, 40 of which were significantly upregulated (VIP > 1, FDR < 0.05, FC > 1.5) and 68 of which significantly were downregulated (VIP > 1, FDR < 0.05, FC < 0.67). Subsequently, KEGG analysis revealed that these upregulated metabolites were mainly enriched in glycerolipid metabolism, lipid and atherosclerosis, cholesterol metabolism, insulin resistance, regulation of lipolysis in adipocytes, vitamin digestion and absorption, fat digestion and absorption (Corrected P < 0.05). Downregulated metabolites were mainly enriched in steroid hormone biosynthesis (Corrected P < 0.05).

Nine MPO-ANCA-GN patients with paired plasma and six MPO-ANCA-GN patients with paired urine during the active and remission phase were included in the study. A total of 504 differential metabolites in plasma samples were identified between the active and remission phase based on VIP value > 1, P < 0.05, and FC > 1.5 or FC < 0.6. Of these, 425 metabolites were downregulated, while 79 lipid metabolites were upregulated in the active group. MPO-ANCA-GN patients were divided into two groups according to Mayo Clinic/Renal Pathology Society Chronicity Score: Minimal-mild group and Moderate-severe group. In plasma samples, our data showed that 3-Methoxysalicylic Acid, Carnitine C20:5, and isoanxanthopterin presented good ability in distinguishing between the minimal-mild group and the moderate-severe group, with an AUC > 0.7. In urine samples, cyclohexylamine and arachidonic acid (AUC > 0.8) can distinguish the two groups well. Conclusion: We identified many novel potential metabolic biomarkers in urine and plasma samples for evaluating disease activity, therapeutic resistance, and risk of relapse in patients with MPO-ANCA-GN.
Figure 1: A) Lobulated glomerulus with membranoproliferative pattern due to severe endocapillary and mesangial proliferation (H&E 40x). B) Immunofluorescence showing bright glomerular C3 staining within mesangium and along capillary walls. (20x).
HERPES ZOSTER IN LUPUS NEPHRITIS: AN UNDERESTIMATED COMPLICATION
Francesco Reggiani¹,², Silvia Cardi¹, Fabio Tumminello¹, Marta Calatroni¹,² and Gabriella Luisa Moroni²
¹Humanitas University, Italy and ²Humanitas Research Hospital, Cascina Perseghetto, Italy

Background and Aims: Herpes zoster (HZ) is a known complication of lupus nephritis (LN) because of the drug-related immunosuppression. In fact, high dose corticosteroids (CS) and immunosuppressive (IS) therapy are almost always used in this setting. Our aim is to evaluate the predisposing factors for the development of HZ in patients with LN.

Method: Retrospective cohort study on 292 LN patients. Demographic and clinical data are expressed as numbers or percentages in case of discrete variables, whereas, in case of continuous variables, they are expressed as median and interquartile range (IQR). The demographic characteristics have been analyzed with Mann-Whitney U test and Fisher’s test where appropriate. A univariate and multivariate logistic regression has been performed to identify potential risk factors.

Results: The incidence of HZ in our cohort is 22.6% (66/226). The patients’ characteristics are shown in Table 1. HZ patients are older (54 vs 45 yo, p<0.001). No differences were found in the clinical characteristics at LN diagnosis, except for higher chronicity index in HZ patients (2 vs 1, p = 0.03). No difference was found in the initial IS therapy. Higher cumulative dose of CS was used in patients with HZ (48.9 vs 21.5 grams, p<0.0001). At univariate and multivariate logistic regression (Table 2) age, female sex, the presence of a proliferative form at renal biopsy (class III or IV) and cumulative CS dose greater than 100 grams are linked to a higher risk for HZ.

Conclusion: Incidence of HZ in our LN cohort is high (22.6%). HZ patients are older, while non-significative differences in clinical presentation or initial IS therapy are present. Age, female sex, the presence of a proliferative form at biopsy and greater cumulative CS dose seems to be a risk factor for HZ development in LN patients. According to these data and to the possible evolution of HZ infection in disseminated forms, HZ vaccination should be strongly recommended in LN patients.
Table 1: Characteristics of the patients.

<table>
<thead>
<tr>
<th></th>
<th>HZ pts (n = 66)</th>
<th>Controls (n = 226)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>54 (IQR 41-64)</td>
<td>45 (IQR 37-54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Sex (female)</strong></td>
<td>92.4% (61/66)</td>
<td>88.5% (199/226)</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Histological Class</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proliferative forms (III &amp; IV)</td>
<td>81.0% (51/63)</td>
<td>74.9% (158/211)</td>
<td>0.62</td>
</tr>
<tr>
<td>Non proliferative forms (II &amp; V)</td>
<td>19.0% (12/63)</td>
<td>25.1% (53/211)</td>
<td></td>
</tr>
<tr>
<td><strong>Activity index</strong></td>
<td>6 (IQR 3-10)</td>
<td>6 (IQR 3-9)</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>Chronicity index</strong></td>
<td>2 (IQR 1-4)</td>
<td>1 (IQR 0-3)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Creatinine (mg/dL)</strong></td>
<td>0.9 (IQR 0.7-1.4)</td>
<td>0.9 (IQR 0.7-1.3)</td>
<td>0.91</td>
</tr>
<tr>
<td><strong>Proteinuria (g/24h)</strong></td>
<td>4.0 (IQR 3.8-5.3)</td>
<td>3.2 (IQR 2.0-5.4)</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>WBC (n/mmc)</strong></td>
<td>5800 (IQR 4100-7600)</td>
<td>5600 (IQR 3900-7490)</td>
<td>0.63</td>
</tr>
<tr>
<td><strong>C3 (mg/dL)</strong></td>
<td>54.0 (IQR 46.0-73.0)</td>
<td>58.5 (IQR 48.0-79.0)</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>C4 (mg/dL)</strong></td>
<td>11.0 (IQR 5.5-14.6)</td>
<td>1.8 (IQR 5-18.0)</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>IS at induction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>54.7% (29/53)</td>
<td>47.7% (83/174)</td>
<td>0.11</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>5.7% (3/53)</td>
<td>15.5% (27/174)</td>
<td></td>
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<tr>
<td>Mycophenolate</td>
<td>18.9% (10/53)</td>
<td>24.7% (43/174)</td>
<td></td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>9.4% (5/53)</td>
<td>3.5% (6/174)</td>
<td></td>
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<tr>
<td>Rituximab</td>
<td>11.3% (6/53)</td>
<td>8.6% (15/174)</td>
<td></td>
</tr>
<tr>
<td><strong>Cumulative CS dose (grams)</strong></td>
<td>48.9 (IQR 20.6-87.3)</td>
<td>21.5 (IQR 10.4-45.5)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 2: Univariate and multivariate logistic regression.

<table>
<thead>
<tr>
<th></th>
<th>Univariate logistic regression</th>
<th>Multivariate logistic regression</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>1.032</td>
<td>1.013</td>
</tr>
<tr>
<td><strong>Sex (female)</strong></td>
<td>1.655</td>
<td>0.611</td>
</tr>
<tr>
<td>Proliferative form at renal biopsy</td>
<td>1.426</td>
<td>0.707</td>
</tr>
<tr>
<td><strong>Activity index</strong></td>
<td>1.01</td>
<td>0.948</td>
</tr>
<tr>
<td><strong>Chronicity index</strong></td>
<td>1.028</td>
<td>0.791</td>
</tr>
<tr>
<td><strong>Creatinine</strong></td>
<td>0.966</td>
<td>0.884</td>
</tr>
<tr>
<td><strong>Proteinuria</strong></td>
<td>5.510</td>
<td>2.008</td>
</tr>
<tr>
<td><strong>Cumulative CS dose &gt; 100 grams</strong></td>
<td>48.9 (IQR 20.6-87.3)</td>
<td>21.5 (IQR 10.4-45.5)</td>
</tr>
</tbody>
</table>

Abstracts
Anti-PLA2R antibodies were negative in all three cases. Tissue samples from patients 1 and 2 were positive for FAT1 antigen using laser microdissection and tandem mass spectrometry (MS/MS) of glomeruli. The third patient was negative for FAT1. Clinical and biopsy findings in our cohort of HSCT-associated MN are summarised in Tables 1 and 2.

**Conclusion:** MN can occur at different points in time, sometimes even years, after HSCT. It can be successfully treated with steroids and immunosuppressants, achieving long-term remission. Most patients with HSCT-associated MN are FAT1-positive, although it is not the only antigen associated with MN in HSCT patients. In the future, serum testing for anti-FAT1 antibodies in patients with HSCT could be of similar significance in diagnosing FAT1-associated MN as PLA2R antibodies are for PLA2R-associated MN.

**REFERENCES**

BACKGROUND AND AIM: Urinary albumin:creatinine ratio (UACR) is an important biomarker of active glomerulonephritis, a common complication of antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis. In most glomerular diseases, high UACR levels and low estimated glomerular filtration rates are associated with the long-term risk of end-stage kidney disease, cardiovascular disease, and death.[1] In the double-dummy, double-blind, controlled ADVOCATE Phase 3 trial, patients were randomized to receive avacopan, an oral C5a receptor (C5aR) antagonist that blocks C5a-mediated neutrophil activation and migration, or a prednisone taper. All patients received background immunosuppression with either cyclophosphamide followed by azathioprine, or rituximab. Primary endpoints were remission at week 26 and sustained remission at week 52. Prespecified secondary endpoints included the evaluation of kidney function.[2] The effect of avacopan on UACR in patients with ANCA-associated vasculitis is described.

METHOD: This post hoc analysis compared the time to achieve the maximum mean difference in percent change in UACR from baseline between the avacopan and prednisone taper groups using Kaplan-Meier survival analysis. Change in UACR from baseline was a prespecified secondary endpoint but was not adjusted for multiplicity. This analysis included patients from the ADVOCATE trial with kidney involvement (based on the Birmingham Vasculitis Activity Score) and a UACR of at least 10 mg/g at baseline.

RESULTS: The baseline geometric mean UACR mg/g (range) in the avacopan group (n = 125) and the prednisone taper group (n = 128) was 433 (20 to 6461) and 312 (11 to 5367), respectively. A statistically significant UACR reduction (based on least-square means) in the avacopan group compared to the prednisone taper group occurred as early as week 2 (−25% vs. 6%, p = 0.0068, difference between groups: −29%, 95% confidence interval (CI) [−45%, −9%]). UACR continued to decrease at week 4 to the maximum difference between the two groups (−40% vs. 0%, p < 0.0001, difference between groups: −40%, 95% CI [−53%, −22%]) (Figure 1). UACR was
comparable between the two groups by week 13 (−55% vs. −49%, \( p = 0.3028 \), difference between groups: −12%, 95% CI [−32%, 13%]). During the 52-week treatment period, 84% (105/125) of patients in the avacopan group achieved a 40% UACR reduction from baseline within a median time of 29 days (95% CI [29, 88]), compared to 83% (106/128) of patients in the prednisone taper group within a median time of 92 days (95% CI [91, 180]) (logrank \( p = 0.0450 \)) (Figure 2). At week 52, there was a greater overall mean improvement in estimated glomerular filtration rate (eGFR) of 7.6 mL/min/1.73 m² in the avacopan group compared to 4.6 mL/min/1.73 m² in the prednisone taper group (\( p = 0.0432 \)).

**Conclusion:** In the ADVOCATE trial, UACR, an important early indicator of improving kidney function, improved three times faster in the avacopan group compared to the prednisone taper group. The rapid reduction in UACR seen in patients with ANCA-associated vasculitis receiving avacopan suggests more

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**Figure 1:** Percent Change in UACR from Baseline in the Avacopan vs Prednisone Taper Groups in Patients with Kidney Involvement and UACR ≥ 10 mg/g.

**Figure 2:** Time to 40% Reduction Urinary Albumin:Creatinine Ratio (UACR) in the Avacopan vs Prednisone Taper Groups.
rapid control of glomerular inflammation which may have contributed to the observed subsequent greater improvement in eGFR.

REFERENCES


#3523

**EFFECT OF IMMUNOSUPPRESSIVE TREATMENTS ON RENAL OUTCOMES AFTER GROSS HEMATURIA-RELATED ACUTE KIDNEY INJURY IN IGA NEPHROPATHY**

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**Background and Aims:** Macroscopic hematuria bouts are one of the most characteristic presentations of IgA nephropathy (IgAN). Acute kidney injury (AKI) is a well-known complication of these episodes of gross hematuria. Although the first descriptions of AKI associated with macroscopic hematuria (AKI-MH) reported a good prognosis in young patients, more recent studies have shown that a substantial number of adult and elderly patients with this unique type of IgAN did not completely recover their baseline kidney function after AKI-MH. Although guidelines recommend a conservative approach for AKI-MH, immunosuppressive therapy (IT) is frequently used in real-world clinical practice. Aim of this study was to analyse the influence of different therapeutic strategies (immunosuppressive or conservative) on kidney function recovery after an episode of biopsy-proven AKI-MH in IgAN patients 40 years.

**Method:** Retrospective study including 91 IgAN patients from 17 nephrology departments who presented with AKI-MH. Secondary types of IgAN and IgA vasculitis were excluded. All the patients had at least one measurement of serum creatinine (Scr) and eGFR before AKI-MH. Kidney function recovery after AKI-MH was defined by the ratio between Scr at a given time after AKI-MH and the last determination of Scr before AKI-MH onset (baseline Scr). No recovery was defined by a Scr > 75% of baseline Scr or the need of kidney replacement therapy (KRT); partial recovery by a Scr <75% and ≥25% of baseline Scr; and complete recovery by a Scr <25% of baseline Scr. End stage kidney disease (ESKD) was defined by an eGFR <15 ml/min/1.73 m² or KRT. Outcomes were the proportion of patients with complete, partial or no recovery of kidney function at 6 and 12 months after MH-AKI and kidney survival (defined as a status free of ESKD or death) at 1, 2 and 5 years and at the end of follow-up. Follow-up was 59±36 months.

**Results:** Mean age was 65±16 years and 72 patients (79%) were men. Mean Scr and eGFR before AKI-MH were 1.2±0.47 mg/dL and 65±24.9 mg/min/1.73 m², respectively, and 37 patients (41%) had CKD (eGFR <60 mg/min/1.73 m²) at baseline. Mean Scr and eGFR at presentation were 4.3±2.8 mg/dL and 19.3±13.4 mg/min/1.73 m², respectively. Thirty-two patients (35%) required acute dialysis at presentation. The most remarkable histological lesions were intratubular erythrocyte casts and tubular necrosis in all the patients. In addition, mesangial proliferation was found in 64%, endocapillary hypercellularity in 25%, segmental glomerulosclerosis in 41%, T1-T2 tubular atrophy/intertubular fibrosis in 33% and crescents in 4%. Sixty-nine patients (76%) were treated with renin-angiotensin blockers. It was prescribed to 52 (57%) patients: corticosteroids alone in 32 (61%), corticosteroids plus mycophenolate in 12 (23%) and corticosteroids plus cyclophosphamide in 8 (15%). Treated patients were significantly older (69.4±20.1 vs 59.9±20.1; p = 0.01), required acute dialysis in a greater proportion (46% vs 20%; p = 0.01) and had more glomerulosclerosis (51% vs 28%; p = 0.02) than non-treated patients. No differences were found in other clinical or histological parameters. There were no significant differences between treated and not treated patients in the number of cases with complete, partial or no recovery of kidney function at 6 months (25%, 33% and 42% vs 26%, 20% and 54% respectively) and 12 months (28%, 30% and 40% vs 35%, 20% and 43% respectively). Kidney survival at 1, 3, 5 years was similar among treated (75.6%, 52%, respectively) and not treated patients (76%, 68%, 50%, respectively). Adverse events occurred in 27% of IT patients: infections (7 patients), diabetes mellitus and cytopenia (2) and vertebral collapse (1). At the end of follow-up, 27 patients (30%) had developed ESKD, with no differences between treated and untreated, and 17 patients had died, 10 among treated patients and 7 among untreated cases.

Conclusion: Prognosis is very poor in IgAN patients > 40 years who present with AKI-MH. IT does not change this unfavorable prognosis, so new therapeutic alternatives are needed.

#4760

**LUPUS NEPHRITIS RELAPSE AFTER IMMUNOSUPPRESSION WITHDRAWAL: A SPANISH MULTICENTER STUDY**

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1San Carlos University Clinical Hospital, Nephrology, Madrid, Spain, 2Virgen del Rocio Hospital, Spain, 3Dr Peset Hospital, Spain, 4Vall d’Hebron University Hospital, Spain, 512 Octubre Hospital, Spain, 6Gregorio Marañon Hospital, Spain, 7Carlos Haya Hospital, Spain, 8La Paz Hospital, Spain and 9Poniente Hospital, Spain

**Background and Aims:** In lupus nephritis (LN), therapeutic schemas for remission induction are well known but data about duration of maintenance treatment are limited. There is no agreement between clinical practice guidelines about duration and withdrawal of therapy, and literature regarding this topic is scarce. Recently, a RCT has observed that immunosuppression discontinuation after 2–3 years was related to LN relapse when compared with immunosuppression maintenance. However, immunosuppressive agents are related to severe adverse events and toxicity. We conducted this study with the aim to evaluate the incidence of LN relapse in a cohort of patients with discontinuation of immunosuppressive treatment after a first LN flare. We also aimed to determine factors associated to the presence of renal relapse in this population.

**Method:** Multicenter retrospective observational study including patients with biopsy proven LN who have received immunosuppressive treatment that was subsequently discontinued. Patients on prednisone at doses lower than 5 mg per day were allowed to be included. Patients were diagnosed between 1990 and 2018. The study was conducted in Spain. Relapse was defined according to Malvar et al criteria.

**Results:** 113 patients were included, mean age was 34.1±14.56 years-old and 85.8% were women. Serum creatinine at the time of LN diagnosis was 1.09±0.63 mg/dL, and proteinuria 3.16±2.53g/24h, ANA were positive in 85.4%, and anti-DNA Abs in 69.91%. Serum C3 and C4 levels were 72.51±44.06 and 13.04±11.27 respectively. 55.7% presented with class IV LN, 12.39% with class III or IV LN, and 8.85% with class II. Mixed forms were less frequent. In a follow up period of 172.53±162.95 months, 17.7% (n = 20) presented a renal flare after immunosuppressive drugs withdrawal. Time from LN to relapse was 89.05±39.87 months, and time from immunosuppression discontinuation to relapse was 37.75±32.13 months. There were no differences in baseline characteristics between patients who relapsed and patients who did not, neither in histologic characteristics at the time of LN diagnostic biopsy except for glomerulosclerosis, that was less frequent in the relapse group (20% vs 34.41%, p = 0.0435). However, a tendency to a shorter time under immunosuppression in patients who relapsed was observed (73.55±78.06 vs 110.79±206.87 months). Data about treatment withdrawal in each group are summarized in Figure 1. Interestingly, there were no differences between both groups in steroids withdrawal (75% vs 78.49%, p = 0.7327) and hydroxychloroquine withdrawal (33.33% vs 21.74%, p = 0.3933). At the time of immunosuppression discontinuation, patients who relapsed presented lower serum C3 and C4 levels (78.79±24.89 vs 112.26±35.52, p = 0.0080 and 13.82±6.07 vs 23.09±12.56, p = 0.0333), but there were no differences in terms of renal function at this moment. At the end of follow up, patients who relapsed presented more albuminuria (227.87±259.79 vs 78.65±24.77, p = 0.0289) but creatinine levels were similar in both groups (0.84±0.30 vs 0.84±0.30, 0.530). Only one patient died and two patients required renal replacement therapy, all in the no relapse group.

**Conclusion:** In a cohort of 113 patients with biopsy proven LN who were treated con immunosuppression and subsequently discontinued, 17.7% presented renal relapse at a mean time of 37 months after withdrawal. There was a tendency to a short time on immunosuppressive regimens in patients who relapsed. Also, lower serum C3 and C4 levels at the time of immunosuppression withdrawal were associated to renal relapse. At the end of a follow up of 14 years, patients who relapsed those who did not showed a similar maintained renal function but those who relapsed presented lower albuminuria.
Background and Aims: Macrophage Migration Inhibitory Factor (MIF) is a pleiotropic inflammatory cytokine and a primary counter-regulator of glucocorticoids (GCs) that emerged as a pivotal regulator of immune-mediated disorders including glomerulonephritis (GN). MIF occurs in two immunologically distinct, conformational isoforms: reduced MIF, ubiquitously present in various tissues and the circulation of healthy subjects, and oxidized MIF (oxMIF), described as the pathogenic and druggable isoform of MIF [1]. We previously reported a positive correlation between disease severity and urinary oxMIF levels in patients with acute lupus nephritis, suggesting oxMIF contribution to kidney damage [2]. In this study we evaluated the anti-inflammatory effects of oxMIF neutralization using ON104 antibody during crescentic GN.

Method: By advanced antibody engineering we generated the fully human antibody ON104 that is specific and highly affine for human oxMIF and its orthologs. ON104 was tested for its therapeutic potential in a rodent model of GN. Nephritis was induced in male WYK rats by a single intravenous (i.v.) injection of rabbit anti-rat GBM (glomerular basement membrane) serum. On day 4 and day 6 after GN induction, ON104 was administrated intraperitoneally (i.p.). Body weight, proteinuria, and hematuria were assessed.

Results: Treatment with ON104 substantially attenuated clinical signs of GN by preserving kidney function demonstrated by reduced proteinuria, and reduced hematuria. Furthermore, ON104 significantly reduced tissue injury, reduced crescentic glomerulus formation, and increased the percentage of normal glomeruli. On the cellular level, oxMIF neutralization by ON104 reduced CD68+ macrophage accumulation within the inflamed kidneys compared to untreated and isotype Ig-treated rats.

Conclusion: Our findings substantiate the role of oxMIF in the pathogenesis of experimental GN. Thus, targeting oxMIF may represent a new and promising treatment option for kidney diseases.

#6547
ON104, A NOVEL BIOENGINEERED ANTIBODY TARGETING OXIDIZED MACROPHAGE MIGRATION INHIBITORY FACTOR (OXMIF) AMELIORATES EXPERIMENTAL GLOMERULONEPHRITIS

Maroua Ferhat1, Randolph Kerschbaumer1, Frederick Tam2, Maria Prendecki1, Lyndon Costa2, Michael Thiele1 and Christine Landlinger1

1 OncoOne Research & Development GmbH, Vienna, Austria and 2 Imperial College London (ICL), Centre for Inflammatory Disease, London, United Kingdom

Background and Aims: Macrophage Migration Inhibitory Factor (MIF) is a pleiotropic inflammatory cytokine and a primary counter-regulator of glucocorticoids (GCs) that emerged as a pivotal regulator of immune-mediated disorders including glomerulonephritis (GN). MIF occurs in two immunologically distinct, conformational isoforms: reduced MIF, ubiquitously present in various tissues and the circulation of healthy subjects, and oxidized MIF (oxMIF), described as the pathogenic and druggable isoform of MIF [1]. We previously reported a positive correlation between disease severity and urinary oxMIF levels in patients with acute lupus nephritis, suggesting oxMIF contribution to kidney damage [2]. In this study we evaluated the anti-inflammatory effects of oxMIF neutralization using ON104 antibody during crescentic GN.

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Conclusion: Our findings substantiate the role of oxMIF in the pathogenesis of experimental GN. Thus, targeting oxMIF may represent a new and promising treatment option for kidney diseases.

REFERENCES


#3053
CORRELATION OF SYSTEMIC AND IN SITU BIOMARKERS OF COMPLEMENT ACTIVATION WITH HISTOPATHOLOGICAL FEATURES AND PROGNOSIS IN C3 GLOMERULOPATHY

Marie-Sophie Meuleman1, Florent Petitprez2, Anna Duval1, Veronica Fremeaux Bacchi1, Jean-Paul Duong Van Huyen1 and Sophie Chauvet1

1 Centre de Recherche des Cordeliers, Paris, France, 2 Queen’s Medical Research Institute, United Kingdom and 3 Necker Hospital, Paris, France

Background and Aims: C3 glomerulopathy is a rare complement mediated disease, resulting from complement alternative pathway (AP) activation. In addition to AP activation, there are emerging evidence for terminal pathway (TP) implication in kidney damage. A C3G histopathologic index has recently been proposed to evaluate both activity and chronicity parameters. Only a chronicity index > 4 has been independently validated as prognosis factor for end stage kidney disease. We aimed to determine the impact of local activation of the TP on disease phenotype.

Method: C3G histopathological index grading were evaluated via central review of 53 kidney biopsies from 43 patients carrying C3G. C5b-9 staining was performed on 53 FFPE kidney sections and quantified (scoring from grade 0 to 3 for C5b-9 deposits in glomeruli and from 0 to 2 in the tubulointerstitial compartment). Clinical data, C3 and sC5b-9 levels at the time of KB were retrospectively collected.

Results: KB were performed at diagnosis for n = 31. In 22 cases, KB was performed during follow up, under specific treatment (n = 10), without treatment (n = 7), or at disease relapse (n = 5). Twenty-five (47%) were children. Median (Q1-Q3) C3 level at KB was 623 mg/L [236-931] mg/L. Median (Q1-Q3) sC5b-9 level at KB, available in 16, was 374 ng/ml [203-1295]. Median (Q1-Q3) activity and chronicity index were respectively 9[6-12] and 1[0-6]. We confirmed the prognostic impact of chronicity index (p = 0.03) (Figure 1A) without impact of the activity index. Glomerular C5b-9 staining was positive in 47/53 (87%) (grade 1: n = 16 (30%); 2: n = 17 (32%); 3: n = 14 (26%)) and n = 40 (75%) had interstitial C5b-9 staining (grade 1: n = 28 (53%); 2: n = 12 (23%)). Soluble C5b-9 measurement correlated with intensity of C5b-9 glomerular deposit (cof corr = 0.69). As compared to patients with normal C3 level, patients with AP activation had higher proteinuria but kidney function at KB was similar. We found distinct histological features according to C3 plasmatic level (Table 1): patients with low C3 level had higher histological activity index (p = 0.03) and higher glomerular and tubulointerstitial C5b-9 staining (p = 0.001 and p = 0.002 respectively). C5b-9 glomeruli staining allows the identification of 3 groups of KB (1: no or low, 2: medium and 3: high C5b-9 staining) with distinct histological and clinical features. Activity index were higher in groups 2 & 3 (p = 0.05) and chronicity index in groups 1 & 3 (p = 0.003) (Table 2). Renal prognosis was poorer in patients with higher glomerular C5b-9 deposits (Figure 1B). Patients with chronicity index >4 and high C5b-9 staining had the poorest renal survival (Figure 1C).

Figure 1:
Table 1: Histological findings and clinical presentation at the time of KB according to C3 plasma level.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Normal C3</th>
<th>Low C3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>25</td>
<td>28</td>
<td>0.17</td>
</tr>
<tr>
<td>Children n(%)</td>
<td>15 (60)</td>
<td>11 (39)</td>
<td></td>
</tr>
<tr>
<td>eGFR at KB (ml/min/1.73m²) m</td>
<td>65 [22, 100]</td>
<td>63 [35, 102]</td>
<td>0.4</td>
</tr>
<tr>
<td>Proteinuria at KB (g/g) m</td>
<td>3 [1, 5]</td>
<td>4 [3, 6]</td>
<td>0.05</td>
</tr>
<tr>
<td>Activity index (/21) m</td>
<td>7 [4, 10]</td>
<td>10 [7, 12]</td>
<td>0.03</td>
</tr>
<tr>
<td>Chronicity index (/10) m</td>
<td>0 [0, 5]</td>
<td>2 [0, 6]</td>
<td>0.15</td>
</tr>
<tr>
<td>Glomerular C5b-9 grade 2 &amp; 3 n(%)</td>
<td>8 (32)</td>
<td>23 (82)</td>
<td>0.001</td>
</tr>
<tr>
<td>Tubulointerstitial C5b-9 n(%)</td>
<td>14 (56)</td>
<td>25 (94)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Conclusion: Our results suggest that TP activation in glomeruli may have an impact on histological features, contributing therefore to renal prognosis. Deeper exploration of correlation between systemic and in situ complement activation and histological features could allow to better identify patients with worst prognosis or who could benefit from emerging complement inhibition therapeutics.

Table 2: Histological findings and clinical presentation at KB according to glomerular C5b-9 staining.

<table>
<thead>
<tr>
<th>C5b-9 Groups</th>
<th>No/Low</th>
<th>Medium</th>
<th>High</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>22</td>
<td>17</td>
<td>14</td>
<td>0.001</td>
</tr>
<tr>
<td>Children n(%)</td>
<td>9 (41)</td>
<td>14 (82.4)</td>
<td>2 (14.3)</td>
<td>0.718</td>
</tr>
<tr>
<td>eGFR at KB (ml/min/1.73m²) m</td>
<td>57 [29, 93]</td>
<td>96 [24, 100]</td>
<td>47 [28, 92]</td>
<td>0.133</td>
</tr>
<tr>
<td>Proteinuria at KB (g/g) m</td>
<td>3 [1, 6]</td>
<td>4 [3, 6]</td>
<td>4 [3, 6]</td>
<td>0.001</td>
</tr>
<tr>
<td>C3 at KB (mg/l) m</td>
<td>932 [681, 1.120]</td>
<td>619 [214, 829]</td>
<td>206 [156, 492]</td>
<td>0.05</td>
</tr>
<tr>
<td>Activity index (/21) m</td>
<td>6 [4, 10]</td>
<td>11 [7, 12]</td>
<td>10 [7, 11]</td>
<td>0.003</td>
</tr>
<tr>
<td>Chronicity index (/10) m</td>
<td>4 [0, 6]</td>
<td>0 [0, 1]</td>
<td>5 [1, 7]</td>
<td>0.003</td>
</tr>
</tbody>
</table>
TRAINED INNATE IMMUNITY IN RESPONSE TO NUCLEAR ANTIGENS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Nils Rother1, Cansu Yarginlar1, Tomas Post1, Maaike Jacobs1, Inge Jonkman1, Montsy Brouns2, Maarten van der Sande1, Sybren Rinzema3, Joost Martens3, Michiel Vermeulen3, Leo Joosten1,4, Mihai Netea4, Luuk Hilbrands1, Zaheeb Choudry2, Johan Van Der Vlag1 and Raphael Duivenvoorden1

1Radboud University Nijmegen, Nijmegen, Netherlands, 2Horacio Oduber Hospital, Oranjestad, Aruba, 3Radboud University Nijmegen, Nijmegen, Netherlands and 4Radboud University Medical Center, Internal Medicine, Nijmegen, Netherlands

Background and Aims: Systemic lupus erythematosus (SLE) is an autoimmune disease directed against nuclear antigens, including those derived from apoptotic microparticles (MPs) and neutrophil extracellular traps (NETs). Innate immune cells display an hyperreactive phenotype in patients with SLE, with increased expression of immunostimulatory surface markers and increased production of proinflammatory cytokines. We hypothesize that the hyperreactive phenotype of innate immune cells in SLE is caused by the induction of trained immunity. Trained immunity is a de facto innate immune memory elicited by an initial stimulus that induces metabolic and epigenetic changes and results in a more vigorous inflammatory response to subsequent stimuli. Here we aim to investigate whether nuclear autoantigens derived from MPs and NETs can induce trained immunity in SLE patients.

Method: To investigate the capability of MPs and NETs to induce trained immunity we stimulated healthy PBMCs with isolated NETs and MPs or with plasma from SLE patients for 24 hours, washed and rested the cells for five days. Cells were restimulated with lipopolysaccharide (LPS) and Pam3CSK4. To test the activation status of innate immune cells, PBMCs were isolated from patients with SLE and healthy controls and stimulated the cells with different TLR agonists. Cytokine production was measured using ELISA. Immune cell subsets in SLE patients were analyzed by flow cytometry. We performed RNA sequencing and Chromatin immunoprecipitation (ChIP) sequencing for histone 3 lysine 4 trimethylation (H3K4me3) on monocytes from SLE patients and healthy controls.

Results: We found that in vitro both MPs and NETs, as well as plasma from SLE patients, can induce trained immunity. Initial stimulation with MPs, NETs or SLE plasma resulted in increased production of Tumor necrosis factor (TNF) and Interleukin (IL) 6 upon restimulation with different TLR agonists. Assessment of circulating immune cells showed higher percentages of monocytes in SLE patients compared to healthy controls, and we found that circulating monocytes from SLE patients produce increased levels of pro-inflammatory cytokines (IL-6, IL-1ß, TNF) after stimulation with Toll-like receptor agonists, indicating trained immunity. This is accompanied by increased expression of metabolism and inflammation-related genes, underscoring the hyperreactive phenotype typical in trained innate immune cells. Epigenetic analysis of monocytes revealed major changes in H3K4me3, an epigenetic mark associated with trained immunity.

Conclusion: Our findings provide new insight into the pathogenesis of SLE by showing that trained immunity can be elicited by SLE-related antigens present in MPs and NETs, and demonstrating that circulating monocytes from SLE patients have a trained immunity phenotype. Trained immunity yields a possible biomarker for the risk of SLE flares and offers a new potential target for developing therapeutic strategies.
Figure 1: Monocytes in SLE patients are trained by NETs and MPs. (A) Human PBMCs were isolated and stimulated with Heat-killed *candida albicans* (HKCA) as positive control, only medium as negative control (Untrained) or MPs and NETs for 24 hours. After the resting period, cells were restimulated with Pam3CSK4 for 24 hours. IL-6 production was measured in the supernatant. (B) PBMCs were stimulated with 10% plasma of SLE patients or healthy control for 24 hours. After the resting period cells were restimulated with LPS. IL-6 production was measured in the supernatant. (C) PBMCs were isolated from patients with SLE or healthy controls and stimulated with LPS for 24 hours. IL-6 and IL-18 was measured in the supernatant. Data is shown as mean ± SEM. P-values were calculated using one-way ANOVA with Dunnett’s post-test (in A) and unpaired t-test (in B,C). (D) Gene set enrichment analysis using Hallmark gene set collection on differentially expressed genes between SLE patients and controls (FDR < 0.1). (E) Heatmap of differentially regulated H3K4me3 peaks compared between healthy controls and SLE patients’ monocytes (FDR < 0.1).

#4220

NOT JUST AIN? OTHER IMMUNE-CHECKPOINT INHIBITOR LESIONS: A SINGLE INSTITUTION’S EXPERIENCE OVER 12 YEARS
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Mayo Clinic, Rochester, United States of America

**Background and Aims:** Immune-checkpoint inhibitors (ICI) are antineoplastic therapies that unleash the immune-system and have revolutionized cancer outcomes. Though they are a drug class with great potential, their effects are not always limited to the malignant cells and can cause a spectrum of immune-related adverse events (irAEs). Roughly 5% of patients will experience acute kidney injury (AKI) with acute interstitial nephritis (AIN) being the predominant pathologic lesion. Glomerular and vascular lesions are thought to be rare and, as a result, not well-defined. We aim to document glomerular and vascular pathology in this context at our institution.

**Method:** We performed a retrospective review of internal native renal biopsies from 2010-2022 that had known ICI treatment. Standard processing of renal biopsies included light microscopy (LM), immunofluorescence (IF), and electron microscopy (EM). We reviewed the biopsies and pathology reports, as well as clinical data from patient electronic medical records.

**Results:** Our search yielded 32 kidney biopsies; of those, most had AIN (27/32), 8 cases had glomerular pathology, and 1 case had arterial endothelitis. Of the cases with glomerular pathology, 4 had subacute glomerular thrombotic microangiopathy (TMA). Among the cases with TMA, 2 were also treated...
with vascular endothelial growth factor inhibitor (VEGFi), 1 with gemcitabine, and 1 with BRAF-inhibitor therapy. Further, only one of these patients had complement testing, which did not reveal definitive deficiency. One patient had proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID), IgG-κ. One patient had IgA nephropathy (IgAN) and another had membranous nephropathy (MN). Most patients were biopsied for rising serum creatinine (SCr) (median: 1.6 mg/dL; range: 0.55-5.5). I had nephrotic-range proteinuria (median: 1.6 mg/dL; range: 0.55-5.5). I had a history of other known causative drugs. IgAN and MN have been reported in association with neoplasia. PGNMID has been reported in a variety of malignant and nonmalignant conditions, and ICI-use could be a triggering factor. In conclusion, the patterns of glomerular injury reported in a variety of malignant and nonmalignant conditions, and ICI-use and MN have been reported in association with neoplasia. PGNMID has been reported in a variety of malignant and nonmalignant conditions, and ICI-use could be a triggering factor. In conclusion, the patterns of glomerular injury seen in our cohort may be secondary to other concurrent risk factors other than ICI use. Arterial endotheliitis appears to be a rare but significant secondary effect to ICI-use.

#4451
MONOCYTE MIGRATION AND ACTIVATION IN ANCA-ASSOCIATED GLOMERULONEPHRITIS
Yosta Vegting1, Katie Hanford2, Aldo Jongejan3, Perry Moerland1, Gayle Gajadin1, Nelly van der Bom-Baylon1, Tamara Dekker1, Liffert Vogt1, Frederike Bemelman2, Jeffrey Kroon2 and Marc Hilhorst1
1. Amsterdam UMC, University of Amsterdam, Nephrology, Amsterdam, Netherlands, 2. Amsterdam UMC, University of Amsterdam, Experimental Vascular Medicine, Amsterdam, Netherlands and 3. Amsterdam UMC, University of Amsterdam, Epidemiology & Data Science (EDS), Bioinformatics Laboratory, Amsterdam, Netherlands

Background and Aims: Glomerular injury in Anti-Neutrophil Cytoplasmic Antibodies (ANCA)-associated glomerulonephritis (AGN) is associated with macrophage infiltration. To date, their role and origin remain to be fully elucidated. Activated blood monocytes likely transmigrate and differentiate into kidney macrophages depending on the local microenvironment. Even in remission, some studies indicate sustained monocyte activation and upregulation of adhesion markers. The aim of this study was to research the intrinsic migration capacity of monocytes in AGN. Targeting monocyte migration might open new therapeutic avenues in the treatment of AGN.

Method: Transendothelial migration of monocytes was tested in AGN patients with active disease (n = 2), in remission (n = 8) and healthy controls (n = 6). To assess their adhesive and migratory capacity, freshly isolated CD14 positive monocytes were added to confluent TNF-α or IL1β overnight-stimulated Human Aortic Endothelial Cell (HAEC) for 30 minutes and subsequently fixed. Monocyte adhesion and transmigration was visualized by phase-contrast microscopy and quantified using ImageJ. To unravel the potential mechanisms driving these differences in monocyte migration, we performed bulk RNA-sequencing of monocytes from AGN patients with active (n = 4) and stable (n = 10) disease, and healthy controls (HC) (n = 6).

Results: Monocyte adhesion, but not migration, was significantly increased during active disease, independently of the stimuli used to mimic the pro-inflammatory phenotype of endothelial cells (EC) (Figure 1). During remission, decreased adhesion was found on the IL1β-stimulated ECs. While CD11b mRNA expression was upregulated, CD11a expression was downregulated in monocytes from active AGN patients compared to HC. Two genes involved in paracellular monocyte transmigration (JAML, PECAM-1) were significantly decreased. Most AGN patients were treated with corticosteroids at time of experiments.

Conclusion: These results suggest a remarkable increase in monocyte adhesion, but lower intrinsic migration capacity, in a 30 minute time-frame during active AGN. Our findings on migration are surprising in the light of theorized enhanced monocyte extravasation towards diseased AGN kidneys. Therefore, it could be speculated that after a longer period of time, a subset of the adherent monocytes would ultimately migrate and differentiate into kidney macrophages. In remission, long-term immunosuppressive treatment or chronic inflammation might decrease monocyte adhesion. This was the first ex-vivo study to research monocyte migration in AGN, further research is required to validate findings and to develop new therapies targeting monocyte migration.

REFERENCE
HISTOLOGICAL SUBTYPING OF INTERSTITIAL INFILTRATES AND CORRELATION WITH RENAL PROGNOSIS IN ANCA-ASSOCIATED GLOMERULONEPHRITIS

Aglaia Chalkia1, Christos Koutsianas2, Harikleia Gakiopoulou3, Panagiota Giannoul1, Alexandros Panagiotopoulos2, Athanasia Kapota1, Konstantinos Thomas3, Dimitrios Vasiropoulos4 and Dimitrios Petras1

1Hippokration General Hospital, Athens, Greece, Nephrology Department, Athens, Greece, 2National and Kapodistrian University of Athens, School of Medicine, 2nd Department of Medicine and Laboratory, Clinical Immunology - Rheumatology Unit, Hippokration General Hospital of Athens, Athens, Greece and 3National and Kapodistrian University of Athens, School of Medicine, Athens, Greece, 1st Department of Pathology, Athens, Greece

Background and Aims: Interstitial inflammatory infiltrates in ANCA associated glomerulonephritis (AAGN) are frequently observed but their correlation to clinicopathological parameters remains elusive.

Method: Retrospective study of 40 patients with newly diagnosed AAGN. Histological assessments using the presence of interstitial inflammatory cells were performed. Biopsy tissues were investigated by CD3, CD20, CD4, CD8, CD68+(PG-M1), CD138 immunohistochemical staining. We assessed the presence of inflammatory cells in terms of clinical, histopathological parameters as well as the renal prognosis in a large follow-up period [47.87 months (12-216)].

Results: The interstitial infiltrates were consisted of lymphocytes (CD3 T cell> CD 20 B cell) at 83%, followed by plasma cells at 43%, neutrophils at 43%, macrophages at 40% and eosinophils at 20% of the biopsies. CD8 T cells dominated the interstitial area in focal and sclerotic class, while CD8 and CD4 tended to have different expression patterns in the interstitial area (figures 1.2).

Interestingly, we reported that the presence of macrophages was correlated with higher chronicity index [interstitial fibrosis (39% vs 24%, p = 0.015) and creatinine at diagnosis (4.4 vs 2.6 mg/dL, p = 0.011), while the presence of neutrophils, lymphocytes and eosinophils was correlated with higher activity index [cellular crescents (37% vs 6%, p<0.001, 26% vs 9%, p = 0.021, 49% vs 24%, p = 0.021, respectively)]. In terms of short-term renal prognosis, only the macrophages were correlated with worst renal function at the 1st year (Cre 3.2 vs 1.8 mg/dL, p = 0.042). Regarding the long-term renal prognosis, we validated as the most reliably predictive score, amongst Berden classification and Mayo Clinic chronicity score, the ANCA renal risk score (AUC 0.694, p = 0.05) and we found that the low-risk group tended to present less severe inflammation (p = 0.029), while the presence of macrophages and eosinophils was less often present (p = 0.03 and 0.05, respectively) compared to the higher risk groups.

Conclusion: Identifying the differences in histopathological subtypes, in yet underestimated active tubulointerstitial lesions, could be the first step toward improving our understanding of distinct pathophysiological mechanisms and anticipating to specific treatment regimens.

ASSOCIATION BETWEEN INTERLEUKIN-37 RS3811047 POLYMORPHISM AND LUPUS NEPHRITIS IN AN EGYPTIAN POPULATION

Samah Ismaeel1, Hamdy Omar2, Aliia Ellawindy3, Hanan Omar1, Asma Hashem1 and Marwa Tawfeek1

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Background and Aims: Systemic lupus erythematosus (SLE) is a chronic, clinically heterogeneous, autoimmune disorder with unpredictable course and features ranging from mild skin affection to life-threatening involvement of major organs. Interleukin 37 (IL-37) is a cytokine with anti-inflammatory and immune-suppressive effects; it suppresses both innate and adaptive immune responses, thus protecting against excessive inflammation-induced tissue damage.

Aim: investigate the association of IL-37 (rs3811047) polymorphism with lupus nephritis in Egyptian population.

Method: This case-control study comprised 3 groups: 109 SLE patients without nephritis, 97 SLE patients with LN, and 240 healthy controls. History taking, clinical examination, disease activity in SLE patients was assessed and routine laboratory tests were done. Genotyping of the IL-37 rs3811047 polymorphism was done using real time polymerase chain reaction (PCR).

Results: The AA genotype was more frequently represented in LN patients (21.6%) compared to SLE patients without LN (7.3%) (p = 0.007), and carriers of the AA genotype had four times increased susceptibility to acquire LN compared to GG and GA genotype carriers (OR: 4.1). Likewise, the A allele was more represented in LN patients (43%) than in SLE patients without LN (30%) (p = 0.004), and the carriers of the A allele had nearly two times more risk of developing LN compared to carriers of the G allele (OR: 1.79). Moreover, the AA genotype was associated with LN susceptibility under the recessive genetic model (OR = 3.49, CI: 1.47-8.30) (p = 0.002), but not under other genetic models.

Conclusion: The AA genotype of the IL-37 rs3811047 polymorphism contributes to the development of SLE in Egyptian patients with doubled risk of acquiring LN in carriers of the allele A.
THE PROGNOSTIC VALUE OF DIFFERENT HISTOPATHOLOGIC MODELS OF ANCA-ASSOCIATED VASCULITIDES: A PROSPECTIVE STUDY

Michalis Christodoulou1, Eleni Moysidou1, Georgios Lionoulos1, Stamatia Stal1, Konstantinos Bantis1, Christina Nikolaidou2, Asimina Fylaktou2, Aikaterini Papagianni3 and Maria Stangou4

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Background and Aims: Renal histology in ANCA-associated vasculitides-glomerulonephritis (AAV/GN) is characterized by active (inflammation, necrosis, crescents) and chronic lesions (sclerosis, fibrosis), and lately classified by Berden Classification (BC), ANCA renal risk (RRS) and Mayo Chronicity score (MCCS). We aimed to prospectively compare predictive ability of the three classification models in AVV.

Method: 27 AVV/GN patients, 17 females, were estimated at time of diagnosis (T0), based on renal biopsy, commenced on the same treatment protocol, cyclophosphamide+steroids, and followed for 6 months. BC, RRS and MCCS Classification models were initially applied on renal biopsies and results were correlated to renal function at T0, and accordingly, 3 (T3) and 6 (T6) months.

Results: Patients’ median age at presentation was 61.9(18-82) years, ratio BC, RRS and MCCS + a t 3 o r 6 m o n th s o f f o l l o w u p . BC, RRS and MCCS + a t 3 o r 6 m o n th s o f f o l l o w u p .

Conclusion: In the short term follow up, ANCA renal risk could better predict renal function outcome compared to Berden Classification and Mayo Chronicity Score, with high RRS frequently leading to HD. Instead, the sclerotic class in BC was not predictive of poor outcome.

PROPOSAL OF A NOVEL RISK PREDICTION SCORE FOR MAJOR ADVERSE CARDIOVASCULAR EVENTS IN LUPUS NEPHRITIS

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1Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary and 2Semmelweis University, Department of Pathology, Forensic and Insurance Medicine, Budapest, Hungary

Background and Aims: Patients with systemic lupus erythematosus have an increased risk of cardiovascular diseases (CVD) vastly contributing to morbidity and mortality. Besides traditional risk factors, lupus-related factors also contribute to the overall risk. Our major objective was to identify both traditional and non-traditional factors that could aid the prediction of CVD risk and major adverse cardiovascular events (MACE) in this population.

Method: We conducted a single-center retrospective analysis on lupus nephritis patients. Demographic variables, cardiovascular events, clinical and histological data were collected from patients who underwent kidney biopsy between 2005 and 2020 (Figure 1). Chi-square, Mann-Whitney U-test, and logistic regression analyses were performed to investigate risk factors for MACE (IBM SPSS Statistics v28). Receiver Operating Characteristic (ROC) curve was used to determine optimal cut-off values. The study was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (SE RKED 225/2018).

Results: 91 patients were enrolled in this period. The mean age was 37.3±12.3 years, 86% females, and the mean follow-up time was 62±48 months. Fourteen patients (15.4%) suffered at least one MACE, of which 13 (14.3%) occurred during follow up lupus and 8 (8.8%) after the biopsy. Two patients deceased of a cardiovascular event. Out of the traditional risk factors, increased age (35.8±11.1 vs 45.5±15.1 years, p = 0.012) entailed a higher occurrence of MACE. Complete white blood cell (3.54±0.41 vs 3.25±0.87 Giga/liter, p = 0.026) and neutrophil count (2.85±0.63 vs 3.11±0.83 Giga/liter, p = 0.001) were higher, while diastolic blood pressure was lower (89.5±10.96 vs 78.43±6.9 mmHg, p<0.001) at the time of the biopsy in patients with MACE complication. Age, neutrophil count, and diastolic blood pressure were proven to be independent predictors of MACE (Table 1). Based on these observations, we proposed a new model (CANDE: Cardiovascular risk –based on Age, Neutrophil count, and Diastolic blood pressure– Estimation score) that is a stronger predictor of MACE and can be used to calculate MACE risk from the time of the biopsy in lupus nephritis patients (Figure 1).

Conclusion: The higher the score was, the more often the MACE cases were present (Table 1). ROC curve analysis demonstrated that at 0.78 cut-off value the score predicts MACE occurrence at the time of the biopsy with a sensitivity of 0.75 and a specificity of 0.61. The analyses of MACE subgroups revealed that neutrophil-lymphocyte ratio was elevated in patients who were hospitalized because of heart failure (5.66±4.61 vs 9.68±6.46, p = 0.046), while neutrophil-thrombocyte ratio was higher in
patients with coronary revascularization in their medical history (0.023±0.015 vs 0.06±0.028, p = 0.02). This also indicates the importance of neutrophils in CVD risk assessment.

Conclusion: Age, neutrophil count, and diastolic blood pressure are demonstrated to be independent risk factors of MACE in lupus nephritis. The score calculated from these parameters (CANDE) is a stronger predictor of MACE at the time of the biopsy. A larger cohort is needed to validate these promising results.

Table 1: Predictors of major adverse cardiovascular events (MACE) at the time of the kidney biopsy in lupus nephritis patients

<table>
<thead>
<tr>
<th>Predictor</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>OR</th>
<th>95% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>-0.118</td>
<td>0.038</td>
<td>9.447</td>
<td>1</td>
<td>0.002</td>
<td>0.889</td>
<td>0.824 – 0.958</td>
</tr>
<tr>
<td>Neutrophil count (Giga/liter)</td>
<td>0.222</td>
<td>0.094</td>
<td>5.608</td>
<td>1</td>
<td>0.018</td>
<td>1.248</td>
<td>1.039 – 1.499</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.057</td>
<td>0.023</td>
<td>6.516</td>
<td>1</td>
<td>0.011</td>
<td>1.034</td>
<td>1.013 – 1.057</td>
</tr>
</tbody>
</table>

Multivariate logistic regression

<table>
<thead>
<tr>
<th>Predictor</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>OR</th>
<th>95% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>-0.124</td>
<td>0.044</td>
<td>7.78</td>
<td>1</td>
<td>0.005</td>
<td>0.884</td>
<td>0.81 – 0.964</td>
</tr>
<tr>
<td>Neutrophil count (Giga/liter)</td>
<td>0.278</td>
<td>0.119</td>
<td>5.401</td>
<td>1</td>
<td>0.018</td>
<td>1.32</td>
<td>1.044 – 1.668</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.052</td>
<td>0.026</td>
<td>3.899</td>
<td>1</td>
<td>0.051</td>
<td>1.03</td>
<td>1.015 – 1.053</td>
</tr>
</tbody>
</table>

Cut-off value (ROC analysis)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANDE score after the kid biopsy</td>
<td>2.1883</td>
<td>0.75</td>
<td>0.61</td>
</tr>
<tr>
<td>CANDE score – MACE after the biopsy</td>
<td>0.7831</td>
<td>0.75</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Figure 1: Risk factors for major adverse cardiovascular events in lupus nephritis: study design and proposal of the CANDE score (Cardiovascular risk – based on Age, Neutrophil count, and Diastolic blood pressure - Estimation score)

(1) The icons were downloaded from www.dreamstime.com under Royalty-free license, Dreamstime LLC, Brentwood, TN, US.

Table 1: Predictors of major adverse cardiovascular events (MACE) at the time of the kidney biopsy in lupus nephritis patients

<table>
<thead>
<tr>
<th>Predictor</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>OR</th>
<th>95% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>-0.118</td>
<td>0.038</td>
<td>9.447</td>
<td>1</td>
<td>0.002</td>
<td>0.889</td>
<td>0.824 – 0.958</td>
</tr>
<tr>
<td>Neutrophil count (Giga/liter)</td>
<td>0.222</td>
<td>0.094</td>
<td>5.608</td>
<td>1</td>
<td>0.018</td>
<td>1.248</td>
<td>1.039 – 1.499</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.057</td>
<td>0.023</td>
<td>6.516</td>
<td>1</td>
<td>0.011</td>
<td>1.034</td>
<td>1.013 – 1.057</td>
</tr>
</tbody>
</table>

Multivariate logistic regression

<table>
<thead>
<tr>
<th>Predictor</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>OR</th>
<th>95% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>-0.124</td>
<td>0.044</td>
<td>7.78</td>
<td>1</td>
<td>0.005</td>
<td>0.884</td>
<td>0.81 – 0.964</td>
</tr>
<tr>
<td>Neutrophil count (Giga/liter)</td>
<td>0.278</td>
<td>0.119</td>
<td>5.401</td>
<td>1</td>
<td>0.018</td>
<td>1.32</td>
<td>1.044 – 1.668</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.052</td>
<td>0.026</td>
<td>3.899</td>
<td>1</td>
<td>0.051</td>
<td>1.03</td>
<td>1.015 – 1.053</td>
</tr>
</tbody>
</table>

Cut-off value (ROC analysis)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
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</table>

ANCA RENAL RISK SCORE 2023: THE UPDATED AND REVISED ARR

Sebastian Bate1, Dominic Mcgovern2, Francesca Castiglioni3, Marek Myslivecek4, Jennifer Scott5, Gavin Chapman6, Nina Brown7, Lauren Floyd8, Benoit Brilland9, Mehmet Fethullah Aydin10, Duha Ilyas1, Ajay Dhaygude8, Juan-Manuel Mejia11, Jennifer Lees12, Marek Kollar4, Andrea Hinojosa11, Abdulmeccit Yildiz10, Augusto Jean François9, Stephen Roberts13, Thorsten Wiech14, Charles Dickson Pusey15, Rachel Jones2, David Jayne2, Ingeborg Bajema16, Charles Jennette17,
Abstracts

**Background and Aims:** Reliable prediction tools are needed to improve prognostication and personalisation of treatment in anti-neutrophil cytoplasmic antibody (ANCA) glomerulonephritis (GN). We aimed to validate and update the ANCA Renal Risk Score (ARRS) prediction model.

**Method:** The ARRS working group collated a retrospective multicentre international longitudinal cohort from referral centres and registries across the globe to revise the ARRS in a validation and recalibration study. The primary endpoint was end stage kidney disease (ESKD) and patients were censored at last follow-up. Cox proportional hazards models were used to reweight risk factors and develop a modified scoring system. Kaplan-Meier estimates, Harrell’s C statistics and calibration plots were used to assess model performance.

**Results:** Of a total of 1591 patients, 1439 were included in the final analyses (959 in the development cohort, 52% male, median age 64 years). The ARRS demonstrated a discrimination of C = 0.800, comparable to the original cohort. Updating the model found an additional useful cut-off for kidney function (K), and serum creatinine replaced glomerular filtration rate which provided higher reliability (K0: < 250 μmol/l = 0 points, K1: 250-450 μmol/l = 4 points, K2: > 450 μmol/l = 11 points). The risk points for the percentage of normal glomeruli (N) and interstitial fibrosis and tubular atrophy (T) were also reweighted (N0: > 25% = 0 points, N1: 10-25% = 4, N2: < 10% = 7, T0: none, mild or < 25% = 0 points, T1: ≥ mild-moderate or ≥ 25% = 3 points). We created four risk groups based on the sum of points: low (0 – 4 points), moderate (5 – 11), high (12 – 18) and an additional very high-risk (21). The model discrimination was C = 0.831 and a supplemental continuous model was developed to supply a patient-specific annual risk. Three-year kidney survival was 96%, 79%, 54%, and 19%, respectively. The ARRS23 performed similarly well in the validation cohort with excellent calibration.

**Conclusion:** We demonstrated the out-of-sample validity of the ARRS and present here the modified and improved score to optimise prognostication and risk stratification for clinical practice and trials.

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**SARS-COV-2 VACCINATION AS A TRIGGER FOR AUTOIMMUNE GLOMERULOPATHIES, CHANCE OR REALITY?**

Jorge Ivan Zamora Carrillo, Marina Lopez, Marc Patricio, Juan Carlos Leon, Sheila Bermejo Garcia, Irene Agraz Pamplona, Natália Ramos Terrades, Maria Azancot, Néstor Toapanta Gaibor and María José Soler Romeo

Vall d’Hebron University Hospital 119, Nephrology, Barcelona, Spain

**Background and Aims:** The administration of vaccines, such as influenza or pneumococcus, is a known trigger for the appearance of autoimmune glomerulopathies (AIG). Since the start of vaccination against SARS-CoV-2, publications described the appearance of AIG after SARS-CoV-2 vaccine administration. The timing that has been established associated with causality reaches up to 6 weeks after vaccination. Our aim is to analyse the incidence of AIG flares before and after the start of vaccination against SARS-CoV-2 in our center.

---

**Table 1: Incidence of AIG, IgAN, vasculitis and INS before and after start of Spanish vaccination.**

<table>
<thead>
<tr>
<th></th>
<th>Prevaccine</th>
<th>Postvaccine</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AIG</strong></td>
<td>86 (39.4%)</td>
<td>85 (50.6%)</td>
<td>0.029</td>
</tr>
<tr>
<td><strong>IgAN</strong></td>
<td>19 (8.7%)</td>
<td>22 (13.1%)</td>
<td>0.185</td>
</tr>
<tr>
<td><strong>Vasculitis</strong></td>
<td>13 (6.0%)</td>
<td>7 (4.2%)</td>
<td>0.430</td>
</tr>
<tr>
<td><strong>INS</strong></td>
<td>11 (5.0%)</td>
<td>18 (10.7%)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

The percentages correspond to the initial sample size of 386 patients.

AIG: Autoimmune glomerulopathies, IgAN: IgA nephropaty, INS: Idiopathic Nephrotic Syndrome.

**Method:** All persons with a kidney biopsy from January 2019 to March 2022 in our center were included in the study. We compared the incidence of AIG before and after Spanish vaccination (SV) initiation and determined the time-lapse from vaccine and SARS-CoV-2 infection to kidney biopsy. We established 6 weeks as the time limit to associate AIG with vaccine or SARS-CoV-2 infection. We also evaluated the analytical characteristics of the outbreaks. Idiopathic nephritic syndrome (INS) which comprehended minimal change disease (MCD) and primary focal and segmental glomerulosclerosis (GSFS), IgA nephropathy (IgAN) and vasculitis were studied as subgroups. Minimal changes disease (MCD) flares in patients with and without kidney biopsy in that period were also studied.

**Results:** A total of 386 biopsies were studied. Of them, 86/218(39.4%) were AIG performed pre- and 85/168(50.6%) post- national vaccination (p = 0.029). From the group with kidney biopsy after SV, 31 (36.5%) presented with acute renal failure or chronic kidney disease with acute exacerbation, peak of creatinine 3.09 mg/dL (IQ range: 2.01–4.97), serum albumin 3.5 g/dL (IQ range: 2.9–3.9), proteinuria 1959mg/g (IQ range: 563–5558) and 53% with hematuria. The incidence of idiopathic nephritic syndrome (INS) studied separately was also significantly higher post-SV (18-10.7%) than pre-SV (11-5.0%) (p = 0.036). There were no differences in the incidence of vasculitis or IgA nephropathy. Regarding time-lapse between either SARS-CoV-2 vaccine or infection to AIG diagnosis, a total of 17 (20%) took place in the first 6 weeks after SARS-CoV-2 vaccine and only 2 (2.4%) before 6 weeks after SARS-CoV-2 infection. Within those 17 flares, the most common diagnosis was of IgAN (5-29.4%), 14 (82.4%) received an mRNA vaccine and 9 (52.9%) took place after the 1st vaccine dose. We observed a significantly increase of MCD flares post-SV (n = 20) as compared with pre-SV (n = 13) (p = 0.002).

**Conclusion:** The incidence of AIG, INS and MCD flares in our center increased significantly after Spanish vaccination against SARS-CoV-2. Importantly, 20% of AIG flares took place in the first 6 weeks after receiving a vaccine dose, being the first dose the most risky one and IgAN the most frequent diagnosis. Although causality cannot be demonstrated solely with temporal association and general COVID-19 vaccination, further investigation and prospective studies could be of great interest.
RELATION OF KIDNEY BIOPSY FINDINGS TO CLINICAL OUTCOMES IN PATIENTS WITH LUPUS NEPHRITIS TREATED WITH AN ANTAGONISTIC ANTI-CD40 ANTIBODY (BI 655064)

Ingeborg Bajema¹, Helmut Schumacher², Jürgen Steffen³, Simone Deutschel⁴ and David Jayne⁵

¹University Medical Center Groningen, Pathology and Medical Biology, Netherlands, ²Statistical Consultant, Germany, ³Boehringer Ingelheim International GmbH, Germany, ⁴Boehringer Ingelheim RCV GmbH & Co KG, Austria and ⁵Department of Medicine, University of Cambridge, United Kingdom

Background and Aims: Lupus nephritis (LN) is the most serious complication of systemic lupus erythematosus with a high risk of end-stage kidney disease and a high need of better treatment. A recent randomized, double-blind, placebo-controlled, phase II trial tested doses of 120, 180 and 240 mg of the anti-CD40 monoclonal antibody BI 655064 as add-on to standard of care (MMF + glucocorticoids), in patients with active LN (proteinuria > 1 g/day) for 52 weeks. Although the trial did not demonstrate a dose-response relationship for the primary endpoint determined by complete renal response, a potential efficacy benefit of BI 655064 180 mg and 240 mg was found in a post-hoc analysis. We investigated whether a treatment effect was related to findings in the pre-treatment renal biopsy.

Method: Biopsies from 101 patients with LN class III or IV, confirmed in a central review conducted according to a previously established protocol, were included. Protein/creatinine ratio (UPCR, based on spot urine) and eGFR were determined at every visit. For each, the last available UPCR and the last available eGFR values, linear regressions (based on the respective baselines) of all patients irrespective of therapy were calculated, and subjects were classified according to their individual performance, “Better” or “Worse” than the average. The modified activity and chronicity indices as well as all biopsy parameters, which are not already contained in the indices, were compared for differences between the “Better” and “Worse”. Parameters with p < 0.1 in the univariate analyses were entered into a multivariate logistic regression model, and a routine model selection procedure (with p < 0.2) was used to identify parameters predictive for clinical outcome. As monocytes express CD40, which is the target of BI 655064, a further question was whether high dose treatment with BI 655064 (180/240 mg) was beneficial when monocytes were present in the biopsy, using a model which adjusted for all predictors identified in the multivariate model.

Results: The results of the univariate and the multivariate analysis of biopsy parameters are shown in Table 1. Improvement in UPCR was better if the

| Table 1: Association of biopsy parameters with UPCR and eGFR. |
|-------------------------------|-------------------|-------------------|---------------------------------|-------------------|
| Parameter                     | Univariate Analysis | Multivariate Analysis | Effect of Treatment Related to Presence of Monocytes |
|-------------------------------|-------------------|-------------------|---------------------------------|-------------------|
| LN class (IV vs III)          | 0.036             | 2.36 (0.86 – 6.52) | 0.97                           | Monocytes: 3.72 (1.07 – 12.9) |
| Ischemic cells                | 0.072             | 0.13             |                                 |                                 |
| Mesangial sclerosis           | 0.086             | 5.79 (1.43 – 23.4) | 0.014                          |                                 |
| Lymphocytes                   | 0.051             | 1.95 (0.75 – 5.08) | 0.17                           |                                 |
| Microthrombi                  | 0.062             | 10.6 (1.05 – 106) | 0.040                          |                                 |
| Mod Activity index            | 0.069             | 0.79 (0.64 – 0.98) | 0.032                          |                                 |
| Mod Chronicity index          | 0.11              | 0.79 (0.64 – 0.98) | 0.032                          |                                 |
| Lymphocytes                   | 0.086             | 0.45 (0.18 – 1.18) | 0.11                           |                                 |
| Synechia/Adhesions            | 0.029             | 0.45 (0.18 – 1.18) | 0.11                           |                                 |
| Mod Activity index            | 0.049             | 1.16 (0.99 – 1.26) | 0.077                          |                                 |
| Mod Chronicity index          | 0.037             | 0.85 (0.69 – 1.06) | 0.15                           |                                 |

¹Chi² or Wilcoxon test, only parameters with p<0.1 presented

Logistic Regression, only parameters with p<0.2 included

“per unit increase”

for “Better” outcome
modified chronicity index was low. In addition, LN class IV subjects had a marginally better prognosis than class III. The effect of high-dose treatment with BI 655064 was better when monocytes were present. eGFR outcome was better if the modified chronicity index was low and, conversely, the modified activity index was high. Further, the presence of synechia/adesions was a negative predictor for positive outcome. There was no indication for an effect of high-dose treatment with 655064 on eGFR when monocytes were present.

Conclusion: This post-hoc analysis of the BI 655064 trial used a novel approach which investigated whether specific histological lesions in renal biopsies were related to treatment outcome. Although the number of patients was limited, our results suggest that treatment with higher dose anti-CD40 may improve the reduction of proteinuria when monocytes are present in the biopsy. This indicates that specific information from renal biopsies could ultimately improve the choice of treatment for individual LN patients.

#5207
CENTRAL NERVOUS SYSTEM INVOLVEMENT IN EOSINOPHILIC GRANULOMATOsis WITH POLYANGIITIS: A DIAGNOSTIC DILEMMA
Carla Nicolau1, Rui Barata2, Miguel Bigotte Vieira1, Tiago Assis Pereira1, Mário Góis1, Helena Viana1, João Sousa1, Francisco Ribeiro1 and Fernando Nolasco1
1Hospital Curry Cabral, Nephrology, Lisboa, Portugal and 2Hospital Curry Cabral, Lisboa, Portugal

Background: Central nervous system involvement is extremely rare in eosinophilic granulomatosis with polyangiitis, and associated with very poor prognosis. A high index of suspicion is needed to diagnose this entity and initiate prompt treatment for this life-threatening condition.

Case presentation: A 71-year-old man was admitted to our hospital with lower limb weakness, loss of vision in the left eye and diplopia for four weeks. Four months prior to admission he reported unintentional weight loss and wheezing. Laboratory studies revealed anemia, eosinophilia and high antineutrophil cytoplasmic antibodies (ANCA) anti myeloperoxidase (MPO) levels. Brain computerized tomography (CT) was normal. Although corticosteroids were started, addition of other immunosuppressants was delayed due to ongoing infection. During the next three days, the patient presented with worsening kidney function and was drowsy, agitated and combative. Lumbar puncture and brain CT scan showed no acute abnormalities. Therefore, plasmapheresis was started. During the third session of plasmapheresis, the patient became drowsy and non-responsive. Brain CT scan revealed subdural hematoma with uncal herniation. Trepanation and initiation of hemodialysis were required. Kidney biopsy revealed focal proliferative glomerulonephritis with fibrocellular crescents. Magnetic resonance imaging and ophthalmological evaluation showed abnormalities compatible with vasculitic disease. Cyclophosphamide was added to prednisolone, with renal and extra renal manifestations improvement. One year later, the patient is autonomous, with right hand paresis, stable kidney function (serum creatinine 2.5 mg/dL) and negative ANCA MPO serology.

Conclusion: Neurological involvement in GEA is heterogeneous and requires differential diagnosis with central nervous system infections, adverse effects of corticosteroids and complication of plasmapheresis. The diagnosis is challenging and demands a high level of suspicion. Otherwise, it may lead to delayed, erroneous diagnosis and worse survival.

#2630
NETOSIS IS A PREVALENT IMMUNE PROCESS IN LUPUS NEPHRITIS AND NEUTROPHIL ELASTASE SCORING EXPRESSES THE ACTIVITY AND SEVERITY IN DIFFERENT CLASSES
Shaimaa Zaki Abdelmegied1, Manal Salman2, Heba Mahmoud2 and Aya Elgendy3
1Internal Medicine and Nephrology Department, Faculty of Medicine Ain Shams University Cairo, Egypt, 2Pathology Department, Faculty of Medicine Ain Shams University Cairo, Egypt and 3Internal Medicine/Allergy and Clinical Immunology Department, Faculty of medicine Ain Shams University Cairo, Egypt

Background: NETosis is a prevalent immune process in lupus nephritis and its presentation in different lupus classes.

Methods: A cross-sectional study included 45 patients with lupus nephritis who underwent renal biopsy and were classified according to lupus class. NE was done for the detection of NETosis by immunohistochemistry.

Results: The prevalence of (NE) was 88.8% (40/45 cases). NE combined score with cut-off (>3) expresses moderate to severe NETosis. It allowed the detection of active proliferative lupus class III-IV with a sensitivity: 80.0%, specificity: 60.0%, PPV: 58.71%, and NPV: 60.0%. In class III-IV (N = 34 cases): NE combined score >3 was 83.3% (25/30 cases) with features: glomerular deposition >25% of the glomeruli in 60% (19/30 cases), strong intensity (+2) in 63.3% (19/30 cases), diffuse (>50% of the number of the glomeruli) 67.8% (19/28 cases). In non-proliferative lupus class II-V (N = 11 cases) NE combined score >3 was 20% (2/10 cases) and score <3 was 80% (8/10 cases) with features: glomerular deposition <25%/ faint intensity (+1) focal. On comparing both groups as regard NE combined score, distribution, intensity, and focal/diffuse p-value was 0.0002, 0.099, 0.013, and 0.94 respectively. On redistribution of biopsies according to NE combined score >3 vs <3 there was a significant difference in activity index, distribution, intensity, and focal/diffuse p-value 0.0011, 0.0001, 0.0002, 0.0006 while non-significant for chronicity index p-value 0.08914.

Conclusion: NETOSIS is a prevalent immune process in lupus nephritis and NE combined score is a sensitive marker of proliferation that increases with class severity and activity.
Figure 1: NE features in renal biopsy in different proliferative vs non-proliferative SLE class.

Figure 2: Neutrophil elastase more than 25% deposition in the glomeruli.

#6899
MICROVASCULAR LESIONS IN LUPUS NEPHRITIS
Tamara Knezevic1, Ivan Padjen2,3, Vanja Ivkovic4,5, Mario Laganovic1,6, Stela Bulimbasic2,7, Ana Luka2, Marijana Ćorić1,7 and Branimir Anić2,3
1University Hospital Centre Zagreb, Division of Nephrology, Hypertension, Dialysis and Transplantation, ZAGREB, Croatia, 2University Hospital Centre Zagreb, Division of Clinical Immunology and Rheumatology, Zagreb, Croatia, 3University of Zagreb, School of Medicine, Zagreb, Croatia, 4University Hospital Centre Zagreb, Division of Nephrology, Hypertension, Dialysis and Transplantation, Zagreb, Croatia, 5University of Rijeka, Faculty of Health Studies, Rijeka, Croatia, 6Clinical Hospital Merkur, Renal Division, Department of Medicine, Zagreb, Croatia and 7University Hospital Centre Zagreb, Department of Pathology and Cytology, Zagreb, Croatia

Background and Aims: Microvascular lesions (MVL) can be found in the kidneys of lupus nephritis (LN) patients and might be associated with worse outcomes. There are very few studies which evaluated MVLs in these patients and we aimed to provide a comprehensive evaluation of all MVLs, their frequency, characteristics and association with renal outcomes one year after kidney biopsy.

Method: We have conducted a retrospective cohort study to evaluate the characteristics and prognostic significance of MVLs in the kidney of subjects with LN. We have collected data on demographics, clinical and laboratory parameters and histopathology (light, immunofluorescent and electron microscopy). MVLs were characterized according to previous classifications. SLE was diagnosed using the American College of Rheumatology criteria.

Results: A total of 56 patients with biopsy-proven LN were followed up for at least one year after kidney biopsy (79% women, mean age at biopsy 38±13 years). Forty patients (71%) had MVLs in the kidney. The most common MVLs were arteriolar endotheliocyte swelling (54%), arteriolar hyalinosis (25%) and endothelialitis (8%) and the frequency distribution of all microvascular lesions is shown in Figure. Median number of lesions in the MVL group was 1 (interquartile range 1 to 2) and subjects had up to 6 MVLs. There was no difference in the median number of MVLs across LN classes (p=0.05). Proteinuria was highest in class V (5.5 g/day, p = 0.06 vs. all other classes). Subjects with MVLs had lower baseline proteinuria compared with those with no lesions (3.6 vs. 5.4 g/day, p = 0.037), but there was no difference in serum creatinine (92 vs. 119 umol/L, p = 0.25). There were no differences in the occurrence or number of MVLs across LN classes (p = 0.63). The number of MVLs was not correlated with proteinuria (p=0.05). There was no difference in the frequency of proliferative lupus between MVL and no MVL groups (79% vs. 60%, p = 0.15). A total of 48% of subjects achieved complete response (CR), 27% achieved partial response (PR) and 25% had no response (NR). MVLs were not associated with response (defined as CR or PR) in a multivariate regression model (OR 3.5 [0.5, 24.6]).

Conclusion: MVLs are common in LN. They were associated with lower baseline proteinuria, but not with proliferative LN or renal outcomes. The association with proteinuria warrants further research.

#5028
CHANGING PATTERNS IN CLINICAL-HISTOLOGICAL PRESENTATION AND OUTCOMES OVER THE LAST FOUR DECADES IN PATIENTS WITH MICROSCOPIC POLYANGIITIS (MPA)
Martina Uzzo1,2, Filippo Sala1,3, Francesco Reggiani1,4, Vincenzo L’imperio5, Marta Calatroni2,4, Umberto Maggiore6, Gabriella Luisa Moroni1,2 and Renato Alberto Sinico1,4
1University of Milano-Bicocca, Department of clinical and sperimental sciences, Milano, Italy, 2Humanitas Research Hospital, Nephrology and Dialysis Unit, Monza, Italy, 3Humanitas Research Hospital, Nephrology and Dialysis Unit, Cusca Perseghetto, Italy, 4Ospedale San Gerardo, Nephrology and Dialysis Unit, Monza, Italy, 5Ospedale San Gerardo, Department of Medicine and Surgery, Pathology Unit, Monza, Italy and 6University of Parma, Department of Medicine and Surgery, Nephrology and Dialysis Unit, Parma, Italy

Background and Aims: Recent data seem to indicate an increasing age of patients affected by MPA over the last decades, which may result from the wider availability of anti-neutrophil cytoplasmic antibody (ANCA) testing and to a greater awareness of the disease. It is not known whether the changing MPA has been mirrored by a change in the pattern of clinical outcomes. We aimed at assessing the changes in demographic, clinical and histological presentation, and outcomes of MPA patients over a 42-year period.

Method: We performed a multicenter retrospective cohort study. Patients diagnosed with MPA between 1980 and the 31st of January 2022 were grouped in two periods (p), based on the year of diagnosis: p1980-2001 and p2002-2022. We tested the baseline differences using the Mann-Whitney test and the Fisher’s exact. We estimated the crude patient survival using the Kaplan-Meier
Figure 1: Crude cumulative incidence curves (Aalen–Johansen estimator) computed with the time from MPA diagnosis to the first event as absorbing state (ESKD or death, whichever came first).

Figure 2: Crude probability of each outcome at each time point since MPA diagnosis, that results from fitting the multiple state model. Unlike the model in which ESKD is an absorbing state (Figure 1), the multistate model allows that patients starting dialysis remain at risk of dying.
estimator and the cumulative incidence of competing events death/dialysis using Aalen-Johansen estimator. The probability of end-stage kidney disease (ESKD) and death at each time point since MPA diagnosis was estimated through a multistate model, which accounted for patients who died after starting dialysis. We used Cox proportional hazards, Fine-Gray regression, and multistate regression models to adjust for potential confounding factors such as age, kidney function and clinical symptoms at the time of diagnosis.

Results: Out of 201 patients, 187 had non-missing follow-up to ESKD and/or death and could be included in the study. There were 77 patients in p1980-2001, and 110 patients in p2002-2022. Compared to p1980-2001, patients in p2002-2022 were older (66.2 (14.0) vs 57.7 (15.8); P < 0.001) and had better kidney function (eGFR (MDRD), mL/min/1.73m²: 25.9 (24.8) vs 21.5 (28.2); P = 0.0011). The prevalence of the sclerotic class according to the Berden histopathological classification was lower in p2002-2022 (4.8 vs 18.2%; P = 0.0016). There were mild differences in the pattern of clinical symptoms, with a lower prevalence of constitutional symptoms (83.6 vs 94.8%; P = 0.021) and a higher prevalence of pulmonary disease (40 vs 20.8%; P = 0.040) and peripheral neuropathy (17.3 vs 5.2%; P = 0.013) in p2002-2022. Crude and adjusted patient survival was similar. However, the risk of ESKD decreased during p2002-2002 compared to p1980-2001 (Figure 1; crude Subhazard ratio of ESKD: 6.30 [95%CI: 0.16 to 0.57; P < 0.001]). The difference in the probability of ESKD remained significant even after accounting for death after ESKD (Figure 2), and after adjusting for potential confounders (Hazard ratio of ESKD since MPA diagnosis in multistate models: 0.33 [95%CI: 0.18 to 0.63; P < 0.001]).

Conclusion: Clinical presentation of MPA has become less severe in the last decades, leading to a reduced risk of ESKD, despite a comparable risk of death. Older age, changing clinical patterns and better kidney function at the time of diagnosis do not fully account for the reduction in ESKD, which may be instead related to new induction and maintenance therapies as well as to a greater awareness of the disease.

#5128

PREDICTIVE FACTORS OF RENAL RECOVERY AND END-STAGE KIDNEY DISEASE IN PATIENTS WITH SEVERE ANCA-ASSOCIATED VASCULITIS WITH GLOMERULONEPHRITIS

Martina Casal Moura1, Dalia Zubidat2, Marc Patricio1, Maria José Soler Romeo3, Fernanda Dos Santos2, Luca Nardelli2, Juan León Román4,5,6, Círia Sousa2, Ladan Zand6, Kenneth Warrington4, Sanjeev Sethi4, Ulrich Specks7 and Fernando Custodio Fervenza2,8,9

1Mayo Clinic College of Medicine and Science, Division of Pulmonary and Critical Care Medicine, Department of Medicine, United States of America
2Mayo Clinic College of Medicine and Science, Division of Nephrology and Hypertension, Department of Medicine, United States of America
3Hospital Universitari Vall d’Hebron, Servicio de Nefrología, Spain
4Mayo Clinic College of Medicine and Science, Division of Rheumatology, Department of Medicine, United States of America
5Mayo Clinic College of Medicine and Science, Department of Laboratory Medicine and Pathology, United States of America
618yearswithbiopsy-provenpureormixedISN/RPS

Background and Aims: A significant number of patients with anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) with glomerulonephritis (AAV-GN) still progress to end-stage kidney disease (ESKD, eGFR <15mL/min/1.73m²) despite advances in remission-induction treatment.

Method: A retrospective cohort study on MPO- or PR3-ANCA positive patients with AAV (MPA or GPA) and ESKD at presentation. Renal recovery, treatment.

Results: We analyzed 166 patients with biopsy proven active kidney involvement and eGFR <15mL/min/1.73m² at the time of AAV-GN diagnosis. Patients received glucocorticoids with CYC (n = 84) or with RTX (n = 72) for remission-induction, and 49 also received PLEX. The predictors of renal recovery were erythrocyte sedimentation rate, SCr at diagnosis and minimal or mild chronicity changes. We analyzed 71 patients who started dialysis with or without PLEX within 4 weeks from AAV-GN diagnosis. The predictors for dialysis discontinuation were minimal chronicity changes in kidney biopsy at the time of diagnosis (OR 6.138, [95%CI 1.389-27.118]; P = 0.017) and focal glomerular involvement (OR 5.017,[95%CI 1.287-19.567];p = 0.020). Predictors for maintenance in ESKD at 12 months included higher serum creatinine (SCr) at the time of diagnosis (IRR 1.086, [95%CI 1.005-1.173],p = 0.037), moderate (IRR 3.797,[95%CI 1.090-13.225],p = 0.036), or severe chronicity changes in kidney biopsies (IRR 5.883,[95%CI 1.542-22.439],p = 0.009).

Conclusion: In our cohort, kidney recovery, dialysis discontinuation, and maintenance of ESKD in patients with AAV-GN and eGFR<15mL/min/1.73m² depended on SCr and histologic findings on kidney biopsies at the time of diagnosis and was not affected by the addition of PLEX.
Table 1: Patient characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total sample (N = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>42.1 (16.4)</td>
</tr>
<tr>
<td>Age at SLE diagnosis, mean (SD), years</td>
<td>29.8 (15.3)</td>
</tr>
<tr>
<td>Female, %</td>
<td>86.7</td>
</tr>
<tr>
<td>Race and ethnicity, %</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>53.3</td>
</tr>
<tr>
<td>White</td>
<td>36.7</td>
</tr>
<tr>
<td>Medications (ever), %</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>100</td>
</tr>
<tr>
<td>Immunosuppressants/biologics</td>
<td></td>
</tr>
<tr>
<td>Azathioprine</td>
<td>40.0</td>
</tr>
<tr>
<td>Belimumab</td>
<td>20.0</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>26.7</td>
</tr>
<tr>
<td>Mycophenolate mofetil/mycophenolic acid</td>
<td>93.3</td>
</tr>
<tr>
<td>Rituximab</td>
<td>20.0</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>23.3</td>
</tr>
<tr>
<td>LN classification, %</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>29.6</td>
</tr>
<tr>
<td>Class IV</td>
<td>25.9</td>
</tr>
<tr>
<td>Class V</td>
<td>18.5</td>
</tr>
<tr>
<td>Mixed</td>
<td>25.9</td>
</tr>
<tr>
<td>Dialysis (ever), %</td>
<td>10.0</td>
</tr>
<tr>
<td>Renal transplant, %</td>
<td>13.3</td>
</tr>
<tr>
<td>Biopsy-proven LN within the past year and currently receiving immunosuppressants/biologic therapy, %</td>
<td>13.3</td>
</tr>
<tr>
<td>Biopsy-proven LN 1–5 years prior and currently receiving immunosuppressants/biologic therapy, %</td>
<td>43.3</td>
</tr>
<tr>
<td>Biopsy-proven LN &gt;5 years prior and currently receiving immunosuppressants/biologic therapy, %</td>
<td>33.3</td>
</tr>
<tr>
<td>Biopsy-proven LN &gt;5 years prior and no longer receiving immunosuppressants/biologic therapy, %</td>
<td>3.3</td>
</tr>
<tr>
<td>Women who have been pregnant or are currently pregnant and received immunosuppressants/biologic therapy during pregnancy, %</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Figure 1: Thematic overview of prominent themes that emerged through qualitative analysis. Representative quotes are included to punctuate the main findings.
Background and Aims: SLE is a chronic autoimmune disorder that can affect all organ systems. Clinically evident renal disease known as Lupus Nephritis (LN) occurs in up to 50% patients of SLE and up to 10% of LN patients develop ESRD. LN carries a significant morbidity and mortality and requires an early aggressive management. Our Aim is to study the effect of IV Cyclophosphamide (CYC) vs Mycophenolate Mofetil (MMF) as Induction regimen in proliferative Lupus Nephritis patients of North- East India.

Method: This is a prospective observational study conducted in the department of Nephrology, Gauhati Medical College, over a period of 1 year. Haematological and biochemical assay including serum creatinine, blood urea, serum albumin, ANA, Anti ds DNA, C3 and C4,24h urine protein, estimated glomerular filtration rate (eGFR) of all patients were taken into account. Renal biopsy was performed under ultrasonographic guidance. SLEDAI Score and Activity and Chronicity Indexes were calculated for all patients. Statistical analysis was done by SPSS Version 22 for windows. Two tailed p<0.05 was considered to be statistically significant. A total of 64 biopsy proven LN patients of Class III, Class IV and Class V (Plus Class III/ Class IV) were enrolled in the study. We randomly assigned 34 patients with Class III through IV lupus nephritis to IV CYC (NIH protocol/monthly) and 30 patients to MMF (2 gm/day) for 24 weeks as Induction Regimen. Both the groups received prednisone, tapered from a maximum starting dosage of 60 mg/day.

All the patients were followed up for 6 months. Complete Response (CR) was considered when proteinuria<0.5g and Partial Response (PR) when 0.5g<proteinuria<3g or there is reduction in proteinuria by at least 50%. Baseline characteristics and CR and PR were compared between the two groups.

Results: Of the total 64 patients, 57 patients (89%) were female, and 7 patients were male (11%) with the mean age of 31±9.45 years. 24% patients had Class III LN and 76% had class IV LN. Complete Response was achieved in 13 patients (43%) in the MMF group and in 15 patients (44%) in CYC group. Partial Response was achieved in 11 patients (36.67%) in CYC group and 6 patients (20%) in MMF group. No response was seen in 7 patients (20.6%) in MMF group and 6 patients (18.7%) in CYC group.

Conclusion: The Northeastern population of India consists of various ethnic groups and there are records of variation in response to the Regimens in different geographical areas. In our study from North-east India, IV Cyclophosphamide and Mycophenolate Mofetil showed similar efficacy as Induction Regimen in proliferative Lupus Nephritis. However, there were higher rates of infection in the Cyclophosphamide group.

<table>
<thead>
<tr>
<th>RESPONSE</th>
<th>CYC Group (N%)</th>
<th>MMF Group (N%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>15/44%</td>
<td>13/43%</td>
<td>0.23</td>
</tr>
<tr>
<td>Partial response</td>
<td>12/35%</td>
<td>11/36.67%</td>
<td>0.26</td>
</tr>
<tr>
<td>No response</td>
<td>7/20.6%</td>
<td>6/20%</td>
<td>0.39</td>
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</table>

<table>
<thead>
<tr>
<th>ADVERSE EFFECTS</th>
<th>CYC (N = 34)</th>
<th>MMF (N = 30)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Infections</td>
<td>24</td>
<td>5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4</td>
<td>8</td>
<td>0.48</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>Anaemia</td>
<td>9</td>
<td>3</td>
<td>0.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>CYC Group</th>
<th>MMF Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria (gm/24 hrs)</td>
<td>0.48±0.92</td>
<td>0.56±0.43</td>
<td>0.18</td>
</tr>
<tr>
<td>S. Albumin</td>
<td>3.92±1.47</td>
<td>4.17±1.26</td>
<td>0.12</td>
</tr>
<tr>
<td>S. Creatinine</td>
<td>0.72±0.6</td>
<td>0.86±0.5</td>
<td>0.15</td>
</tr>
</tbody>
</table>
Figure 1: Intersection immune associated genes of arsenic trioxide in systemic lupus erythematosus (SLE). (A) The heatmap showed the transcriptional expression of differentially expressed genes (DEGs) in both GSE144390 and GSE50772 dataset (merged dataset). (B) Venn diagram indicated 476 total predicted targets of Arsenic Trioxide (ATO) using four databases. (C) The transcription expression of 12 intersection genes (DEGs genes, immune related genes, and arsenic trioxide targeted genes) in SLE. *p<0.05, **p<0.01, ***p<0.001.

Figure 2: Single-sample GSEA (ssGSEA) analysis of eight intersection genes in the infiltration of immune cells in systemic lupus erythematosus (SLE). The heatmap showing a total of 8 types of immune cells had significant associations with intersection genes expression in SLE. aDCs, activated Dendritic Cells; DCs, Dendritic Cells; iDCs, immature Dendritic Cells; pDCs, plasmacytoid Dendritic Cells; Tfh cell, Follicular helper T cell; Th1 cells, T helper1 cells; Th2 cells, T helper2 cells; Treg cell, Regulatory T cell; TIL, Tumor-Infiltrating Lymphocytes.
NOD-like receptor signalling pathway (p = 1.93E-09). Ten types of immune cells showed significant difference with intersection genes expression in SLE using ssGSEA approach. MMP9 was the most significantly associated with immune cells and showed positive correlations with macrophages and neutrophils. A significant TF-MMP9-miRNA regulatory network was constructed using cytoscape software. Pilot data from our in vitro studies suggested that ATO might down regulate MMP9 expression in PBMCs obtained from LN patients during disease remission (n = 3).

Conclusion: ATO interacts with immune cells in LN patients via different inflammatory pathways and may downregulate MMP9 expression in PBMCs.

PROTEINURIA AND PROGRESSION OF IGA NEPHROPATHY. HAVE WE REACHED THE POINT OF NO RETURN?

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Virgen del Rocio Hospital, Nephrology, Seville, Spain

Background and Aims: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide, associated with an incidence of 2.5/100,000 cases per year and progression to end-stage kidney disease (ESKD) in 20% patients within 10 years. Proteinuria has been identified as the greatest risk factor for ESKD in IgAN. The aim was to evaluate the correlation between proteinuria and major adverse renal events (MARE). We define MARE as 40% decline in glomerular filtration rate (eGFR), initiation of kidney replacement therapy (either dialysis or kidney transplantation) or death whether from renal cause or cardiovascular-related.

Method: In this retrospective observational single-center study, we included all biopsy-proven IgAN patients older than 18 years with proteinuria >500 mg/24h, diagnosed between 2006-2017 and followed up to January 2022. Clinical, analytical, and histological findings were collected at time of diagnosis and during follow-up. Uni and multivariable Cox regression were performed to establish correlation between our data and the main event. A linear mixed-effects model was used to estimate eGFR slope.

Results: A total of 124 patients were included. Mean age and eGFR were 40 ±15 years and 59 ml/min (IQR: 33-94 ml/min) respectively, with a median proteinuria of 1.44 g/24h (IQR: 0.7-2.3). 64% of patients were treated with corticosteroids. In the multivariate analysis, we found that IFTA >25% had a statistically significant risk of MARE (IFTA T1 HR 3.1; 95% CI 1.52-6.6; p = 0.002; IFTA T2 HR 6.6; 95% CI 1.46-16.12; p <0.001), history of cardiovascular disease presented 3.7 times higher risk of MARE (HR 3.7; 95% CI 1.46-9.6 p = 0.015). Patients with proteinuria >3 g/24h showed significantly higher hazard ratio (HR 2.36 95%CI 1.16-4.8 p = 0.01) for MARE. In the 3-year linear mixed-effects model, patients with proteinuria above 3 g/24h had an annual eGFR slope of -6.3 ml/min (-9.6 to -3.1 95% CI). Nevertheless, proteinuria between 1.5 to 3 g/24h had a similar behaviour as our reference group (proteinuria <1.5 g/24h). These results might provide new evidence supporting a more conservative approach and start receiving glucocorticoids if proteinuria is >3 g/24h.

REFERENCES

SERUM BIOMARKERS AS PREDICTORS OF RENAL DAMAGE IN ANCA-ASSOCIATED VASCULITIDES
António Silva Inácio1, Patricia Domingues1, Ana Piedade1, Teresa Furtado1, Beatriz Mendes1, Ricardo Verde1, Jesuïna Duarte2, Patricia Valério Santos1, Ana Farinha1, Miriam Karina Soto Rios1 and Liliana Cunha1
1Centro Hospitalar De Setúbal E.P.E., Nephrology, Setúbal, Portugal and 2Centro Hospitalar De Setúbal E.P.E., Clinical Pathology, Setúbal, Portugal

Background and aims: Despite therapeutic advances, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) carry poor renal and survival outcomes. Prognostic elements are needed to guide treatment. Several studies explored determinants of AAV outcomes, but predictive factors are not well established. Poor prognosis factors have been lower glomerular filtration rate, lower serum C3, C3 deposition on immunofluorescence (IF), and recently platelet count below 250 × 109/L. Histopathological lesions have also been related to renal outcomes. In this study we aim to correlate serum immune and inflammatory biomarkers with renal histological lesions' severity.

Methods: We retrospectively analysed histopathological findings of adults with biopsy-proven AAV renal involvement through Berden's histopathological classification (BHC) classes, Brix's renal risk score (BRS), interstitial fibrosis and tubular atrophy (IFTA) and crescentic glomeruli percentages (%), C3 positive IF and presence of interstitial hemorrhage (IH). Patients' ANCA titer (ANCAD) measured by ELISA, serum C3 and C-reactive protein (CRP) were documented at diagnosis. ANCA titer was also registered at last follow-up date (ANCAF). Univariate statistical analysis was used to correlate every biomarker with every histologic variable mentioned. C3 and CRP were used as continuous variables and ANCA titers as continuous and categorical variables. As a continuous variable, ANCA titers above laboratorial detection values, proliferative classes and the activity index at kidney biopsy (Table 2). Variables included in Table 1 with values of antiC1q antibodies and we found significant correlation for serum creatinine, active urinary sediment, C3 and C4 values, proliferative classes and the activity index at kidney biopsy (Table 2).

Results: We included 46 patients with biopsy-proven AAV kidney involvement from January 2006 to January 2023, 65.2% male (n = 30), median age 66.5 (60.75-74.5), 78.3% (36) MPO, 15.2% (7) PR3 and 6.5% (3) seronegative; and 12.8% (5) 100-134 and 43.6% (20) > 134. According to BHC, biopsies were: 17.4% (8) global sclerotic, 28.3% (13) mixed, 39.1% (18) crescentic, and 15.2% (7) 100-134 and 43.6% (> 134). ANCA positive biopsies were 28.3% (16) global sclerotic, 28.3% (13) mixed, 39.1% (18) crescentic, and 15.2% (7) 100-134 and 43.6% (> 134).

Conclusions: ANCA titer at diagnosis, serum C3 and CRP did not correlate with histological severity and chronicity lesions in our population. Nonetheless, larger cohorts, systematization of biopsy findings and studies on newer biomarkers might bring helpful information to expected prognosis and initial Furtapace approaches. A positive correlation between ANCA levels at the last follow-up date and medium and high-risk BRS groups on initial biopsy might be further explored in larger studies.

#5081

THE VALUE OF ANTI-C1Q ANTIBODIES IN PREDICTING THE CLINICAL-HISTOLOGICAL FEATURES OF LUPUS NEPHRITIS PATIENTS AT TIME OF KIDNEY BIOPSY

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1Humanitas University, Nephrology, Milan, Italy, 2University of Milano Bicocca, Italy, 3Humanitas Research Hospital, Rozzano Milan, Italy, 4Fondazione IRCCS Ca' Grande PoliClinico Maggiore, Milan, Italy and 5Humanitas Research Hospital, Nephrology, Rozzano Milan, Italy

Background and Aims: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with renal involvement in around 50% of patients. Delayed diagnosis of lupus nephritis (LN) is associated with higher risk of end-stage kidney disease (EKD) and mortality. Kidney biopsy remains the gold standard for diagnosis and management of LN, but in the last decades there is an interest for new serum biomarkers. Anti-C1q antibodies are autoantibodies associated with LN. Nevertheless, few studies have correlated the association of anti-C1q antibodies with active LN with focus on renal histology.

Method: We evaluated clinical and histological data of 59 patients with biopsy proven LN. Kidney biopsies were categorized according to the ISN/RNP Classification. We evaluated the correlation of the main clinicopathologic features with values of anti-C1q antibodies, measured by a commercial kit with a clinically validated ELISA test. Normal values of anti-C1q were < 20 UA, medium values were between 20 and 80 UA and high values were > 80 UA. Demographic and clinical data were expressed as numbers or percentage for discrete variables and as continuous variables as mean and standard deviation. The correlation between anti-C1q levels and clinicopathological characteristics have been explored using Spearman's test.

Results: At the presentation of 59 patients with LN, the mean age was 34 years and the time of SLE disease before the onset of LN was 73.2 months. 9 patients were male, mean serum creatinine was 1 mg/dL, glomerular filtration rate (eGFR) was 88.53 ml/min, proteinuria was 4.35 g/day and microscopic hematuria was present in 79% of pts. Kidney biopsies were classified as non-proliferative (class II and V) in 18.4% of patients and proliferative (class III and IV) in 77.6% of patients. We evaluated the correlation between all variables included in Table 1 with values of antiC1q antibodies and we found significant results for serum creatinine, active urinary sediment, C3 and C4 values, proliferative classes and the activity index at kidney biopsy (Table 2).

Table 1: Clinical and histological characteristics at presentation of LN in 59 patients. RSP/ISN Classification for kidney biopsy classes.

| Time of SLE before LN (months) | 73.2 ± 89.9 |
| Male sex, n (%) | 9 (18) |
| Age (years) | 34 ± 13.21 |
| Serum Creatinine (mg/dL) | 1 ± 0.41 |
| eGFR CKD-EPI (ml/min) | 88.53 ± 31.16 |
| Proteinuria (g/24 h) | 4.35 ± 3.43 |
| RBC in the Urinary Sediment n./HPF | 17 ± 24 |
| Arterial hypertension (%) | 49.15 |
| Hematocrit (%) | 31.11 ± 7.09 |
| White blood cells /ul | 5558 ± 2367.52 |
| Platelets /ul | 232100 ± 96.310 |
| Class II n° (%) | 3 (6.1) |
| Class III n° (%) | 5 (10.2) |
| Class IV n° (%) | 19 (38.8) |
| Class V n° (%) | 6 (12.2) |
| Class VI n° (%) | 1 (2) |
| Class V + III n° (%) | 7 (14.3) |
| Class V + IV n° (%) | 8 (16.3) |
| Activity Index (n) | 7.84 ± 5.69 |
| Chronicity index (n) | 2.02 ± 2.1 |
| Antiphospholipid antibodies, n° (%) | 41 (69.5) |
| C3 (mg/dL) | 50.32 ± 27.56 |
| C4 (mg/dL) | 8.33 ± 6.21 |
| ANA positivity, n° (%) | 59 (100%) |
| Anti-DNA positivity, n° (%) | 53 (89.8) |
| Anti Ro antibodies, n° (%) | 18 (30.5) |
| Anti Sm antibodies, n° (%) | 18 (30.5) |
| Anti RNP antibodies, n° (%) | 22 (37.3) |
Table 2: Trend/significant correlation of anti-C1q antibodies values at diagnosis of lupus nephritis with patient's clinical and histological characteristics. RSP/ISN Classification for kidney biopsy classes.

<table>
<thead>
<tr>
<th>Clinical-histological variables</th>
<th>Anti-C1q antibodies</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine ≥ 0.8 mg/dl</td>
<td>67.58 ± 39.28</td>
<td>0.08</td>
</tr>
<tr>
<td>RBC/HPF urine sediment &gt; 0</td>
<td>82.33 ± 62.16</td>
<td>0.07</td>
</tr>
<tr>
<td>C3 &lt; 90 mg/dl</td>
<td>91.83 ± 69.97</td>
<td>0.03</td>
</tr>
<tr>
<td>C4 &lt; 15 mg/dl</td>
<td>90.73 ± 69.69</td>
<td>0.05</td>
</tr>
<tr>
<td>Class II + % of pts 9</td>
<td>27.95 ± 31.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Class III + % of pts 38</td>
<td>101.89 ± 69.1</td>
<td></td>
</tr>
<tr>
<td>Activity index ≥ 4</td>
<td>110.02 ± 68.34</td>
<td>0.00</td>
</tr>
</tbody>
</table>

### #5348
THE EFFECTS OF RITUXIMAB IN NON-HCV-RELATED MIXED CRYOglobulINEMIC VASCULITIS

Annalisa Guarino, Nunziante Caruso, Giovanni Geraci, Roberta Longo, Giorgio Amore, Gianluca Rabajoli, Roberta Fenoglio, Savino Sciascia and Dario Roccatello

Torino, Italy

**Background and Aims:** Remarkable results in severe HCV-related cryoglobulinemic vasculitis have been obtained with Rituximab. Details of the clinical characteristics and effective treatment of non-HCV-related cryoglobulinemic syndrome are presently lacking.

**Method:** This paper reports on a prospective single-Center open study aimed at evaluating the clinical presentation and effects of Rituximab administered alone in patients with severe non-HCV-related cryoglobulinemic syndrome.

**Results:** The study group included 11 patients followed for at least 6 months. Three patients had type 1 cryoglobulinemia, 6 had type II and the remaining 2 patients had type III. Mean cryocrit was 2.5%. Four out of 11 patients had symptomatic sicca complex with anti-SSA (Ro/anti SSB (La) antibodies. All 11 patients presented with biopsy-proven renal involvement, 4 out of 11 with leukocytoclastic vasculitis, 8 with involvement of the peripheral nervous system. Renal biopsy revealed diffuse membranoproliferative glomerulonephritis (MPGN) in 9 out of 11 patients. Extracapillary proliferation and necrosis of the glomerular tuft was observed in 1 of these 9 cases. Intermittent nephritis together with mesangial expansion and capillary immune deposits were observed in 1 patient. Prevalent interstitial fibrosis and glomerular sclerosis were detected in the remaining case. Patients underwent treatment with rituximab alone. After 6 months we observed a remarkable improvement in the necrotizing skin ulcers and a substantial amelioration of the electrophysiological parameters of motor and sensory peripheral neuropathy. Improvement in both renal function (from 2.8 to 1.4 mg/dl, p < 0.001) and proteinuria (from 4.2 g/24 to 0.4 g/24 h, p < 0.001) was found in 10 out of 11 patients, while 1 could not be fully treated because of a severe infusion reaction and sudden development of anti-Rituximab antibodies. Good renal response was confirmed at the end of follow-up (38.4 months). Three patients had a relapse at 6, 12, and 48 months, respectively.

**Conclusion:** In our cohort the administration of 4 once-weekly infusions of Rituximab followed by 2 more infusions after 1 and 2 months proved to be effective in the management of these rare patients.

### #5386
ONCO-NEPHROLOGY: THE ROLE OF KIDNEY BIOPSY IN THE MANAGEMENT OF SIDE EFFECTS OF TARGETED THERAPIES

Nunziante Caruso, Stefania Lalloni, Martina Marchisio, Marco Morrone, Gianluca Rabajoli, Andrea Careddu, Giovanni Geraci, Roberta Fenoglio, Savino Sciascia and Dario Roccatello

Torino, Italy

**Background and Aims:** The introduction of innovative therapies, resulting from revisiting cancer as a disease of the immune system, has changed the scenario of complications. These new classes of drugs, such as targeted therapies and immune checkpoint inhibitors, assure substantial advantages in cancer therapy, despite some side affecting various organs, including the kidney. Histological evaluations of kidney disorders induced by targeted/immunotherapy are limited.

**Method:** In this study we examined the histological features of patients treated with new cancer agents who underwent kidney biopsy for new onset kidney failure and/or urinary abnormalities.

**Results:** The cohort included 30 adult patients. The most frequently administered therapies were immunotherapy (30%), targeted therapy (26.7%), immunotherapy plus targeted therapy (13.3%), immunotherapy plus chemotherapy (13.3%), targeted therapy plus chemotherapy (16.7%). The most common histological finding was tubular interstitial nephritis (30%) that was associated with acute tubular necrosis in 4 cases, and thrombotic microangiopathy (23.3%). After kidney biopsy, 16 of the 30 patients were treated according to the histological diagnosis. Fourteen patients were treated with steroids. One patient with membranous nephropathy was treated with a single dose of rituximab. A patient with severe thrombotic microangiopathy requiring dialysis received a treatment with eculizumab for 3 months. Overall some renal response was obtained in all patients treated with glucocorticoids, while complete kidney response was achieved in the patient treated with rituximab. Cancer treatment was resumed without change in 21 out of 30 patients.

**Conclusion:** Kidney biopsy is critical for the management of kidney toxicities and should be strongly encouraged for patients showing adverse kidney effects of novel cancer agents.

### #5679
PATIENT OUTCOME IN A SWEDISH SINGLE-CENTRE COHORT OF ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT

Ylva Ostdlund, Aso Saeed and Karlo Mihovilovic

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**Background and Aims:** End-stage kidney disease and premature death are common in patients with antineutrophil cytoplasmic antibody (ANCA) - associated vasculitis (AAV) with renal involvement. Poor patient outcome is attributed to multiple factors comprising a delay in diagnosis and treatment, inadequate efficacy of treatments, and complications due to toxic effects of given immunosuppressive therapy. The aim of the present study was to evaluate clinical and prognostic features of a Swedish cohort of patients with renal AAV and to investigate the pattern of immunosuppressive treatment and predictors of renal and patient survival.

**Method:** Ninety-one patients diagnosed with AAV with renal involvement between 01 March 2002 and 30 October 2018 in a single-centre were included in the present retrospective study.

**Results:** Among these ninety-one patients, 52 (57%) were diagnosed with PR3-ANCA, and 39 (43%) with MPO-ANCA. Patients with PR3-ANCA and MPO-ANCA were received comparable induction therapy. However, the frequency of PLEX was significantly higher in patients with PR3-ANCA versus MPO-ANCA (44% vs. 21% respectively; P = 0.025). Overall renal survival at 1- and 5-year was 91% and 69% respectively with no significant differences between patients with PR3-ANCA and MPO-ANCA. Overall, 1-year and 5-year patient survival were 92% and 77% respectively. The overall survival time was 11.5 years and 95% confidence interval (CI) of 9.9 to 13.0 years. Mean survival time in patients with PR3-ANCA was 10.8; 95% CI 8.8 to 12.7 years versus 11.7; 95% CI 9.6 to 13.8 years in those with PR3-ANCA. Cox regression analysis showed that advancing age significantly predicted higher mortality risk, whereas MPO-ANCA subtype significantly predicted lower mortality risk (Figure 1). Infection (25%), malignancy (22%), and cardiovascular events (16%) were the major causes of death in the present cohort. In a subgroup of thirty-two patients with eGFR <15 ml/min per 1.73 m² or undergoing dialysis at time of diagnosis. Twenty-three patients (72%) were treated with PLEX, whereas 9 patients (28%) did not receive PLEX as a part of remission induction therapy. Treatment with PLEX had no effects on overall 1-year patient and renal survival.

**Conclusion:** In this cohort of patients with AAV with renal involvement the overall 1-year renal and patient survival were high. Advancing age significantly predicted higher mortality risk, while MPO-ANCA subtype significantly predicted lower mortality risk. Treatment with PLEX had no effects on 1-year patient and renal survival in a subgroup of patients with severe renal involvement with AAV.
Figure 1:

#5861
NEW-ONSET OR EXACERBATIONS OF GLOMERULONEPHRITIS FOLLOWING SARSCOV2 VACCINE: A REVIEW OF THE LITERATURE
Chiara Rimoldi1, Lucia Del Vecchio1, Mariag Giulia Magatti1,2, Marco Allinovi3, Beniamina Gallelli1, Marco D'amico1,2, Giulio Pucci Bella1,2 and Gianvincenzo Melfa1

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Background and Aims: Following vaccination against SarsCoV2 several cases of new-onset glomerulonephritis or exacerbations of glomerular diseases have been reported [1, 2]. No literature review has been published yet on the subject.

Method: We searched for single case or case series through the PubMed portal search and through the abstract search submitted to the EDTA and the American Society of Nephrology in 2021 and 2022 (last view on the 15th of December 2022).

Results: A total of 138 cases were analyzed, of which 127 complete for all the variables. The mean age was 52.6±20.75 years (min 12, max 99), M/F 67/63. The majority of patients received mRNA vaccine (BNT16b2 Pfizer (n = 70, 51%), mRNA-1273 Moderna (n = 42, 30.7%), followed by AZD1222 AstraZeneca (n = 10, 7.3%) and Ad26.COV2.S Johnson & Johnson (n = 4, 2.9%). A minority of cases were associate with Covaxin and Sinovac (Figure 1).

Most cases were reported from the European continent (39.4%, n = 54), followed by North America (35.8%, n = 49) and Asia (21.9%, n = 30). A minority of cases were reported from Australia and Central/South America. The onset of glomerulonephritis occurred after a mean of 17.8 days±22.82 (min 1, max 89). In 37.4% of cases (n = 49), glomerulonephritis occurred after the first dose, in 61.8% after the second (n = 81), only 1 case after the third one. Regarding mRNA vaccine, in most cases, the disease occurred after the second dose (n = 78, 70.9% of cases, p < 0.001). Gross hematuria as the initial symptom was significantly related to mRNA vaccination (27/27 cases), 30 cases (24.8%) showed nephrotic syndrome at onset. The most prevalent diagnosis was IgA nephropathy (n = 36, 26.3%), followed by vasculitis (n = 33, 24%), Minimal Change Disease (n = 26, 19%), and membranous nephropathy (n = 14, 10.2%) (Figure 2). Interesting, 6 cases (4.4%) of anti-GBM GN were reported. Compared to patients with glomerulonephritis, those with systemic vasculitis were older (59.84±19.43 vs 49.21±21.21 years), with a slightly shorter onset time (14.9±12.67 days, vs 16.6±24.14 days). Both vasculitis and glomerulonephritis generally occurred more frequently following mRNA vaccination. For vasculitis, ANCA-MPO was more frequent (n = 15, 45.45%), followed by ANCA PR3 (n = 10, 30.3%), and finally IgA vasculitis (n = 3, 9%). Two cases (6.06%) were ANCA negative. New-onset glomerulonephritis accounted for 78.8% (n = 108), while relapses accounted for 21.2% (n = 29). There was no significant difference between the type of vaccine and de-novo or relapse glomerulonephritis. Patients were treated with steroid only (43.4%, n = 56), steroid and immunosuppressant (n = 21, 61.3%), rituximab alone or in combination (n = 26, 20.15%), conservative therapy (24, 18.6%). 6 patients (4.4%) underwent dialysis, 2.9% (n = 4) received plasmapheresis. 80 patients (69%) responded effectively to therapy, achieving complete remission, 19% (n = 22) achieved partial remission, while 2.1% (n = 14) did not respond to therapy. Evolution towards ESKD occurred in 11 cases (8%).

Conclusion: New-onset glomerulonephritis or exacerbations of glomerular diseases that were in remission is a possible complication of SarsCov2 vaccination. Most patients received mRNA vaccine; more than half of the patient developed or worsened the GN after the second dose.

REFERENCES
PREDICTORS OF MORTALITY IN ANCA-ASSOCIATED VASCULITIS: WHAT IS THE ROLE OF SERUM BIOMARKERS?
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Background and Aims: ANCA-Associated vasculitis (AAV) is an autoimmune disease with necrotizing inflammation of small vessels as the main manifestation. AAV is a severe disease with high level of mortality. Severity markers are needed to better tailor treatment. ANCA titers have not always been correlated with disease severity and mortality. Other inflammation markers have also been used such as C3 and C-reactive protein (CRP). The aim of this study is to correlate ANCA titers, C3 and CRP values with mortality in patients with renal vasculitis.

Method: We retrospectively analyzed all adult patients between June 2006 and December 2022 with a renal AAV in the nephrology department of São Bernardo Hospital. Demographic, clinical and laboratory findings of all patients were recorded. ANCA titers at the time of diagnosis (ANCAd), remission (ANCArm), relapse (ANCArl) and last follow-up (ANCAf) dates were registered. C3 levels were measured at diagnosis (dC3) and at the last follow-up (fC3) dates. CRP was measured at diagnosis (CRPd), remission (CRPrm) and last follow-up (CRPf). ANCA titers was analysed as continuous and categorical variables. C3 and CRP were used as continuous variables. We analyse the association between ANCA titers, C3, CPR values and mortality with univariate analysis. Multivariable adjusted cox regression analysis was performed for assessing predictive variables associated with mortality.

Results: We included 58 AAV patients with kidney involvement, with mean age of 69±10 years old, 54.4% were male (n = 31), 82.7% (n = 48) MPO-ANCA+, 12.1% (n = 7) PR3-ANCA+ and 5.2% (n = 3) seronegative. Median follow-up was 32.2 months. 20 (34.5%) patients died. At admission, categorization by ANCA titer revealed 5.2% (3) 0-19 UI/mL, 10.3% (6) 20-39,
and CT scan showed features of small bowel obstruction with transition at stercoralis (Figure 1). Bronchoesophageal lavage was done which revealed biopsy was taken. The duodenal biopsy showed features of strongyloidiasis revealed diffused edema, erythema, and superficial ulceration in duodenum and bilateral raised Eco pattern in kidneys rest were normal. Upper GI endoscopy showed features of strongyloidosis.

HRCT chest revealed bilateral ground glass opacities and a calcified nodule 8mm3, urea-92mg/dL, creatinine-2mg/dL. ECG showed sinus tachycardia, and total leucocyte count-8600, eosinophilia with absolute eosinophil count 1900/μL. The laboratory investigations on admission showed hemoglobin-15 g/dL, platelet 31.2 vs 52.1 ± 29.3 ml/min, respectively; p = 0.78). 17.6% of patients reached the composite endpoint, while 12.3% progressed to ESRD. Those with SARS-CoV-2 infection were more likely to reach the composite endpoint compared to those without infection [prevalence of composite endpoint, 26.7% vs. 14.8%, p = 0.006; OR, 2.1 (95%CI, 1.23-3.58), p = 0.006 (Figure 1). Similarly, there was a significant decline of eGFR in the first year of follow-up between the two study groups [-2.24 (-24.8; 20.9) vs. +2.31 (-16.8; 27.5) ml/min, respectively, p = 0.004]. In multivariate Cox proportional hazards regression analysis, the independent predictors of the composite endpoint were baseline eGFR (HR, 0.94; 95%CI, 0.92-0.96, p < 0.05), age (HR, 1.02-4.29, p = 0.04) (Figure 2). The results remained consistent when restricting the analysis to ESRD as an endpoint. When taking into account the severity of SARS-CoV-2 infection, a severe infection was the most important predictor of the composite endpoint (HR, 2.1; 95%CI, 1.02-4.29, p = 0.04) (Figure 2). The results remained consistent when restricting the analysis to ESRD as an endpoint. When taking into account the severity of SARS-CoV-2 infection, a severe infection was the most important predictor of the composite endpoint (HR, 2.1; 95%CI, 1.02-4.29, p = 0.04) (Figure 2). The results remained consistent when restricting the analysis to ESRD as an endpoint. When taking into account the severity of SARS-CoV-2 infection, a severe infection was the most important predictor of the composite endpoint (HR, 2.1; 95%CI, 1.02-4.29, p = 0.04) (Figure 2). The results remained consistent when restricting the analysis to ESRD as an endpoint. When taking into account the severity of SARS-CoV-2 infection, a severe infection was the most important predictor of the composite endpoint (HR, 2.1; 95%CI, 1.02-4.29, p = 0.04) (Figure 2).
EXPLAINABILITY OF A DEEP LEARNING BASED CLASSIFICATION MODEL FOR ANCA-ASSOCIATED GLOMERULONEPHRITIS

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Background and Aims: The histopathological classification for ANCA-associated glomerulonephritis (ANCA-GN) is a well-established tool to reflect the variety of patterns and severity of lesions that can occur in renal biopsies of patients with ANCA-associated vasculitis. As with many fields, medicine saw a rapid emergence of Artificial Intelligence (AI) and Deep learning (DL) approaches. In the field of digital pathology AI can now serve as decision-support for pathologists, with the potential for gains in productivity and time-saving. It was demonstrated previously that AI can aid in identifying histopathological classes of renal diseases, e.g. of diabetic nephropathy. Although these models reach high prediction accuracies, their black box structure makes them very non-transparent. The disadvantage is that the networks' decisions are not easily interpretable by humans and it is not clear what information in the input data underlies their decisions. This necessitates the use of Explainable AI (XAI), so that decisions made by AI models become accessible for validation by a human expert.

Method: Renal biopsy slides of 80 patients with ANCA-GN from 3 European centers, who underwent a diagnostic renal biopsy between 1991 and 2011, were included. On the scanned slides glomeruli were labelled as ‘normal’, ‘sclerotic’, ‘crescentic’ or ‘abnormal - other’. We developed a DL-based computational pipeline, which detects and classifies the glomeruli. We investigated the explainability of our model, using XAI techniques to shed light on the decision-making criteria of our trained DL classifier using saliency maps. These maps were analyzed by pathologists to compare the decision-making criteria of humans and the DL model.

Results: Our DL model shows a prediction accuracy of 93% for classifying glomeruli. The saliency maps from our trained DL models help us to better understand the decision-making criteria of the DL black box.

Conclusion: AI and DL play an increasingly important role in (nephro)pathology. To ultimately enable safe implementation of these models in clinical practice, validation of their decisions is needed. To achieve this, we used XAI techniques, which showed great potential for illuminating the decision-making criteria of the DL black box.

Figure 1: GradCAM saliency map for glomerulus with crescent and focal sclerosis.
THE VALUE OF THE HISTOLOGICAL CLASSIFICATIONS OF ANCA ASSOCIATED VASCULITIS IN PREDICTING LONG TERM KIDNEY SURVIVAL

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Background and Aims: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are a group of multisystemic autoimmune diseases characterized by necrotizing inflammation of small vessels, with a predilection for the kidney. The prognostic value of histological classification of ANCA-glomerulonephritis (ANCA-GN) is discussed. In 2010, Berden and colleagues proposed a prognostic classification based on glomerular involvement; in 2018, Brix et al. introduced the ANCA Renal Risk Score, which includes histological features and glomerular filtration rate; in 2017 the Mayo Clinic Chronicity Score, that considers chronic histological lesions, was designed and assessed in ANCA-GN. We aimed to identify which score is the best tool to predict end-stage kidney disease or death in a cohort of ANCA-GN patients.

Method: Patients who underwent kidney biopsy in two Italian centers within 32 years were retrospectively collected. Inclusion criteria: age >18 years, and at least one year of follow-up. A minimum of 10 glomeruli was considered adequate for a biopsy. Renal biopsies were classified according to Berden’s classification, Renal Risk Score and Mayo Clinic Chronicity Score. The primary end point of the study was the development of end-stage kidney disease (ESKD) at 5 years, defined as the chronic need of renal replacement therapy (RRT) or glomerular filtration rate (GFR) <15 ml/min. The secondary endpoint was a composite endpoint of ESKD or death for all causes.

Results: Of the 152 patients 84 were male, the median age was 63.8 years (Figure 1). Mean eGFR at diagnosis was 21.32 ml/min/1.73 m². 32.2% of patients were PR-3 positive, 50.6% were MPO positive, 17.2% were ANCA-negative. After a mean follow-up of 71.7 ± 66.7 months, 59 patients (38.8%) were on chronic dialysis or with a GFR <15 ml/min; among them, 20 patients died. The pure kidney survival rate (without ESKD or GFR <15 ml/min) was 79% at 1 year, 65% at 5 years, 59.8% at 10 years. Figure 2 reported the pure kidney survival rates of the patients assigned to every class of the three scores that we considered in this study. Fig. 3, Fig. 4, Fig. 5 show Kaplan-Meyer curves for the secondary outcome (ESKD+death); patients are classified according to the Berden’s score (Fig. 2), the Renal Risk Score (Fig. 3) and Mayo Clinic Chronicity Score (Fig. 4).

Conclusion: Berden histopathological classification and Renal Risk Score are predictive of renal prognosis when we consider the primary outcome (ESKD or GFR <15 ml/min) and when we consider the composite outcome (ESKD + death). The Mayo Clinic Chronicity Score allows a reliable stratification of the patients only when we consider the composite outcome (ESKD and death).
Figure 3:

Figure 4:

Figure 5:
CLINICAL CHARACTERISTICS OF PATIENTS WITH LUPUS NEPHRITIS CLASS III–V: ANALYSIS OF INTERNATIONAL REAL-WORLD DATA

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Background and Aims: Lupus nephritis (LN) is a severe renal manifestation of systemic lupus erythematosus (SLE) that negatively impacts morbidity and mortality; however, real-world data for LN is scarce. This study describes: the proportion of patients with SLE managed by rheumatologists (rheum-managed) and by nephrologists (neph-managed) with LN class III–V; the proportion of patients with a Safety of Estrogens in Lupus Erythematosus National Assessment - SLE Disease Activity Index (SELENA-SLEDAI) score ≥ 8 by region; extra-renal organ systems involvement by region; flaring by region; and EQ-5D and EQ-visual analogue scale (VAS) scores by estimated glomerular filtration rate (eGFR).

Method: Data were drawn from the Adelphi Lupus Disease Specific Programme, a cross-sectional, multi-subscriber survey of physicians and their consulting patients conducted April 2021–May 2022 in China, Japan, EU5 (France, Germany, Italy, Spain and the UK) and the USA. Physicians provided demographic and clinical data for 5–6 consecutive adult patients consulting for SLE/LN. LN class III–V was assessed by the physician at data collection. SELENA-SLEDAI scores were derived by physician assessment of patients’ current clinical manifestations. Patients had the opportunity to complete an EQ-5D form. All analyses were descriptive.

Results: Overall, 9% (183/2148) of rheum- and 48% (364/766) of neph-managed patients had LN. Most patients with LN had a SELENA-SLEDAI score ≥ 8 (70% of rheum- and 76% of neph-managed; Table 1), compared with 48% (1032/2148) of rheum-managed patients with SLE alone. The proportion of neph-managed patients with LN with a SELENA-SLEDAI score ≥ 8 varied by region, from 58% in the USA to 87% in China. In total, 62% of rheum- and 43% of neph-managed patients with LN had ever flared (any organ system; Table 1). The proportion of rheum-managed patients with LN who had ever flared ranged from 52% in China + Japan to 75% in EU5. The proportion of patients with LN currently experiencing a flare was similar between rheum- (31%) and neph-managed (35%) patients, but varied by region, with the highest proportion for rheum-managed patients in China (59%) and lowest in the USA (18%). In subgroups with ≥15 patients, EQ-5D and EQ-VAS scores generally worsened as eGFR lowered (Figure 1).

Conclusion: Patients with LN class III–V had high disease burden (SELENA-SLEDAI scores ≥ 8) and flaring that varied by region, suggesting a need for more efficacious treatments for patients with LN.

Table 1: Summary of outcomes among patients with LN by region and management.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>China</th>
<th>China + Japan</th>
<th>EU5</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LN n = 183</td>
<td>LN n = 364</td>
<td>LN n = 55</td>
<td>LN n = 113</td>
<td>LN n = 63</td>
</tr>
<tr>
<td>SELENA-SLEDAI score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;8</td>
<td>54 (30)</td>
<td>89 (24)</td>
<td>12 (22)</td>
<td>15 (13)</td>
<td>17 (27)</td>
</tr>
<tr>
<td>≥8</td>
<td>129 (70)</td>
<td>275 (76)</td>
<td>43 (78)</td>
<td>98 (87)</td>
<td>46 (73)</td>
</tr>
<tr>
<td>SELENA-SLEDAI organ involvement (reported in ≥30% of rheum- or neph-managed total population)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>132 (72)</td>
<td>313 (86)</td>
<td>37 (67)</td>
<td>106 (94)</td>
<td>42 (67)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>96 (52)</td>
<td>166 (46)</td>
<td>26 (47)</td>
<td>50 (44)</td>
<td>29 (46)</td>
</tr>
<tr>
<td>Constitutional*</td>
<td>68 (37)</td>
<td>120 (33)</td>
<td>28 (51)</td>
<td>58 (51)</td>
<td>32 (51)</td>
</tr>
<tr>
<td>Mucocutaneous</td>
<td>59 (32)</td>
<td>95 (26)</td>
<td>19 (35)</td>
<td>45 (40)</td>
<td>21 (33)</td>
</tr>
<tr>
<td>Ever flared†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>113 (62)</td>
<td>156 (43)</td>
<td>32 (58)</td>
<td>56 (50)</td>
<td>33 (52)</td>
</tr>
<tr>
<td>No</td>
<td>61 (33)</td>
<td>177 (49)</td>
<td>20 (36)</td>
<td>51 (45)</td>
<td>25 (40)</td>
</tr>
<tr>
<td>Unsure</td>
<td>9 (5)</td>
<td>31 (9)</td>
<td>3 (5)</td>
<td>6 (5)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Current flare</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(among patients ever flared†)</td>
<td>35 (31)</td>
<td>54 (35)</td>
<td>19 (39)</td>
<td>34 (61)</td>
<td>19 (38)</td>
</tr>
</tbody>
</table>

*Includes fatigue, fever, weight loss; † any organ system.
CLINICAL UTILITY OF SEROLOGICAL TEST AT TIME OF BIOPSY
Mårten Segelmark1,2, Maria Weiner3 and Björn Peters4
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Background and Aims: It is common practice to order serological tests at time of renal biopsy, but the diagnostic value in different clinical settings is largely unknown. We utilized data from the national Swedish Renal Biopsy Registry to analyze the positive and negative post-test likelihood of four common diagnoses depending on the results of frequently used serological tests.

Method: Data on all biopsies performed during the period 2015-01-01 – 2020-12-31 was retrieved from the Swedish Renal Biopsy Registry. All biopsies are classified into one of the following five biopsy indications: the nephrotic syndrome (nephrosis), acute/subacute nephritic syndrome (nephritis), other acute kidney injury (AKI), chronic kidney disease stage 1-2 (CKD 1-2), and CKD 3-5. Biopsy results are given as SNOMED codes by the pathologist and a clinical diagnosis using the ERA coding system by the nephrologist. Results from the following serological tests were analyzed: C3, C4, ANA, anti-dsDNA, ANCA (PR3 and/or MPO-ANCA) and anti-phospholipid antibodies. Pre-test likelihood, positive post-test (PPL) and negative post-test likelihood (NPL) for the diagnoses IgA nephropathy (IgAN), diabetic nephropathy (DN), ANCA-associated vasculitis (AAV) and lupus nephritis (LN) were analyzed. The diagnostic yield was defined as the ratio between the PPL and NPL.

Results: Out of a total of 3165 individuals that had undergone kidney biopsy, there were 694 (21.9%) patients assigned a diagnosis of IgAN, 378 (11.9%) with DN, 342 (10.8%) with AAV and 117 (3.7%) with LN. The proportion of patients being tested varied from 17% for anti-phospholipid antibodies to 77% for ANCA. The highest diagnostic yield was found for ANCA in AAV where the PPL/NPL ratio was 154. In patients with nephrosis the ratio went up to 290 mainly because of a very low NPL (0.2%). The next best diagnostic yield was seen in SLE were both ANA and anti-dsDNA exhibited a PPL/NPL ratio of 26. The best yield for ANA was found when the biopsy indication was nephrosis where the PPL was 33% and the NPL 0.54% and the ratio 61. For anti-dsDNA the best yield was in AKI with a ratio of 46 (PPL 55%, NPL 1.1%). The best test to make a diagnosis less likely was anti-phospholipid antibodies in diabetic nephropathy. The test was never positive in any of the 42 patients with this diagnosis however the same result slightly increased the likelihood of AAV. A positive result for C3(reduced levels) also reduced the likelihood of DN and the likelihood av diabetic nephropathy, the PPL / NPL ratio was 13. C4 and ANCA being, on the other hand, reduced the likelihood for IgAN with a ratio in the same range.

Conclusion: While the utility of ANCA, ANA and anti-dsDNA is well known, it is less known when a positive test substantially reduced the likelihood of a disease. Here we present data showing that a positive test for C3 decreases the likelihood of DN, while the likelihood is much less affected by C4. The opposite is seen for IgAN.

Figure 1: EQ-5D (A) and EQ-VAS (B) scores by eGFR* among rheum- and neph-managed patients with LN†
* eGFR was inferred by chronic kidney disease stage: stage 1/2 = eGFR ≥ 60 ml/min/1.73 m²; stage 3a/b = eGFR 30–59 ml/min/1.73 m²; stage 4 = eGFR 15–29 ml/min/1.73 m²; stage 5 = eGFR <15 ml/min/1.73 m²; † included only patients with a chronic kidney disease stage.
SD, standard deviation.

#5414

Abstracts

i326
#5627
SYSTEMATIC HISTOLOGICAL SCORING OF TUBULOINTERSTITIAL LESIONS CORRELATE WITH CLINICAL PARAMETERS IN ANCA-ASSOCIATED GLOMERULONEPHRITIS
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Background and Aims: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a small vessel vasculitis affecting multiple organ systems, including the kidney. Small vessels in the kidney include small-sized arteries (interlobular artery, afferent and efferent arteriole), capillaries (glomerular and peritubular capillary) and venules. Although crescentic ANCA glomerulonephritis (GN) is a common histological finding reflecting glomerular small vessel vasculitis, it is reasonable that manifestation of AAV could also contribute to interstitial small vessel vasculitis. Therefore, we here aimed to expand our current knowledge focusing on interstitial vasculitis in ANCA GN by systematic histological scoring of vascular lesions analogous to Banff.

Method: A total number of 49 kidney biopsies with confirmed renal involvement of AAV at the University Medical Center Göttingen were retrospectively included between 2015 till 2020. A renal pathologist evaluated all biopsies and was blinded to clinical data collection and analysis. A detailed methodological section is provided in the Supplementary material and methods section.

Results: Since previous studies established that crescentic ANCA GN associates with severe kidney injury and acute deterioration of kidney function in AAV, we first systematically scored interstitial vasculitis in association with requirement of renal replacement therapy (RRT). Among all active and chronic tubulointerstitial lesions analogous to the Banff scoring system, the only association between severe kidney injury requiring RRT was observed for interstitial vasculitis in AAV reflected by peritubular capillaritis (ptc) and arteritis (v, p = 0.0002) and arteritis (v, p = 0.0069), affecting 5/49 (10.2%) and 11/49 (22.4%) of renal biopsies, respectively. Since it is known that severe deterioration of kidney function also correlates with crescentic ANCA GN, we next directly compared glomerular and tubulointerstitial lesions. The fraction of normal glomeruli was inversely associated with interstitial fibrosis (ci), total (t) and inflammation in IFTA (i-IFTA), whereas glomerular crescents were associated with interstitial inflammation (i), tubulitis (t) and total inflammation (ti). In contrast, global glomerular sclerosis associated with less interstitial inflammation (i) but correlated with interstitial fibrosis (ci) and tubular atrophy (ct), confirming established mechanisms that chronic glomerular injury leads to tubular atrophy and interstitial fibrosis. Interestingly, no association between interstitial vasculitis (ptc and v correlating with severe kidney injury) and any glomerular lesion in ANCA GN (also correlating with severe kidney injury) was observed, thereby confirming that interstitial vasculitis contributes to severe kidney injury independent of ANCA GN. By contrast, short-term renal recovery from RRT was equal in both groups, suggesting a distinct association with acute decline of kidney function at disease onset.

Conclusion: Taken together, by using the Banff scoring system we here expand our current knowledge of renal interstitial lesions in AAV revealing peritubular capillaritis and arteritis as important histological alterations associated with severe kidney injury in a considerable subset of AAV. Furthermore, our findings that interstitial vasculitis did not correlate with crescentic ANCA GN implicate that the characteristics of each vasculitis manifestation are independent and could further improve our understanding of mechanisms contributing to renal injury. These observations suggest that interstitial vasculitis in AAV may also affect long-term prognosis requiring further investigation.

#3191
RISK OF CKD IN LUPUS NEPHRITIS: CORRELATION WITH DURATION OF REMISSION AND DEVELOPMENT OF RENAL AND EXTRArenal FLARES
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Background and Aims: Achievement of remission and prevention of SLE flares are important therapy targets in patients with SLE in order to avoid the development of systemic chronic damage. In patients with lupus nephritis, the correlation between the duration of remission, the occurrence of SLE flares and the development of CKD is unclear. The aims of this study are to investigate a) the risk of CKD in patients with lupus nephritis b) the correlation between the risk of CKD and the development of renal and extrarenal SLE flares c)
the correlation between the risk of CKD and the achievement and duration of remission and the probability and predictors of renal and extra-renal remission.

**Method:** This is a retrospective multicentric study of prospectively collected data. Patients were included if they were >18 years old, they had a histological diagnosis of lupus nephritis and they had at least 5 years of follow up after the diagnosis. CKD was defined as eGFR <60 ml/min/1.73m² without active urinary sediment for at least 3 months. Remission was defined as normal renal function (serum creatinine <1.0 mg/dl, eGFR >60 ml/min/1.73m²), proteinuria <0.5 g/24h and cSLEDAI = 0 for at least 1 year. The probability of developing flares and achieving remission was estimated using Cox regression analysis.

**Results:** CKD developed in 57 patients out of the 303 included in the study (18.8%) during a median follow-up of 14.8 years. During the observation 257 patients achieved remission in a median time of 1.4 (0.7-3.6) years, while 46 patients never achieved it. 115 patients maintained remission until the end of follow-up (9.5 (5.8-14.5) years), while 142 developed a flare after a median time of 3.6 (2.3-5.9) years from the beginning of remission. Altogether, in these 142 patients, 174 SLE flares developed during a median follow-up of 17.8 (13.3-24.2) years: 132 renal flares (20 with serum creatinine increase, 112 with proteinuria) and 42 extra-renal flares. CKD developed in 11 patients with creatinine flares (55%), 19 patients with proteinuric flares (16.9%) and 1 patient with extra-renal flares (2.4%) (p<0.0001). The longer was the duration of remission, the lower the probability that remission was interrupted (Figure 1A) by the development of a SLE flare: the risk of flare reduced from 10% when the remission lasted less than 5 years, to 5% if the remission lasted 5-10 years and to 2% if the remission lasted more than 10 years (Figure 1B). CKD developed in 26 out of the 46 patients who never achieved remission (56%), in 31 patients among those who achieved remission but developed SLE flares (21.8%) and in none among those who maintained remission until the end of the observation (p<0.0001). We found that 3 years of persistent remission significantly reduced the risk of CKD development (Figure 2). At multivariate Cox regression analysis, age >40 years (OR: 1.017; 95% CI: 1.005-1.028; p = 0.004), therapy with hydroxychloroquine (OR: 1.384; 95% CI: 1.109-1.661; p = 0.021) and absence of arterial hypertension (OR: 0.699; 95% CI: 0.425-0.975; p = 0.011) were independent predictors of remission.

**Conclusion:** in patients with lupus nephritis, the risk of CKD is significantly higher if renal-extrarenal remission is not achieved or if it is interrupted by SLE flares. In particular, the risk of CKD is very high in patients who develop renal flares with creatinine increase. A longer duration of remission is related to a lower risk of SLE flares and of CKD: in particular, 3 years of remission protect from the development of CKD. Age older than 40 years, therapy with hydroxychloroquine and absence of arterial hypertension are associated with the achievement of remission.

![Figure 1](image1.png) **Figure 1:** A) probability of persistence of remission in relation to the duration of remission. B) risk of SLE flares in relation to the duration of remission.

![Figure 2](image2.png) **Figure 2:** CKD free survival in patients with at least 3 years of remission and in patients without 3 years of remission.
LONG-TERM CLINICAL OUTCOMES OF PATIENTS WITH LUPUS NEPHRITIS TREATED WITH AN INTENSIFIED B-CELL DEPLETION PROTOCOL WITHOUT MAINTENANCE THERAPY

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Background and Aims: The aim of this prospective study is to investigate the long term safety and efficacy of intensified B-cell depletion therapy (IBCDT) in patients with active lupus nephritis (LN), in comparison to a conventional immunosuppressant therapy, followed by a 3 year maintenance micophenolate mofetil (MMF) regimen.

Method: Thirty patients were administered an IBCDT (4 weekly rituximab [RTX] 375 mg/m2 and 2 more doses after 1 and 2 months; 2 infusions of 10 mg/kg cyclophosphamide [CYC], 3 methylprednisolone pulses), followed by oral prednisone (tapered to 5 mg/d by the third month). No immunosuppressant maintenance therapy was given. Thirty patients matched for LN class and age were selected as controls: 20 received 3 methylprednisolone pulses days followed by oral prednisone and micophenolate mofetil (MMF) 2 to 3 g/d, whereas 10 were given the Euro Lupus CYC, MMF (1-2 g/daily) or azathioprine (AZA, 1-2 mg/kg/day) were given for > 3 years as a maintenance therapy.

Results: At 12 months, complete renal remission was observed in 93% of patients on IBCDT, in 62.7% on MMF, and in 75% on CYC (P = 0.001). The dose of oral prednisone was lower in the IBCDT group (mean ± SD 2.9 ± 5.0 mg/d) than MMF (10.5 ± 8.0 mg/d, P = 0.01) or CYC group (7.5 ± 9.0 mg/d, P = 0.01). Mean follow-up after treatment was 45 months (interquartile range [IQR] 36-120 months), 48.6 months (IQR 36-120 months), and 45.3 (IQR 36-120 months) months for IBCDT, MMF, and CYC, respectively. At their last follow-up visit, we observed no significant differences in proteinuria and serum creatinine, nor in the frequency of new flares among the 3 groups.

Conclusion: In biopsy-proven LN, the IBCDT without further immunosuppressive maintenance therapy was shown to be as effective as conventional regimen of MMF or CYC followed by >3-year maintenance either MMF or AZA regimen. Moreover, the use of IBCDT was associated with a marked reduction of glaucoma levels at cumulative dose.

MULTICENTER STUDY TO ASSESS THE FREQUENCY OF ADVERSE EVENTS FROM VACCINATION AGAINST SARS-COV2 IN PATIENTS WITH PAUCI-IMMUNE GLOMERULONEPHRITIS

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Background and Aims: The present study aims to investigate the frequency of adverse events of SARS-CoV2 vaccination in patients with pauci-immune glomerulonephritis with a median age of 46±18 years and 71% male were included. 15% of patients were hypertensive and 4% were diabetic. 90% had antihypertensive treatment, and 44% immunosuppressive treatment. In renal biopsy according to Oxford classification: M1: 11.4%, E1:8.8%, S1:22%; T1:10.5%. The basal creatinine was 1.3 ± 0.47 mg/dl (eGFR 16 ± 116 ml/min/1.73m2), and proteinuria (uPCR) 500 mg/g (IQR 30-3220). The patients were followed for a median of 83 months (IQR 0-111 months). Seven patients progressed, defined as a loss of >40% of glomerular filtration rate (GFR), FH and FHR-1 plasma levels were significantly higher in IgAN cases (FH: cases 2400±659 nM vs controls 1980±573 nM, P = 0.002), (FHR-1: cases 97±256 vs controls 379±152 nM, P = 0.011), but the patients had a lowest FH/FHR-1 ratio (FH/FHR-1 cases 5.4±2.58 vs controls 6.3±3.67, p = 0.061). The levels of FH-2 and FHR-4A were also elevated in IgAN cases (FH-2: cases 214±127 vs controls 132±71 nM, P < 0.0001), (FHR-4A: cases 45±22 vs controls 31±14 nM, P < 0.001), while protein levels of FHR-1 and FHR-5 are higher in plasma samples from IgAN patients than in controls. The contribution of other FH proteins to IgAN is so far unknown. The objective of this study is to determine the role of FH and FHR proteins in the renal progression of IgAN, and to establish whether plasma levels of these proteins could at least partially explain the heterogeneity observed in the patients.

Method: Plasma levels of FH, FHR-1, FHR-2, FHR-4A and FHR-5 was carried out in patients diagnosed with IgAN by renal biopsy (n = 45), and compared with a control group (n = 45). Protein levels observed in the IgAN patients were subsequently compared according to renal progression.

Results: Forty-five IgAN patients with a mean age of 46±18 years and 71% male were included. 15% of patients were hypertensive and 4% were diabetic. 90% had antihypertensive treatment, and 44% immunosuppressive treatment. In renal biopsy according to Oxford classification: M1: 11.4%, E1:8.8%, S1:22%; T1:10.5%. The basal creatinine was 1.3 ± 0.47 mg/dl (eGFR 16 ± 116 ml/min/1.73m2), and proteinuria (uPCR) 500 mg/g (IQR 30-3220). The patients were followed for a median of 83 months (IQR 0-111 months). Seven patients progressed, defined as a loss of >40% of glomerular filtration rate (GFR), FH and FHR-1 plasma levels were significantly higher in IgAN cases (FH: cases 2400±659 nM vs controls 1980±573 nM, P = 0.002), (FHR-1: cases 97±256 vs controls 379±152 nM, P = 0.011), but the patients had a lowest FH/FHR-1 ratio (FH/FHR-1 cases 5.4±2.58 vs controls 6.3±3.67, p = 0.061). The levels of FH-2 and FHR-4A were also elevated in IgAN cases (FH-2: cases 214±127 vs controls 132±71 nM, P < 0.0001), (FHR-4A: cases 45±22 vs controls 31±14 nM, P < 0.001), while no differences in FHR-5 levels were found (FHR-5: cases 25.7 ± 17 vs controls 27 ± 15, p = 0.7). When the patients who progressed and those who did not progressed were compared, it was observed that, as previously described, FH-1 levels showed a tendency to be higher in progressing patients (566±333 vs 451±203 nM, p = 0.2), and a lower FH/FHR-1 ratio (4.1±2.4 vs 5.8±2.6, p = 0.1). Moreover, we also observed a similar trend in the other FHR proteins: (FHR-2: 304±106 vs 195±118 nM, p = 0.043); (FHR-4: 53±26 vs 43±21, p = 0.29); (FHR-5: 41±35 vs 23±8.9 nM, p = 0.2).

Conclusion: We observed increased levels of several FH proteins and FHRs/FH ratios in our IgAN cohort. We confirm that FH-1 is implicated in renal progression, and we also show that other proteins of the family (FHR-2, FHR-4, and FHR-5) also contribute, suggesting that dysregulation of the alternative Complement pathway by FHR proteins is involved in IgAN. Genetic studies in the CFH-CFHR region may provide additional evidence to our protein findings.
#6193 MULTICENTER RETROSPECTIVE STUDY EVALUATING THE CLINICAL PICTURE AND OUTCOME OF THE SARS-COV2 INFECTION AMONG PATIENTS WITH GLOMERULAR DISEASES
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Background and Aims: This is a retrospective study aiming to describe the clinical picture and outcome of sars-cov2 infection in patients with glomerular diseases (GD) and its impact in the probability of relapse of the primary disease.

Methods: Patients with biopsy-proven GD, who had been infected by sars-cov2 were studied. Patients who ended up in end-stage kidney disease prior to infection were excluded. We recorded demographics, histopathological diagnosis, past medical history, immunosuppressive regimens which were given for the GD, status of GD at the time of infection, clinical picture and outcome of the infection including specific symptoms, requirement for hospitalization, duration of hospitalization and outcome of Covid-19. The probability of relapse following Covid-19 was also estimated in patients who were infected and those who did not.

Results: To date 312 patients have been included in the study, of whom 214 (68.5%) were diagnosed with Covid-19, while the remaining 98 did not. Infected patients were younger compared with those not infected [44 (28-59,75) vs. 53 (38-64) years, p < 0.001]. The mean time from the diagnostic biopsy to Covid-19 was 67,6±(±9,3) months. 82.5% of the infected patients were vaccinated against sars-cov2 and 49.1% were treated with immunosuppressive therapy at vaccination. 28(13%) of the infected patients required admission to hospital, with a mean duration of 8,3±(±5,1) days. 84.2% of the infected patients experienced complete recovery of the infection, 4 (1.5%) due to Covid-19 and 24 (11%) had Covid-19 related symptoms for more than 3 months. Among patients who had achieved remission of the GD prior to the infection, the frequency of relapse of the primary disease was higher in patients with Covid-19 versus not infected patients (11.9% vs. 2.1%, p = 0.007).

Conclusions: According to our findings, the sars-cov2 infection appears to have a significant impact in patients with GD not only due to the increased morbidity but also by increasing the probability for relapse of the primary disease.

#6325 A LONG TERM EXPERIENCE OF MANAGEMENT OF BIOPSY-PROVEN RENAL AL AMYLOIDOSIS WITH DARATUMUMAB MONOTHERAPY
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Background and Aims: Daratumumab is an anti-CD38 monoclonal antibody recently approved as a first-line therapy on top of standard therapy for the treatment of multiple myeloma and AL amyloidosis. The mechanism of action of Daratumumab is based on its ability to bind CD38, a transmembrane receptor expressed in particular by pathogenic plasma cells, inducing their death through multiple intra and extracellular signaling mechanisms and thus interrupting the production of monoclonal light chains and consequently the deposition of new amyloid substance. The following data describe the good results reported by our group and the long-term experience achieved in recent years on the efficacy of daratumumab used in monotherapy.

Methods: This paper describes 17 patients affected by AL amyloidosis who were treated with Daratumumab alone, 24 iv administrations and a dose of 16 mg/kg. All of them had an histological confirmation and staging of renal involvement before treatment was started and were ineligible for ASCT. A bone marrow biopsy excluded overt multiple myeloma and the patient could either be naïve or refractory. Haematological and organ response was evaluated every 4 infusions by checking NTproBNP, dFLC and FLC ratio, serum creatinine, Upt (24h), serum and urine IF; responses were defined by using the International Society for Amyloidosis extended criteria. When feasible, the patient who underwent the whole cycle of therapy underwent a second kidney biopsy at the end of the treatment.

Results: 1 mean age at diagnosis was 73 years. 16 out of 17 patients had proteinuria (in the nephrotic range in 11) that was associated with renal function impairment in 11. Two patients were on dialysis at the time of therapy initiation, the patient completed the treatment: 13 over 17 underwent at least 12 infusions. At this time, the 12 th administrations 11 out of 13 pts (84.6%) had an overall hematological response. 6 pts (46.5%) achieved a complete hematological response, 5 pts had a very good partial response (38%), and 2 were non responders (15.3%). As regard to renal response 5/13 had already achieved an organ response; 6 didn’t meet renal response criteria yet; the 2 patients who were in dialysis at the time of therapy initiation, remained on dialysis. 1 of them had a complete hematological and cardiac responses, the remaining pt didn’t have any response. 7/9 achieved a renal response; the 2 remaining patients who were in dialysis at the time of therapy initiation, remained on dialysis. A significant decrease in 24-hour proteinuria from 6,02 g/24 hours (range 0.8 – 16,8) to 1,28 g/die (range 0.9 – 3,6 g/die, p < 0.005) with stabilization or improvement of sCr (from 1.66 mg/dl to 1.1 mg/dl, p = 0.17) were observed. 8/9 patients with cardiac involvement obtained at least amelioration. At the end of follow-up (mean 30 months, range 19–46) 5 patients have persistent hematological and renal response. One patient with initial partial response had a relapse and initiated a treatment with Bortezomib plus cyclophosphamide and dexamethasone. Two patients died to COVD infection and cardiovascular disease respectively. The last patient is still alive and is currently being treated with a second line of therapy, because no hematologic or organ response was achieved with Daratumumab. 7 patients underwent a second kidney biopsy at the end of the treatment. Histological findings showed stable deposits in 6 over 7 cases, while the last one showed a reduction in the extent and amount of amyloid deposits.

Conclusion: The optimal management of patients with AL amyloidosis remains to be defined. In particular patients who are ineligible for transplant continue to have a poor outcome. In recent years daratumumab has emerged as an appealing therapeutic alternative as shown by several reports. However, in clinical trials daratumumab was always added to bortezomib, cyclophosphamide and dexamethasone. Two patients died to COVD infection and cardiovascular disease respectively. The last patient is still alive and is currently being treated with a second line of therapy, because no hematologic or organ response was achieved with Daratumumab. 7 patients underwent a second kidney biopsy at the end of the treatment. Histological findings showed stable deposits in 6 over 7 cases, while the last one showed a reduction in the extent and amount of amyloid deposits.

#6452 SEVERE INFECTIONS AND IMMUNOSUPPRESSIVE MAINTENANCE THERAPY IN PATIENTS WITH LUPUS NEPHRITIS: DATA FROM A SINGLE CENTER PROSPECTIVE STUDY
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Background and Aims: Systemic lupus erythematosus is a multi-organ, multi-systemic autoimmune disease with significant burden on generally young patients. Renal involvement is relatively frequent, recent studies cite a prevalence of 15–60% of patients, and 25% develop end-stage renal disease after 10 years of disease onset. We studied the incidence of severe infections in 67 lupic patients with biopsy proven lupus nephritis treated with immunosuppressive maintenance therapy: mycophenolate mofetil, azathioprine, calcineurin inhibitors associated with corticosteroids. Severe infections are a major cause of death in lupic patients.

Methods: We concluded a single center prospective study to assess the incidence of severe infections in patients with biopsy proven lupus nephritis. Patients received standard induction therapy (Euro lupus, NIH, MMF, CNIs induction regimens) and were assigned to maintenance therapy to either AZA, MMF, CNIs or patients who received both AZA and MMF in the course of the disease (a switch in therapy was made), alongside standard doses of
corticosteroids. We used SPSS version 16 for the statistical analysis and data was extracted from the electronic medical records.

**Results:** We included patients diagnosed with systemic lupus erythematosus who had renal biopsy performed between January 2008 – December 2018. Patients were followed-up until May 2020. We included 67 patients, out of which 58 patients were female (86.5%). Median age at diagnosis of lupus disease was 29 years (min 10 years, max 62 years). Median duration of the disease was 10 years (min 1.5 years, max 30 years). Median duration of corticosteroid treatment was 10.1 years (min 1.58 years, max 29). 1 patient had class I, 2 had class II, 12 had class III, 32 had class IV, 12 had class V, 1 had class VI, 1 had classes III+V, 1 had classes IV+V of lupus nephritis (ISN classification of lupus nephritis). The induction regimens received by the patients were: Eurovalop (21 patients), NIH (23 patients), MMF (14 patients) and CNIs (9 patients). Treatments administered for the maintenance period were MMF (5 patients), AZA (5 patients), CNIs (9 patients), and patients who had a switch in therapy, receiving both MMF and AZA during the study (26 patients) due to financial reasons, pregnancies, adverse effects, patient preference. We registered severe infections in 16 patients – 3 patients had severe viral infections, 9 had bacterial and 4 had both viral and bacterial severe infections. We did not obtain statistical significance (Chi square statistic = 1.568, p = 0.06) for the association of a specific immunosuppressive treatment modality with infection development. In our study, the duration of administration of each immunosuppressive therapy expressed in years was not associated with the number of severe infections (Independent-Samples Mann-Whitney U Test, p<0.05).

**Conclusion:** We could not identify significant differences regarding infection rates in patients treated with MMF or AZA, CNIs, MMF and AZA. We therefore suggest that all patients receiving the immunosuppressive regimens described should be considered at equal risk of severe infections.

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**#5643**  
**TUBULOINTERSTITIAL NEPHRITIS AND UVETIS (TINU) SYNDROME: A REPORT OF 6 CASES WITH RENAL BIOPSY AND ELECTRON MICROSCOPY EVALUATION.**

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**Background and Aims:** Tubulointerstitial nephritis with uveitis (TINU) syndrome is a rare, but probably under-diagnosed, immune-mediated clinical entity, characterized by simultaneous renal and ocular manifestations. Diagnosis requires exclusion of all other causes of tubulointerstitial nephritis (TIN). We present six patients with clinical, laboratory and renal biopsy findings consistent with TINU syndrome.

**Method:** Medical records review. All patients underwent renal biopsy. Histochemical (pas, masson, silver, Congo-red) and immunohistochemical stains for immune cell populations (CD3, CD20, CD4, CD8, PGM1, CD138) and for the assessment of β2-microglobulin were conducted. Electron microscopy (EM) was also performed.

**Results:** All our patients experienced ocular and renal manifestations, defined by bilateral uveitis, photosensitivity, and decline of renal function. In all patients, increased serum creatinine was accompanied by non-nephrotic range proteinuria, glucosuria or “full blown” Fanconi syndrome. The rest of the laboratory evaluation was normal apart from the presence of elevated erythrocyte sedimentation rate and urine β2-microglobulin. Follow-up, ranged from 18 months to 10 years. Histological evaluation revealed interstitial inflammatory infiltration consisting of lymphocytes, with a T-cell predominance, along with several macrophages. Inflammation severity varied, with some showing scarce foci of immune cell clusters, while others demonstrated a dense, diffuse interstitial infiltration. Interestingly, in two cases, non-necrotic, ill-defined granulomas were detected. Tubulitis was also encountered in some patients. A divergence was noted regarding chronicity index, with different levels of tubular atrophy, interstitial fibrosis and global glomerulosclerosis among different cases. β2-Microglobulin immunohistochemical evaluation revealed diminution of cytoplasmic staining in tubular epithelial cells compared to control kidneys. A notable finding derived from EM was the presence, in one patient, of scattered granular electron-dense-deposits along tubular basement membranes. First-line treatment included steroids, supplemented in some cases by additional immunosuppressive agents. Three patients experienced partial or complete response. Progressive renal damage was observed in a case with severe chronic lesions and persistence of inflammation-triggering factor (β2-microglobulin).

**Conclusion:** Our cases seem to represent progressive stages within the continuum of disease evolution. Patients with more prominent inflammation might represent a more initial state, while those with more severe chronicity index, probably depict more advanced stages. While the predominance of T-cells predicates a cell-mediated autoimmune mechanism, as the driving force of the disease occurrence, the presence of immune-complexes in more advanced stages might contribute to the involvement of humoral immunity as a late event during disease course.

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**#5295**  
**SECONDARY MEMBRANOUS NEPHROPATHY WITH IGA DEPOSITS IN A PATIENT WITH PRIMARY CILIARY DYSKINESIA.**

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**Background and Aims:** Membranous nephropathy and IgA nephropathy are two types of common glomerulonephritis worldwide. There are reports of the coexistence of these glomerulopathies, mostly with mesangial expansion and IgA deposits. Furthermore, primary ciliary dyskinesia is rarely associated to glomerulopathy. Thus, we report a case of a patient with primary ciliary dyskinesia demonstrating membranous glomerulopathy associated with IgA and IgG deposits exclusively in glomerular basement membrane, without complement deposition.

**Method:** Case report.

**Results:** A 18 years-old man was referred from the nephroepidiatric outpatient clinic with subnephrotic hematuria and proteinuria. His medical history included a clinical diagnosis of primary ciliary dyskinesia due to a history of several respiratory infections since birth, asthma, rhinitis and bronchiectasis and a 15 years-old brother with a similar history. He was diagnosed with idiopathic thrombocytopenic purpura at age of one year-old and received prednison. At 3 years-old he presented with nephrotic syndrome, hematuria and hypertension, and was treated with intravenous methylprednisolone and oral cyclophosphamide for three months. Renal biopsy demonstrated mesangial expansion and thickening of the glomerular basement membrane (GBM), without adequate material for immunofluorescence. Because proteinuria and hematuria persisted, the prednison dose was increased to 2 mg/kg/day and cyclosporine was started. After 5 years on these medications, persisting with proteinuria, a second biopsy was performed and showed 16 glomeruli, three globally sclerosed and the others with diffuse thickening of the GBM, without other alterations, focal interstitial fibrosis and tubular atrophy and diffuse granular deposits of IgA 1+ and IgG 2+ along the GBM. Cyclosporine and prednison were discontinued. At age of 18 years-old, he was admitted to adult glomerulonephritis clinic with significant developmental delay (weight 28.6kg and height 1.29m), no edema and normal arterial blood pressure with RAAS inhibition. Laboratory tests: Hb 8.9 g/dL, serum iron 12 mcg/dL, Creatinine 0.51 mg/dL, albumine 2.3 g/dL. Serologies were negative for syphilis, hepatitis B and C, HIV, ANA and anti-DNA, with normal complement C3, C4 and C1q. Urinalysis revealed proteinuria 1+, hematuria 16.000/mL and proteinuria 1.400 mg/dL. CT scan showed symmetrical bronchiectasis in both lungs, with mucoid endobronchial impingement and diffuse bronchial parietal thickening; and chronic post-thrombotic changes with calcified thrombi in the left renal vein, extending into the inferior vena cava. A third renal biopsy was performed showing 38 of 45 (84%) globally sclerosed glomeruli without mesangial matrix changes or capular adhesions. GBM was thickened with spikes and holes and reactive podocytes. The tubulointerstitial compartment showed moderate atrophy and fibrosis (40-50%). Immunofluorescence microscopy evidenced strong immunoreactivity of IgG 3+/3+, IgA 3+/3+, Kappa 3+/3+ and Lambda 2+/3+, in granular pattern exclusively in GBM, without C3. Electron microscopy showed four sclerosed glomeruli, without deposits. Immunohistochemistry staining for IgG1 2+/3+, and it was negative for PLA2R, NELL-1, THSD7A, Exostosin-1 and 2, IgG 2, IgG3 and IgG4. The patient was maintained with supportive treatment, with RAAS inhibition and SGLT2 inhibitors, without immunosuppression.

**Conclusion:** This case highlights the codominance of IgG1 and IgA deposits along the GBM, without proliferation or mesangial deposition and without complement activation, in a patient with membranous nephropathy and primary ciliary dyskinesia, a condition rarely associated with glomerulopathies. Although rare, such renal biopsy findings reinforce the need for a better understanding of the different mechanisms of membranous nephritis, in
addition to better understanding and management of treatment in this situation.

#2898

UNMET NEEDS AND POOR LONG-TERM RENAL OUTCOMES IN EUROPEAN PATIENTS WITH LUPUS NEPHRITIS

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Background and Aims: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE), associated with substantial morbidity and increased risk of end-stage renal disease (ESRD). Despite currently used therapies, a notable proportion of patients may not achieve sustained remission, leading to adverse disease outcomes. This study aims to summarize evidence on the long-term outcomes, burden of comorbidities, and real-world (RW) effectiveness of therapy in European patients with LN.

Method: A targeted literature review was conducted using MEDLINE/Pubmed and Embase to identify studies in patients with LN. Search strategies were developed for each database to identify relevant peer-reviewed articles published in English from March 2012 - March 2022 and conference abstracts from 2019 – March 2022. All records were screened according to pre-specified inclusion/exclusion criteria. Only studies conducted in a European setting were summarized here.

Results: Of 4,216 total records, 55 studies reported long-term outcomes of LN and RW effectiveness of treatment in European adults. Up to 36% of patients with SLE developed LN, and nearly all LN cases occurred within 5 years of SLE diagnosis. Patients with LN often suffered from serious infection (19-35%), cardiovascular disease (CVD) (26%), chronic kidney disease (CKD)/ESRD (6-22%) and were more likely to experience cardio- and cerebrovascular events than patients with SLE only (p < 0.001). Patients with LN had a higher risk of mortality compared to those with SLE only or other lupus manifestations (p < 0.001), and deaths were often due to infections (8-32%), CVD (22-58%), or malignancies (5-27%). CKD/ESRD also contributed to poor survival – patients with ESRD had 3-times higher risk of death compared to those with LN only (p < 0.001). The majority of RW studies evaluated effectiveness of standard of care (SOC) induction and/or maintenance therapy, mostly with mycophenolate mofetil and cyclophosphamide. Treatment response rates varied across the studies likely due to heterogeneity in study design, drug dosing, and patient population; comparative studies did not find significant differences in response rates between the regimens. Overall, 30-86% of patients with LN achieved complete renal response/remission (CRR) within the first year of starting SOC therapy. However, one study reported that only 38% of patients maintained CRR while on SOC over a 5-year period, suggesting inadequate long-term maintenance on existing therapies. Patients who were non-responders (NR) after 1 year had a significantly increased risk of mortality and CKD compared to responders (p < 0.005). Patients achieving CRR had significantly longer survival compared to NR patients (95 vs 55%, p < 0.0001), further highlighting the value of achieving response in terms of long-term renal outcomes. Despite initial response to current therapies, 20-35% of patients experienced a renal relapse/flare while on maintenance therapy, with one study noting significantly increased risk of proteinuric flares with azathioprine compared to other maintenance therapies (p = 0.001). Limited studies focused on patients with severe refractory LN.

Conclusion: European adults with LN have considerable comorbidity burden and poor long-term renal outcomes. Few patients achieve and maintain renal remission with SOC, and a notable proportion of patients experience renal relapse despite initial response to therapy. Given the impact that achieving CRR has on long-term outcomes, there is a need for effective therapies that provide sustained remission, especially for patients with severe/refractory LN.

#5769

MEASURING PROTEINURIA AT 12 MONTHS IN LUPUS NEPHRITIS: A USEFUL TOOL?

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Background and Aims: Lupus nephritis is a well known manifestation of systemic lupus erythematosus (SLE) and it can progress to end stage kidney disease (ESKD) in 10-30% of patients [1]. Several studies have been conducted to find out whether proteinuria detected earlier in the course of lupus nephritis is associated with worse kidney related outcomes, such as progression to chronic kidney disease [2].

Method: We retrospectively reviewed a cohort of 67 patients referred to our center with the diagnosis of lupus nephritis until 2019. We evaluated proteinuria (g/g) in a random urine sample measured 12 months after diagnosis and beginning of treatment of lupus nephritis and divided patients into two groups: those with proteinuria less than or equal to 0.3 g/g – group 1 (n = 11; 35%) and those with proteinuria superior to 0.3 g/g – group 2 (n = 20; 65%) that had measures of our variables of interest. These groups were compared regarding a continuous variable: serum creatinine measured in the first year of follow up, as evaluated in previous studies [3]. We compared the median of serum creatinine values between group 1 and group 2 using Mann-Whitney test, due to the absence of normal distribution of serum creatinine. We also compared the median of serum creatinine in the 7th year to proteinuria measured at 3 and 6 months.

Results: Mean follow up was 13.36 ± 7.8 years and 81.7% (n = 57) were women, with a median age of 33.0 ±12.85 years. A total of 8 patients (11.9%) progressed to ESKD defined by the need for renal replacement therapy or being surviving to renal transplantation. Only 1 patient died due to a nosocomial infection. We had a sample of 31 patients, 26 women and 5 men (p = 0.591) (missing n = 36). Baseline median serum creatinine in group 1 was 0.95 mg/dl and in group 2 was 0.78 mg/dl (p = 0.086). We obtained a median serum creatinine of 0.69 mg/dl (Interquartile range (IQR): 0.61-0.87) in group 1 versus 0.92 mg/dl (IQR: 0.66-1.25) in group 2 (p = 0.04). Medians of serum creatinine in the 7th year regarding proteinuria measured at 3 and 6 months were not significantly different (p = 0.05).

Conclusion: In our cohort, the group with a higher persistent proteinuria (>0.3 g/g), one year after lupus nephritis diagnosis, had a significantly higher serum creatinine (7 years after diagnosis). Although previous studies have shown that reducing proteinuria to less than 0.3–0.8/g.d⁻¹ by 1 year of treatment predicts good long-term kidney outcomes, our particular data suggest that further reducing to less than 0.3 g/g may provide additional benefit in the long run [2], even though, due to our reduced sample, more investigation is required. From the above mentioned, one may consider 12 months proteinuria
as a potential predictor to long-term renal outcomes with lupus nephritis. More studies are necessary to validate this hypothesis.

REFERENCES


#6612 ACUTE KIDNEY INJURY ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITOR THERAPY: REPORT OF 4 CASES

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Background and Aims: Immunotheapy using immune checkpoint inhibitors (ICIs) is the cornerstone of modern cancer therapy. Despite significant clinical benefits, ICIs are associated with remarkable adverse events of autoimmune nature involving various organs. Acute Kidney Injury (AKI) occurs more rarely, mainly with the appearance of acute interstitial nephritis. We present a series of patients with AKI after administration of immunotherapy with ICIs.

Method: Patient 1 with metastatic small cell lung cancer on immunotherapy with atezolizumab presented with purpura on the trunk and lower extremities, AKI, microscopic glomerular hematuria, and proteinuria. Patient 2 with esophageal malignancy on immunotherapy with pembrolizumab and worsening renal function. Patient 3 with endometrial malignancy on immunotherapy with pembrolizumab developed AKI, nephrotic syndrome and microscopic hematuria. Patient 4 with melanoma on immunotherapy with pembrolizumab presented with microscopic hematuria and rash.

Results: A kidney biopsy was performed in all 4 patients unraveling the following: Patient 1: pauci-immune necrotizing glomerulonephritis with fibrinoid necrosis and inflammation in the wall of a vessel. Patient 2: acute interstitial nephritis with intense inflammation. Patient 3: findings consistent with focal segmental glomerulosclerosis (FSGS, NOS), without evidence of immune complex disease. Patient 4: focal segmental glomerulosclerosis, moderate interstitial fibrosis and interstitial nephritis in remission. The patient had already been treated with glucocorticoid. In all 4 patients immunotherapy was temporarily discontinued and they were treated with intravenous pulses of methyl-prednisolone followed by oral glucocorticoids, with significant improvement of kidney function and resolution of all extra renal manifestation i.e skin rash etc. Escalation of immunosuppressive therapy with the addition of another agent was avoided in order not to cause relapse of the malignancy.

Conclusion: AKI is a rare but potentially serious complication of ICIs. Temporal discontinuation of the implicated agent is of major importance while treatment with glucocorticoids may be critical for kidney function. Yet, constant vigilance and sustained collaboration among medical specialists are becoming essential in the increasing use of immunotherapy.

#6663 PRIMARY SJÖGREN SYNDROME WITH BIOPSY PROVEN RENAL INVOLVEMENT: A SINGLE CENTER EXPERIENCE

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Background and Aims: Primary Sjögren’s syndrome (pSS) is a chronic systemic autoimmune disease characterized by inflammation and destruction of the exocrine glands and the involvement of multiple organs. A wide variety of kidney manifestations associated with pSS have been described. The prevalence of kidney involvement is not clear. Our aim was to describe the renal involvement of patients with pSS diagnosed by kidney biopsy (KB). We also analyzed the clinical manifestations, laboratory and immunological characteristics, clinical outcomes, treatments received in patients with pSS referred to a specialized kidney centre.

Method: Observational, retrospective study of adult patients (age > 18 years) diagnosed with pSS (EULAR criteria) referred and treated at a kidney referral centre (Fundació Puigvert) in Barcelona, Spain. We collected data from the clinical records registry including demographic variables, laboratory parameters, biopsy results and adverse outcomes, defined by the need of renal replacement therapy (RRT) and/or death. Absolute frequencies, percentages, means and standard deviations were used for statistical analysis. Multivariate analysis was performed as appropriate in SPSS V28.0

Results: A total of 27 patients with pSS underwent KB from January 1994 to July 2022; all patients were female, with a median age of 58.4 years (SD ± 12.4); 85% were Caucasian. The mean baseline glomerular filtration rate (eGFR) was 65.9 mL/min (SD ± 16) (before nephrologist referral), with 8 of 27 patients (29.6%) having eGFR less than 60 mL/min at baseline. The main indication for nephrological evaluation was acute kidney injury (AKI) (63%), followed by the presence of non-nephrotic proteinuria with dysmorphic haematuria (29.6%). The most common finding in KB was acute interstitial nephritis (AIN) (55.6%), as an isolated AIN kidney lesion in twelve patients (44.4%). Mild interstitial nephritis was noted in the context of a predominant glomerular lesion in three other patients (one membranoproliferative glomerulonephritis, one IgA nephropathy and one AA amyloidosis). Nine patients (33.3%) had glomerular lesion (see Table 1). In 18.5% of patients, the diagnosis of pSS was made after the renal biopsy. The percentage of patients receiving ACEI/ARB was 77.8%. A total of 25 patients received some type of immunosuppression (IS). Corticosteroids being the most frequently used (77.8%), followed by the combination IS treatment (44%) and rituximab (33.3%). At the time of the KB, the mean eGFR was 46.3 mL/min (SD ± 24), compared to eGFR of 45.2 mL/min (SD ± 22) one-year after KB. During follow-up, seven patients (25.9%) required RRT and three (11.1%) died from non-renal causes, mainly by infections associated with immunosuppression. Factors associated with adverse renal outcomes were AKI (p = 0.01), baseline eGFR CKD-EPI less than 60 mL/min (p = 0.005), presence of anti-Ro60 antibodies (p = 0.046), use of plasmapheresis (p = 0.013), use of cyclophosphamide (p = 0.013) and the presence of tubulointerstitial atrophy with glomerular sclerosis on kidney biopsy (p = 0.010).

Conclusion: Our study included a larger cohort than previously reported before in a single centre. In our cohort of patients with pSS who were evaluated by KB, AIN was the leading cause of renal involvement, as has been seen in other studies. The presence of eGFR below 60 mL/min at baseline and the finding of chronicity in the KB are associated with an adverse outcome, as well as is the presence of AKI. Early referral to nephrologist may be important for prognosis, and KB is necessary for accurate diagnosis of kidney involvement to allow targeted treatment.
#6809
PULSE VERSUS DAILY ORAL CYCLOPHOSPHAMIDE IN ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT: A SINGLE CENTER EXPERIENCE
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Background and Aims: We aimed to compare the risk of death, relapse and infections requiring hospital admission of ANCA-associated vasculitis (AAV) patients according to the induction of remission scheme used: daily oral (PO) cyclophosphamide or pulse intravenous (IV) cyclophosphamide.

Method: We identified all newly diagnosed AAV patients treated with PO or IV cyclophosphamide between January 1998 and December 2022 admitted to the CHVNGe Nephrology Department. Data were analyzed with SPSS v28© using parametric and non-parametric tests and Kaplan Meyer survival analysis.

Results: We identified 74 cases of de novo vasculitis, 50 of them received PO cyclophosphamide and 24 received IV cyclophosphamide. Median age at presentation was 68,30 ± 16,06 years PO and 68,00 ± 10,41 years IV. Median duration of follow-up was 3,8 years ± 2,98 for both groups, 6,21 years PO and 3,88 years IV. One-year survival was 84% in PO and 91,3% in IV patients; 15 (30%) PO and 5 (20,8%) IV patients had at least one relapse. Neoplasms occurred in 3 (6%) patients in the PO group and 1 (4,2%) patient in the IV group. The number of patients admitted with one or more infections was 22 (44%) in the PO group and 9 (37,5%) in the IV group. Renal survival was 26 (52%) PO and 15 (62,5%) IV. There was no difference in survival (p = 0,176), renal survival (p = 0,113), risk of relapse (p = 0,283) and infection (p = 0,196) between the two groups.

Conclusion: There was no difference in renal or overall survival, confirming the previous published data. Contrasting with CYCLOPS, our analysis does not confirm an increased risk of relapse in the IV group. One particularly interesting data is that the number of infections in IV route was lower than PO, corroborating the data on lower cumulative doses and therefore lower risk of infection in previous studies. Potential bias of this study is the small sample of patients enrolled in the two groups and the duration of follow up. Despite the reduction in the cumulative dose of cyclophosphamide, we continue to have significant adverse effects, which can also be explained by the dose of corticosteroid previously used, therefore strategies to reduce the toxicity associated with treatment without compromising efficacy are important goals for future research. Treatments need to be optimized and customized according to the severity of the patient's disease and the risk of recurrence.

#3741
A CASE OF PODOCYTIC INFOLDING GLOMERULOPATHY WITH DIABETES MELLITUS, NEPHROTIC RANGE PROTEINURIA AND POSITIVE ANTI-PLA2R IN SERUM
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Background and Aims: Podocytic infolding glomerulopathy (PIG) is a rare glomerular abnormality which was first proposed as a new disease entity in 2008. It is characterized by glomerular basement membrane (GBM) bubbling viewable by light microscopy, due to extensive trapping of podocytic cytoplasm fragments and cell membrane projections within the GBM. Electron microscopy reveals podocyte infolding and invagination into the glomerular basement membranes (GBMs). Most of the cases reported worldwide, indicate that PIG usually co-exists with autoimmune diseases. In this case we present a diabetic patient with no other autoimmune disease in his medical history, whose biopsy was characterized as PIG.

Method: A 60-year-old Caucasian man with a 5-year history of type II diabetes mellitus, hyperlipidemia, hypertension, hyperuricemia and benign colon polyps, was noted by his family physician to have proteinuria. He had been treated with an angiotensin II receptor blocker, statin, and allopurinol for 5 years and he was well regulated. At the point of admission, his 24-h urine collection showed 4,5gr of urine protein. His creatinine at the time was normal (0,89mg/dl), no hypoalbuminemia, no edema or deregulation of hyperlipidemia was noted. His fundoscopy at this point had no diabetic lesions. In the immunological work up, we found normal values of autoantibodies ANA, anti-dsDNA, anti-ENA, complement screening C3, C4, serum and urine protein electrophoresis - immunofixation. Everything was within normal limits except from serum autoantibodies to PhospholipaseA2 Receptor of podocytes which was tested with ELISA and valued 35 RU/mL (<20RU/mL).

In the following 9 months his proteinuria remained at the same levels. Due to the persistent nephrotic range proteinuria (>3.5gr/24h) a kidney biopsy was performed. Biopsy was evaluated under light microscope (histochemistry for Congo-Red and immunohistochemistry for C4d, PLA2R and DNAJB9 included), immunofluorescence and electron microscope.

Results: The renal biopsy included 8 glomeruli, 3 of them globally sclerosed (37.5%), the rest enlarged with mild to moderate mesangial matrix increase and thickening of the GBMs, without spikes, pin holes or reduplications. Immunohistochemistry for C4d, PLAR2 and DNAJB9 was negative. Immunofluorescence revealed nothing noticeable (no staining of IgG, IgA, IgM, C3, C1q, C4, κ-λ chains) apart from a moderate linear albumin staining. Without electron microscopy the whole picture was rather reminiscent of mild to moderate lesions of diabetic nephropathy.

On electron microscopy, no classical electron-dense deposits were found. Effacement of podocytes' foot processes was multi-segmental. More importantly, podocytic cytoplasmic processes invaginating into the GBMs were observed, accompanied by scattered endomembranous, partially microspherulif microstructures, sometimes with adjacent unclear small pyknotic areas. The biopsy report concluded that although light microscopy and immunofluorescence findings could indicate diabetic nephropathy, the electron microscopy lesions suggest the diagnosis of PIG.

Conclusion: To our knowledge, this is the first reported case with PIG and anti-PLA2R antibodies detected in the serum, without clear histological evidence of membranous nephropathy. Our patient was diabetic for five years with no diabetic lesions in fundoscopy. Although PIG has been reported mainly in the context of autoimmune diseases, the coexistence with diabetes or its possible role in PIG’s pathogenesis has not been addressed. The treatment of this peculiar morphologically disease, still remains an open query for physicians.
Efficacy and Safety of Monthly-steroid Pulse Therapy and Tonsillectomy in Patients with IgA Nephropathy

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Background and Aims: In Japan, tonsillectomy and corticosteroid therapy is widely performed in patients with IgA nephropathy, to improve kidney outcomes and reduce proteinuria and hematuria. Over the last decade, tonsillectomy and corticosteroid therapy monthly for 3 consecutive months and tonsillectomy without post-treatment. Thereafter, the effects and adverse events were evaluated.

Method: Forty-two patients diagnosed with IgA nephropathy on biopsy at our hospital, with ≥0.3g/day of proteinuria, and who had undergone tonsillectomy and steroid pulse therapy were included in the study. Of these patients, 16 were treated with three months of consecutive steroid pulse therapy without follow-up steroid administration (MSP); the remaining patients were administrated the conventional steroid pulse therapy (SP), including modified Pozzi’s (Lancet 1999) and Hotta’s (AJKD 2001) regimens. We evaluated and compared the time to proteinuria remission and both hematuria and proteinuria remission between the two groups using Kaplan-Meier curve and log-rank test. Remission of proteinuria was defined as three consecutive results of <0.3g/day over 6 months, and that of hematuria was defined as three consecutive results of <5 RBCs/high-power field in the urinary sediment. In addition to efficacy, we compared the incidence rates of adverse events between the two groups.

Results: There were no significant differences in the age, sex, time to diagnosis, histopathological findings according to the Oxford classification, or RAS inhibitor use between the MSP and SP groups. The eGFR(ml/min/1.73m^2) was 81.3 and 78.5, and the urinary protein excretion (g/day) was 1.18, in the MSP and SP groups, respectively. The proteinuria remission rates in the MSP and SP groups were 81% and 69% after one year and 94% and 81% after two years, respectively, with no significant difference. The remission rates of both hematuria and proteinuria were 47% and 46% after one year and 77% and 58% after two years, respectively, with no significant differences. The incident rates of adverse events, including diabetes and infections, was 13% and 54% in the MSP and SP groups, respectively, and was significantly lower in the MSP group (p = 0.005).

Conclusion: Tonsillectomy with monthly steroid pulse therapy was effective and safer than the conventional steroid pulse therapy in patients with IgA nephropathy.
Abstracts

#3786
CORONARY ARTERY CALCIFICATION IN AN SLE PATIENT WITH RENAL: IS IT PATIENT OR DISEASE RELATED?
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Background and Aims: Cardiovascular disease is one of the leading causes of death in SLE patients (Fors Nieves CE, et al. 2016). Coronary artery calcium scores can be used as a predictor CVD events, independent of traditional risk factors. CAC scores quantify the presence and extent of calcified plaque in the coronary arteries. A CAC>0 in the general population is an independent predictor of CVD mortality (Platekani AN, et al. 2015) patients with SLE, especially those aged >45 years, have an increased prevalence of CAC and the presence of renal affection obviously increases this risk. Patients with SLE aged ≤45 years have an increased prevalence of detectable CAC compared with the general population (Yevgeniya Garshkeyn, et al. 2019). We evaluated CAC in SLE with predominantly renal affection.

Method: In this observational study we identified 86 patients with SLE and documented lupus nephritis by renal biopsy ISN/RPS classification 2004, without known coronary artery disease and who had a non-contrast chest CT performed as part of their clinical care, with images retrievable for calculation of CAC scores. Demographics, disease characteristics and comorbidities were ascertained and adjusted for.

Results: 15.1% of patients with SLE, LN (mean age 43±41 years, 84%female,) had CAC>0, 53.8% for age ≤45 years and 46.2% for age >45. Patients with SLE with CAC>0 were older and had longer disease duration and higher disease activity than patients with normal CAC (p.value 0.004, 0.004 and 0.02 respectively). Furthermore, DM was at higher incidence in normal CAC patient and all patients with CAC>0 were hypertensive.

Conclusion: Patients with SLE and LN have an increased prevalence of detectable CAC. Our data suggest that subclinical atherosclerosis in SLE may develop early and it is directly related to disease factors as its duration and pathological activity. Although, patient age is an important risk factor for developing coronary artery calcification. This need a close monitoring and even some cardioprotective interventions.

#4210
ZETOMIPZOMIB DEMONSTRATES CLINICALLY MEANINGFUL IMPROVEMENT IN UPCR IN NPHROTIC RANGE PROTEINURIA PATIENTS: RESULTS FROM THE OPEN-LABEL MISSION STUDY
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1 The Ohio State University Wexner Medical Center, United States of America, 2 NYU School of Medicine, United States of America and 3 Kezar Life Sciences, United States of America

Background and Aims: Prospective cohorts have shown that patients with LN and nephrotic range proteinuria at baseline have a lower probability of achieving renal response [1]. These patients may require more time due to slower proteinuria recovery. Results previously reported on the Phase 2, open-label MISSION study evaluating the safety and tolerability of zetomipzomib in active proliferative LN including patients with nephrotic range proteinuria, demonstrated clinically meaningful renal responses [2]. A post-hoc analysis of MISSION patients with nephrotic range proteinuria is presented here.

Method: In the MISSION Phase 2 study, patients with active proliferative LN (Class III or IV ± V) with 24-hour urine protein to creatinine ratios (UPCR) ≥1.0 mg/mg despite stable background therapy received 60 mg of zetomipzomib subcutaneously once weekly (first dose: 30 mg) in addition to stable background therapy for 24 weeks. End of treatment (EOT) was at Week (W) 25, and end of study (EOS) occurred at W37. The primary endpoint was the number of patients with ≥50% reduction in UPCR from baseline after 24 weeks of treatment. Nephrotic range proteinuria was defined as UPCR ≥3.0 mg/mg at baseline (as per KDIGO 2012 Clinical Practice Guideline for the Management of Glomerular Diseases).

Results: Of 17 evaluable patients who reached EOT, 4 patients had nephrotic range proteinuria, with 3 having hypoalbuminemia (serum albumin ≤3.5 g/dL) at baseline. Patients with nephrotic range proteinuria had mean LN duration of 4.14 years with mean 24-hour UPCR of 5.78 mg/mg, mean serum albumin of 3.0 g/dL, mean blood pressure of 124/81 mmHg and mean eGFR of 122.5 mL/min/1.73 m2. All 4 patients were on concomitant corticosteroids (mean dose: 19.81 mg/d), mycophenolate mofetil, hydroxychloroquine and antihypertensives. After 24 weeks of zetomipzomib treatment, 3/4 patients with nephrotic range proteinuria achieved ≥50% reduction in UPCR at W25 (EOT) and W37 (EOS, 12 weeks post-treatment) (Table 1). Serum albumin levels also improved and normalized by EOS in all 3 patients with hypoalbuminemia at baseline (Table 1). eGFR levels generally remained stable throughout the study. Reduction of daily steroid dose to 10 mg/day was observed in all 4 patients as early as W13 and at EOT/EOS while other background therapy doses

Table 1: Correlational analysis of cell-free circulating DNA, renal engagement, age, sex, BVAS and phenotype for patients during active disease.

<table>
<thead>
<tr>
<th></th>
<th>mtDNA R</th>
<th>p-value</th>
<th>nDNA R</th>
<th>p-value</th>
<th>Ratio R</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Diagnosis (MPA or GPA)</td>
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<td>.498</td>
<td>−0.014</td>
<td>.959</td>
<td>0.142</td>
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<td>ANCA</td>
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<td>.061</td>
<td>0.338</td>
<td>.200</td>
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<td>Age</td>
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<td>−0.218</td>
<td>.418</td>
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<td>.399</td>
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<td>Sex</td>
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<td>.920</td>
<td>−0.096</td>
<td>.723</td>
<td>0.152</td>
<td>.574</td>
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<tr>
<td>Kidney involvement</td>
<td>−0.015</td>
<td>.268</td>
<td>−0.074</td>
<td>.786</td>
<td>−0.015</td>
<td>.957</td>
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<td>BVAS</td>
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<td>−0.178</td>
<td>.525</td>
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<td>mtDNA</td>
<td>0.920</td>
<td>&lt;.001**</td>
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<td>1.01</td>
<td>0.096</td>
<td>.723</td>
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<tr>
<td>nDNA</td>
<td>0.789**</td>
<td>&lt;.001**</td>
<td>0.152</td>
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<td>.786</td>
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<td>Ratio mtDNA/nDNA</td>
<td>0.295</td>
<td>.268</td>
<td>0.015</td>
<td>.268</td>
<td>0.015</td>
<td>.268</td>
</tr>
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</table>

Spearman rank correlation was performed.

**Correlation significant at 0.01 level (two-tailed).

Table 2: Correlational analysis of cell-free circulating DNA, kidney involvement, age, sex, BVAS and phenotype for patients during remission.

<table>
<thead>
<tr>
<th></th>
<th>mtDNA R</th>
<th>p-value</th>
<th>nDNA R</th>
<th>p-value</th>
<th>Ratio R</th>
<th>p-value</th>
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<tbody>
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<td>Diagnosis (MPA or GPA)</td>
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<td>Kidney involvement</td>
<td>0.426</td>
<td>.100</td>
<td>0.308</td>
<td>.245</td>
<td>0.221</td>
<td>.411</td>
</tr>
<tr>
<td>BVAS</td>
<td>0.054</td>
<td>.848</td>
<td>−0.049</td>
<td>.863</td>
<td>0.121</td>
<td>.667</td>
</tr>
<tr>
<td>mtDNA</td>
<td>1.0</td>
<td>&lt;.001**</td>
<td>0.789**</td>
<td>&lt;.001**</td>
<td>0.778</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>nDNA</td>
<td>0.789**</td>
<td>&lt;.001**</td>
<td>1.0</td>
<td>&lt;.001**</td>
<td>1.0</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>Ratio mtDNA/nDNA</td>
<td>0.778</td>
<td>&lt;.001**</td>
<td>0.397</td>
<td>0.128</td>
<td>0.397</td>
<td>0.128</td>
</tr>
</tbody>
</table>

Spearman rank correlation was performed.

**Correlation significant at 0.01 level (two-tailed).
related to the diagnosis and management of glomerulonephritis (PG)

**Method:** In this post-hoc subgroup analysis of MISSION Phase 2 study, zetomipzomib treatment demonstrated clinically meaningful improvement in UPCR and normalization of albumin levels in patients with nephrotic range proteinuria and hypoalbuminemia. These results further support the potential activity of zetomipzomib in hard-to-treat LN patients.

### REFERENCES


### #4414

**GLOMERULONEPHRITIS DIAGNOSIS AND MANAGEMENT: IMPROVING KNOWLEDGE AND COMPETENCE AMONGST NEPHROLOGISTS THROUGH ONLINE CME CASE CHALLENGES**

Sukhbir Bahra¹, Adriana Stan¹, Peter Schoonheim ¹, Rita Moreira Da Silva¹ and David Kavanagh²

¹Medscape, Den Haag, Netherlands and ²Newcastle upon Tyne Hospitals, Newcastle upon Tyne, United Kingdom

**Background and Aims:** Continuing medical education (CME) aims at modeling best practice in promoting positive behavior. We hypothesized that participation in the case-based medical education "Challenging Cases of Glomerulonephritis: How Would You Diagnose and Manage These Patients?" would lead to improved knowledge and competence of nephrologists in the diagnosis and management of glomerulonephritis.

**Method:** The online CME activity consisted of 2 patient case scenarios, and it was delivered as an interactive, text-based format. Using a "test and teach" methodology to elicit cognitive dissonance, clinicians completed multiple-choice questions to test their application of evidence-based recommendations. Each response was followed by detailed, referenced, feedback to improve learners’ knowledge, competence, and confidence on the diagnosis and management of glomerulonephritis. The educational effect was assessed using a repeated-pairs design with pre-/post-assessment, where 3 multiple choice questions assessed knowledge/competence and 1 question assessed confidence. Significance was assessed using paired samples t-test for overall average number of correct responses and for confidence rating, and the McNemar’s test for individual questions (5% significance level, P < 0.05). Cohen’s d estimated the effect size impact on number of correct responses (r<.20 modest, .20-.49 small,.50-.79 moderate, ≥.80 large). Data were collected between July 15 2022 and September 27 2022.

**Results:** Comparison of responses to questions before and after education demonstrated a large educational effect for nephrologists (n = 119; d = 1.36; P < .001). Overall 84% nephrologists improved their knowledge/competence related to the diagnosis and management of glomerulonephritis (P < .001), showing a 76% relative increase in correct responses from pre- to post-CME (51% pre, 90% post). Significant increases in knowledge/competence on rare complement-mediated kidney diseases were reported (P < .001 for all comparison) for:

- Clinical manifestations (64% pre; 97% post)
- Diagnosis (18% pre; 84% post)
- Management (71% pre; 90% post)

**Conclusion:** Around 55% of nephrologists showed a measurable confidence increase (P <.001) in their ability to recognize clinical information suggestive of rare complement-mediated kidney diseases.

### #4709

**PERSONALISED INDUCTION THERAPY IN ANCA GLOMERULONEPHRITIS**

Laura Hamburger¹, Wing Yin Leung¹, Ian Bruce² and Silke Brix³
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**Background and Aims:** Patient and kidney outcome in ANCA glomerulonephritis (GN) remains unsatisfactory. Rituximab use failed to reduce the rate of infectious complications and demonstrates a significant rate of hypogammaglobulinaemia in ANCA vasculitis. Adjusting the rituximab dosage to the individual patient’s need promises a reduction in treatment toxicity.

**Method:** Retrospective analysis of a single centre cohort of ANCA GN patients with disease flares between 2019 – 2022 using a stratified induction immunosuppression with rituximab and cyclophosphamide. Treatment intensity was adjusted to reduce the rate of systemic inflammation and microscopic haematuria, peripheral CD19 cell count depletion and immunoglobulin G (IgG) levels.

**Results:** 45 patients (median age 57 years, 55.7% female, median eGFR 27 mls/min) were treated with a median dose of 1.5 grams Rituximab during induction (interquartile range, IQR 1 – 2 grams). 18 patients received concomitant intravenous cyclophosphamide pulses to control the acute inflammation (median cumulative dose of 2 grams, IQR 1.65 – 3 grams). Peripheral B cell depletion was 91.4% at 3 months and 90.3% at 6 months (<3 CD19 cells/ul). During the initial 12 months treatment, IgG level fell below 7g/l in 20 patients, below 5g/l in nine patients and below 3g/l in one patient. Seven patients required renal replacement therapy at diagnosis (15.6%). Five patients recovered kidney function and three patients developed end stage kidney disease (6.7%). Twelve infections were reported requiring antibiotic treatment (26.7%), seven severe infections were documented requiring hospitalisation (13.3%) and one patient died (2.2%).

**Conclusion:** An early assessment of treatment response assists adjusting vasculitis therapy. Adjusting management to the patient’s individual immunological and treatment response may result in better outcome with less treatment toxicity.

### #4732

**GLUCOCORTICOID-RELATED ADVERSE EFFECTS IN THE TREATMENT OF ANCA-ASSOCIATED VASCUITIS**

David Plappert, Markus Ketteler, Moritz Schanz and Nico Schmid
RBK Stuttgart, Department of General Internal Medicine and Nephrology, Stuttgart, Germany

**Background and Aims:** Upcoming glucocorticoid (GC)-sparing treatment strategies like avacopan could potentially diminish or replace the need of GC therapy for ANCA-associated-vasculitis (AAV) in the future. Therefore, a proper assessment of GC-related morbidity in AAV is required to provide further justification of such therapies. The aim of this study was therefore to assess the incidence of common toxicities and to further investigate the effect of GC-treatment on the incidence and management of diabetes mellitus, arterial hypertension and hypercholesterolemia.

**Method:** In this single-centre-cohort-study we screened medical records for patients with a diagnosis of AAV admitted to the Robert-Bosch-hospital (RBK) in Stuttgart, Germany on a regular basis. We assessed the dosage and duration of immunosuppressive therapy used to treat AAV, as well as the incidence and therapies of arterial hypertension, diabetes mellitus and hypercholesterolemia.
For this study, we observed the vasculitis time course during the acute phase (180 days) after either the initial diagnosis or relapse for each patient.

Results: We included 74 patients admitted to the RBK since 2004 up to the current date. Most common subtype of AAV was GPA (n = 48 patients), followed by MPA (n = 22) and EGPA (n = 4). Including relapses, a total of 127 events were observed. We followed patients for a mean time of 8 years (SD 3.9, 0.9 - 18.0 years). Mean duration of glucocorticoid therapy in total was 4.2 years (SD 3.6, 0.3-14.7 years). All of the patients received prednisolone, whereas 73% of the patients furthermore were administered methylprednisolone for induction therapy. Overall, 34% of the patients were diabetes mellitus (20% pre-existing diabetes, 20% new-onset diabetes). Daily and accumulated GC-dose did not differ between patients with or without diabetes. However, there was a significant higher accumulated GC dose in patients requiring insulin-therapy for diabetes management in comparison to those with oral anti-diabetics (p-value = 0.0214). 89% of the patients were treated with antihypertensive therapy (38% pre-existing hypertension, 51% new-onset hypertension). We found that the accumulated dose of prednisolone within the first 180 days after a vasculitis event was not significantly higher for patients with documented hypertension. However, we detected that the mean accumulated GC dose after a vasculitis event was significantly higher for the subgroup of patients in whom an escalation of antihypertensive therapy was initiated in comparison to the patients whose therapy was stable or even deescalated (p-value = 0.0001). With regard to hypercholesterolaemia, there was no statistical difference in the accumulated GC-dose during the acute course between patients requiring statin-therapy and those who did not.

Conclusion: GC related toxicities are common in patients with AAV. This study provides additional evidence about the incidence of treatment related harms in AAV to further promote importance of alternative reduced dose or GC free treatment approaches. This may be relevant in detecting risk groups for whom upcoming GC-sparing treatment strategies such as avacopan are essential to reduce treatment-related harm.

#5076 MONOCLONAL GAMMOPATHY IN C3 GLOMERULOPATHY: DOES THE BUCKET STOP THERE? Pedro Fragoso1, Luis Rodrigues1,2, Andreia Borges1, Ana Belmira1 and Rui Alves1,2

1Coimbra Hospital and University Centre, Nephrology Department, Coimbra, Portugal and 2Faculty of Medicine, University of Coimbra, University Clinic of Nephrology, Coimbra, Portugal

Background and Aims: C3 glomerulopathy (C3G) is a rare diagnosis, characterized by dysregulation of the alternative pathway of complement, classically presenting in children and young adults. Recently, it has been reported the association between the production of a monoclonal protein and the development of C3G, affecting a larger age span.

Method: We report the case of a 53-year-old male patient, that attended the emergency department due to persistent holocranial headache. He was an IV drug abuser with a history of treated Hepatitis C infection and free lancing with a chain monomolecular protein, identified by the Laboratory Department. On admission, he was hypertensive (187/98 mmHg), and labs showed an acute on chronic kidney disease (serum creatinine 2.35 mg/dl from a basal of 1.5 mg/dl) with an active urinary sediment (38 erythrocytes/field, with dysmorphia), a urinary protein/creatinine ratio of 626 mg/g, and C3 consumption (0.52 g/L). The patient was admitted, and a kidney biopsy was performed.

Results: Further lab results confirmed a serum IgG Lambda monomolecular protein. Autoantibodies screening (ANCA, ANAs, Anti-GBM), ASLO and Rheumatoid Factor were negative. Cryoglobulonemia was detected, and the cryoprecipitate’s immunofixation revealed monoclonal proteins IgG Lambda. HCV viral load was negative. Bone marrow biopsy revealed a small per cent (< 3%) of plasma cells with Lambda light chain restriction. Kidney biopsy’s light microscopy showed increased mesangial matrix and cells, endocapillary hypercellularity, and some glomeruli with lobulated appearance. Five out of 15 glomeruli presented fibrocellular crescents. Immunofluorescence showed C3 dominant staining on capillary walls and in the mesangium, with absent IgG and light chain deposits. A presumptive diagnosis of C3 glomerulopathy was made and the patient was empirically started on corticosteroids (3 pulses of intravenous methylprednisolone, followed by oral prednisolone 1mg/Kg/day), which was followed by paraproein-directed chemotherapy with bortezomib, cyclophosphamide and dexamethasone (VCD). The patient is currently on the third VCD cycle, presenting both renal and haematological responses: recovery of serum creatinine to basal levels (1.54 mg/dl), resolution of haematuria and proteinuria, normalisation of C3 levels. Serum immunofixation is currently negative for monomolecular protein, with normal serum immunoglobulin levels. Electron microscopy revealed electron-dense deposits in the mesangium, and mesangium-capillary transition, supporting the diagnosis of C3 glomerulonephritis. Genetic testing of complement-related genes revealed a rare missense variation of unknown significance (c.4855A>C) on the C3 gene, that has previously been reported in association with C3 glomerulopathy and atypical Haemolytic-Uremic syndrome.

Conclusion: This case represents a monoclonal gammopathy associated- C3 glomerulonephritis with a favourable response to paraprotein-directed chemotherapy. Although the association between monoclonal gammopathy and C3G rests on epidemiologic findings, experimental evidence suggests that several monoclonal proteins have complement dysregulation features, which may enhance alternate complement pathway activation.

Our patient’s response is in line with observational data that have shown improved renal outcomes in patients who achieve a haematological response following monoclonal protein-directed chemotherapy, which further supports the role of monoclonal gammopathy in C3G pathogenesis [1].

Interestingly, the genetic variation identified in our patient might have provided a favourable genetic background for the development of C3G, which is thought to rely upon a complex interaction of triggering events, such as a monoclonal gammopathy, and underlying complement abnormalities, such as genetic variants in complement genes.

REFERENCE

#5133 MONTREAL COGNITIVE ASSESSMENT (MOCA) AND DYSMORPHIC RED BLOOD CELLS IN PATIENTS WITH IMMUNOGLOBULIN A NEPHROPATHY

Anna Popova1,2, Marija Halturina 3, Kārlis Račenis1,2, Mikus Saulīte1,2, Jānis Selīls1,2, Anna Jana Saulīte2,1, Aivars Petersons1,2, Juta Kroica3, Haris铈 Cernesvskis1,2, Kristine Oleinika2,4,5, Baiba Silsēre4,5, Aivars Lejnieks2,7 and Viktorija Kuzema2,6

1Pauls Stradins Clinical University Hospital, Nephrology Department, Riga, Latvia, 2Riga Stradins University, Riga, Latvia, 3University of Latvia, Latvia, 4Boston Children’s Hospital, Boston, United States of America, 5Harvard Medical School, United States of America, 6Pauls Stradins Clinical University Hospital, Latvia and 7Riga Stradins University, Riga, Latvia

Background and Aims: Patients with chronic kidney disease (CKD) are at an increased risk of cognitive dysfunction, which is characterized by deficits in executive functions, memory and attention. Previous studies have suggested that albuminuria and lower estimated glomerular filtration rate (eGFR) are related to mild cognitive impairment (MCI) and dementia. There are no studies that have noticed connection between glomerular activity presented by dysmorphic red blood cells (RBC) count and cognitive evaluation results. The aim of the study was to investigate the association of cognitive decline with renal function and other potential risk factors such as albuminuria, proteinuria, and hematuria in patients with immunoglobulin A nephropathy (IgAN).

Method: A prospective study that took place from January 2020 till January 2022 at Pauls Stradins Clinical University Hospital Nephrology center included patients with IgAN. Diabetes mellitus, oncology, acute inflammation processes, transplantation in anamnesis were exclusion criteria. Demographic, anamnestic, clinical, laboratory data for renal function evaluation were collected. GFR was calculated using CKD-EPI Creatinine Equation. Urine spot protein/creatinine ratio was used for proteinuria measurement. Urine microscopy was performed by a nephrologist. Patients were assessed with a MoCA. Results of MoCA have been compared with potential risk factors.

Results: Sixty-five patients were included in the study. The mean age of the participants was 42.06 ± 10.71 years (IQR 35.47-75, range 21-65), with predominance of male sex (62.1%), mainly with higher education (45.5%). Dialysis was performed in 7 patients. The average duration of illness was 89.97 months ± 97.95 (IQR 31.5-120, range 1-456 months/38 years). Average GFR was 59.26 ± 38.66 (IQR 20.25-91.75, range 3-131) ml/min/1.73m2, urea 12.57±9.88 (IQR 6.3-15.45, range 4-62). Patients did not have anemia, average hemoglobin 135.20±14.8. Average proteinuria was 0.53±0.99 g/g (IQR 0.06-0.52, range 0.06-6.20), albuminuria - 69.34±107.3 g/mol (IQR 10.95-69.4, range 0.45-620). Average hematuria was 116.68±239.67 RBC/mlk (IQR 9.99-92.1, range 1.5-1421.3), while dysmorphic RBC count was 4.02±9.88 (IQR 6.3-15.45, range 4-62). Patients did not have anemia, average hemoglobin 135.20±14.8. Average proteinuria was 0.53±0.99 g/g (IQR 0.06-0.52, range 0.06-6.20), albuminuria - 69.34±107.3 g/mol (IQR 10.95-69.4, range 0.45-620). Average hematuria was 116.68±239.67 RBC/mlk (IQR 9.99-92.1, range 1.5-1421.3), while dysmorphic RBC count was 4.02±9.88 (IQR 6.3-15.45, range 4-62). Average hematuria was 116.68±239.67 RBC/mlk (IQR 9.99-92.1, range 1.5-1421.3), while dysmorphic RBC count was 4.02±9.88 (IQR 6.3-15.45, range 4-62). Average hematuria was 116.68±239.67 RBC/mlk (IQR 9.99-92.1, range 1.5-1421.3), while dysmorphic RBC count was 4.02±9.88 (IQR 6.3-15.45, range 4-62).
Patients age correlated with memory task score (p = 0.002, r = -0.42). Dysmorphic RBC count in urine sediment correlated with attention task (p = 0.002, r = -0.42).

Conclusion: Mild cognitive impairment is frequent even in our young age IgAN patient's cohort. Even small age difference plays role in MoCA evaluation score. No correlations have been found between proteinuria or albuminuria and MoCA score. Association between dysmorphic RBC and cognitive decline should be studied in bigger cohorts’ studies.

RE-ASSESSMENT OF PATHOLOGICAL DATA OF VASCULITIS PATIENTS WITH RENAL INVOLVEMENT ACCORDING TO CURRENT SCORING SYSTEMS AND CLINICAL CORRELATION

Deniz Eräl1, Dilek Barutcu Atas2, Murat Tuğcu1, Arzu Velioğlu1, Izzet Hakkı Arikân1, Fatma Alibaz-Oner1, Haner Direskeneli3, Ebru Asicioglu2 and Z. Serhan Tuglular2

1 Marmara University School of Medicine, Internal Medicine, Istanbul, Turkey, 2 Marmara University School of Medicine, Nephrology, Istanbul, Turkey and 3 Marmara University School of Medicine, Rheumatology, Istanbul, Turkey

Background and Aims: Renal involvement is responsible for substantial morbidity and mortality in ANCA associated vasculitis (AAV) patients. Predicting renal prognosis in AAV patients with renal involvement has been a challenge over the last decade. To date Berden Classification which focuses on glomerular lesions at renal biopsy proposed in 2010, Mayo Clinic Chronicity Score also including non-glomerular histopathological chronicity findings proposed in 2017 and adding eGFR at diagnosis to glomerular and non-glomerular chronicity findings at renal biopsy constructing ANCA Renal Risk Score (ARRS) proposed in 2018 have all addressed the latter challenge. In this study, we aimed to validate the impact of these 3 classification systems on the renal and patient survival in our ANCA associated glomerulonephritis (AAGN) patient population.

Method: Thirty-seven AAV patients with biopsy proven renal involvement who have been treated and followed-up at our multidisciplinary vasculitis clinic at Marmara University School of Medicine, Istanbul, Turkey between 2000-2020 were included in the study. Renal biopsies were re-evaluated by our pathologist and patients were grouped according to Berden Classification, Mayo Chronicity Score and ARRS. Renal survival and mortality analyses were carried out for 3 classification systems in order to evaluate their success at predicting prognosis and survival.

Results: Evaluated according to Berden Classification, 40.5% (n = 15) were classified as focal, 8.1% (n = 3) were sclerotic, 40.5% (n = 15) were crescentic and 10.8% (n = 4) were mixed. Focal group was associated with best renal prognosis and patients in mixed group had poorest renal prognosis. Differences in renal survival rates (p = 0.111) and patient survival rates (p = 0.129) among Berden Classification groups were not statistically significant. According to Mayo Chronicity Score, 16.2% of the patients were scored as minimal, 51.4% were as mild and 32.4 were in medium group. None of the patients were classified as severe. Compared to minimal group, mild and medium groups were found to be significantly associated with CKD development (p = 0.002). Mortality rates were similar between the groups according to Mayo Chronicity Score (p = 0.143). In renal survival analysis, mild and medium groups were associated with decreased renal survival (p = 0.046). When evaluated for ARRS, 29.4% of the patients were in low risk group, 45.9% of the patients were in medium risk group and 24.3% of the patients were in high risk group. Medium and high risk groups were associated with higher probability of progression to CKD (p = 0.000). Renal survival was found to be poorest in high risk group and best in low risk group (p = 0.017). Although mortality rates were higher in medium risk group than lower and higher risk groups, the difference has not reached statistical significance (0(0%) vs. 7 (38.9%) vs. 2 (22.2%); p = 0.067). Renal survival in AAGN patients according to Berden Classification, Mayo Chronicity Score and ARRS parameters are shown in Figure 1.

Conclusion: Recent classification systems were evaluated among our AAGN patients and our results showed that addition of eGFR at diagnosis to glomerular and non-glomerular histopathological findings were predictive of renal prognosis. Mayo Chronicity Score and ARRS systems can be used to predict patients’ renal reserve at diagnosis and also they can be used as a prognostic tool to predict patients’ probability of progressing to chronic kidney disease, end stage kidney disease.

Figure 1: Renal survival in AAGN patients according to Berden Classification, Mayo Chronicity Score and ARRS parameters.
THE PREDICTIVE VALUE OF URINARY CONGOPHILIA AS A BIOMARKER IN PREGNANT AND NON-PREGNANT WOMEN WITH LUPUS NEPHRITIS

Dalia Younis1, Rasha Samir Shemies1, Ghada El-Kannishy1, Alaa Mosbah1, Mahmoud Zakaria2, Amira Awadalla2 and Sherouk Elnagar1

1Faculty of Medicine Mansoura University, Egypt and 2Urology and Nephrology Center, Egypt

Background and Aims: Endoplasmic reticulum (ER) stress with protein misfolding has been introduced as a key pathogenetic mechanism in patients with lupus nephritis (LN). Pregnancy is thought to exaggerate ER stress in conjunction with autophagy inhibition. This probably explains disease flares during pregnancy; however, this is not fully addressed. The detection of the abnormally misfolded proteins is made using the Congo red stain, which is referred to as congophilia. This study aimed to assess the predictive value of urinary congophilia as a marker of protein misfolding in pregnant and non-pregnant women with lupus nephritis.

Method: Urine samples from non-pregnant lupus nephritis patients (n = 45) and pregnant women with lupus nephritis (n = 12), as well as pregnant healthy controls (n = 38) were collected. Urinary congophilia was assessed by Congo Red Dot Blot assay. The disease activity was defined according to SLE Disease Activity Index (SLEDAI) criteria. Renal biopsy was done for 26 adults of non-pregnant lupus nephritis patients at time of urine sampling as it was clinically indicated and modified NIH activity index was assessed.

Results: The median and range values for SLEDAI score were 14(4-34) for non-pregnant LN patients, and 4(0-6) for pregnant women with LN (Table 1). Congo red retention (CRR) was significantly higher for non-pregnant LN patients (24.18%(0.75-126.29%)), in comparison with pregnant LN patients (0.67%(0.31-27.69%), P = 0.001), and healthy controls (0.33%(0.18-2.7%), P≤0.001). There was a significant positive correlation between CRR on one hand, and anti-ds-DNA (r = 0.791, P≤0.001), as well as SLEDAI score (r = 0.623, P≤0.001) on the other hand. However, no significant correlation has been found between CRR with renal histopathological activity index (r = 0.2, P = 0.425). CRR at a cut point ≥ 21.85% had 83% sensitivity, and 58% specificity to capture high LN activity status (NIH-AI > 10) versus lower LN activity status (Fig. 1).

Conclusion: Urinary congophilia may add diagnostic value in patients with lupus nephritis and can be a reliable marker of disease activity. CRR is related to disease activity rather than pregnancy.

Figure 1: ROC curve to test the diagnostic accuracy assessment of CRR to capture high LN activity status (NIH-AI >10) versus lower LN activity status (NIH-AI ≤10). CRR at a cut point ≥ 21.85% had 83% sensitivity, and 58% specificity to capture high LN activity status (NIH-AI >10) versus lower LN activity status.

Table 1: Sociodemographic, clinical, and laboratory characteristics of participant at sampling time.

<table>
<thead>
<tr>
<th></th>
<th>Pregnant lupus nephritis N = (12)</th>
<th>Non-pregnant lupus nephritis N = (45)</th>
<th>Pregnant healthy controls N = (38)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>27.42 ± 5.78</td>
<td>29.47 ± 10.42</td>
<td>26.69 ± 5.84</td>
<td>0.342</td>
</tr>
<tr>
<td>WBC, (× 10³/mm³)</td>
<td>8.2 (2.30-17.4)</td>
<td>5.7 (1.7 - 16.10)</td>
<td>9 (5.1 - 16.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>HB, g/dl</td>
<td>10.17 ± 1.94</td>
<td>9.1 ± 2.1</td>
<td>10.99 ± 1.41</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PLT, (× 10³/mm³)</td>
<td>211 (82-287)</td>
<td>237 (75-526)</td>
<td>220 (34-398)</td>
<td>0.505</td>
</tr>
<tr>
<td>24hr. urinary protein, mg/day</td>
<td>1748 (200-7387)</td>
<td>2492.5 (311-12000)</td>
<td>NA</td>
<td>0.374</td>
</tr>
<tr>
<td>Serum creatinine, mg/dl</td>
<td>1.1 (0.5-2.7)</td>
<td>1.7 (0.6-11.9)</td>
<td>0.6 (0.3-0.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Albumin, gm/dl</td>
<td>2.75 (1.9-3.7)</td>
<td>2.95 (1.6-3.5)</td>
<td>3.5 (2.8-4.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>INR</td>
<td>1(1-1.04)</td>
<td>1 (1-1.3)</td>
<td>1 (1-1.3)</td>
<td>0.401</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>29.5 (21-40)</td>
<td>22 (8-47)</td>
<td>26.5 (16-38)</td>
<td>0.093</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>22(18-25)</td>
<td>21 (10-42)</td>
<td>23 (16-80)</td>
<td>0.448</td>
</tr>
<tr>
<td>Anti-ds-DNA, U/ml</td>
<td>5.9±2.03</td>
<td>74.52±56.5</td>
<td>NA</td>
<td>0.001</td>
</tr>
<tr>
<td>ESR</td>
<td>79±17.7</td>
<td>66.8±35.5</td>
<td>NA</td>
<td>0.842</td>
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<td>SLEDAI</td>
<td>4(0-6)</td>
<td>14(4-34)</td>
<td>NA</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CRR, %</td>
<td>0.67(0.31-27.69)</td>
<td>24.18(0.75-126.29)</td>
<td>0.33(0.18-2.7)</td>
<td>≤ 0.001</td>
</tr>
</tbody>
</table>
Background and Aims: The spectrum of glomerular lesion that occurs in the context of plasma cell dyscrasias (PCD) is wide, including type I and type II membranoproliferative glomerulonephritis (MPGN), focal proliferative GN, membranous nephropathy (MN), minimal change disease and amyloidosis. A clear-cut link between hematological dyscrasias and glomerulopathy is often offered by the finding of paraproteins in the kidney or by kidney leucocytic infiltration and, in these scenarios, malignancy treatment is often found to be also effective towards the glomerulopathy. In the context of PCD in which proliferation of the B-cell clone does not lead to plasma-cell terminal differentiation such as chronic lymphocytic leukemia (CLL), the physiopathological link with glomerulonephritis is not well established and it’s hard to determine whether the combination of these two disorders is fortuitous. With regarding to MN, it’s now well established that this histopathological pattern must be related to the presence of circulating autoantibodies, where anti-PLA2R antibodies usually been associated with primary MN. To our knowledge association between LLC and anti-PLA2R associated MN has not been described.

Case report: We report the case of a 76-year-old man who was admitted in February 2022 with anasarca and acute kidney injury. He had recently been evaluated by a hematologist in the context of suspected chronic lymphocytic leukemia (CLL). Laboratory findings, along with typical CLL white blood cell count, showed decreased kidney function from baseline and were compatible with nephrotic syndrome, with proteinuria progressively increasing up to 27 gr/24 h in the following weeks. CLL was confirmed by lymphocyte typing. A total body CT scan showed mediastinal, abdominal and inguinal lymphadenopathies, but no suspected neoplastic lesions. Screening for autoimmunity tested completely negative, as well as infectious screening for common hepatic viruses (HBV, HAV, HCV), EBV, CMV, HIV, Parvovirus B19. Lymph node biopsy showed no aspects of aggressive lymphoproliferative disease and hematological consultation only indicated clinical and laboratory follow-up of LLC, with no further indication to specific therapies. A kidney biopsy was performed showing diffuse thickening of the basement membrane (Fig. 1) with granular deposition of Ig (+++) and C3 (+++) along the glomerular capillary walls at immunofluorescence. Electron microscopy revealed subepithelial immune deposits (Fig. 2) with initial incorporation from the glomerular basement membrane (GBM). Anti PLAS antibodies, found negative at first determination, subsequently tested positive at high titre (ELISA 1356.4 U/ml). A diagnosis of stage two membranous nephropathy was made, and the patient was treated with Rituximab 375 mg/m2 every week for four weeks. Clinical stability was obtained with repeated intravenous administration of diuretics (furosemide 60 mg + canrenone 200 mg) along with albumin. Nevertheless, nephrotic syndrome persisted, and kidney function progressively decreased with serum creatinine up to 2.8 mg/dL. Immunophenotype, which showed reduction but no suppression of CD19+ lymphocytes, was again repeated on November 2022 and showed typical LLC findings (CD 19+, CD 20+, CD 23+, CD 5+). Anti PLASR antibodies gradually decreased instead, reaching a value of ELISA 1.8 U/ml in November 2022 and persisted negative until present. The patient recovered from nephrotic syndrome in Autumn 2022 and is currently on stage G3B chronic kidney disease with persistent sub-nephrotic proteinuria in supportive treatment.

Conclusion: Simultaneous diagnosis of primary MN and LLC led us to ask ourselves whether this patient could benefit from LLC-specific chemotherapy, even though there were no signs of aggressive hematological disease and no clear link with the nephropathy. We think that further investigations are required to deeply understand the connection between hematological and renal disorders, in order to identify whether there are two diseases to treat separately or two sides of the same disease to treat as one.

#5332
COVID-19 INFECTION MODIFIES GLOMERULAR DISEASE EVOLUTION
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Background and Aims: A fibrotic effect of the SARS-CoV2 virus (Covid-19) has been described and the risk for acute renal failure in glomerular disease (GD) patients; however, the long-term renal effect in these patients is unknown. We evaluate the impact of the Covid-19 infection on eGFR, the influence of proteinuria, the effect of the drugs used to control glomerulonephritis and the use of Paxlovid (nirmatrelvir/ritonavir) for covid infection control.

Method: We retrospectively evaluate the eGFR (mL/min/1.73m2) at month 12 and 6 before infection (pre-infection period), during infection, 6 months after infection and at the last visit post-infection in renal biopsy-proven glomerulonephritis patients. Patients were included from January/2020 to July/2022. All patients were followed up for six months or more from infection.

Results: Forty-seven patients were included. The mean follow-up was 13 months (min: 6–max = 33). Sex Female 24 (52%), Age (mean[SD]) = 47 (14) years. 39(85%) were vaccinated before infection. At infection time, 31(66%) of the patients presented proteinuria (protein/creatinine ratio > 0.2 mg/mg), 27(54%) received oral steroids, 27(54%) mycophenolate, 24(51%) prednisone, and 27(54%) renin-angiotensin system inhibitors (RASi). Four (8%) started chronic renal replacement therapy during the follow-up, and 12(25%) required hospital admission. During the pre-infection period, eGFR remained stable (mean change (95%CI): -2.2 (-8.2 to 3.7) mL/min/1.73m2, P = 1. Compared with month six before infection, eGFR decreased at the end of the follow-up by 9.1 (95% CI: 0.96 to 17.2) mL/min/1.73m2, P = 0.019. After stratifying by the presence of proteinuria, eGFR decreased only in those with proteinuria 14.5 (95%CI: 3.7 to 25.4) mL/min/1.73m2, while no changes were observed in those without proteinuria. No changes in proteinuria level after infection were observed. No interaction between drugs used, hospitalisation requirements and eGFR evolution was observed. In the sub-group of patients treated with Paxlovid (all previously vaccinated) after six months of follow-up, no patients observed.

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required hospitalisation; however, eGFR evolution was similar to the whole group, which decreased only in those with proteinuria at baseline.

**Conclusion:** The Covid-19 infection in proteinuric GD patients changed the renal function evolution dramatically. The medication used (mycophenolate, steroid and RASi), including Paxlovid, did not influence this evolution. At the end of the follow-up, the accelerated renal function deterioration continues. Urgent therapeutic measures for controlling eGFR decline in these patients are needed.

#5902
**KIDNEY INVOLVEMENT IN HAEMATOLOGICAL MALIGNANCIES: THE IMPORTANCE OF EARLY NEPHROLOGICAL REFERRAL**

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**Background and Aims:** Kidney is often injured in the setting of hematological malignancies. Although, kidney involvement negatively influences the prognosis of these patients, often the referral to clinical nephrology is late. The aims of this study were to investigate the long-term outcomes of haematological diseases with renal involvement demonstrated by kidney biopsy and the association between nephrological referral earliness and survival.

**Method:** Monocentric retrospective study evaluating overall survival (OS) (time to death) and renal free survival (RFS) (time to renal replacement therapy) in patients affected by hematologic malignancies with renal involvement demonstrated by kidney biopsy. Data have been collected by January 1st 2009 to December 30th 2021. Results reported as median (min-max) and percentage (%).

**Results:** 46 patients; M/F = 1.3; age: 70 years (39.5-91.2). Follow-up: 17.8 months (0.13-125.4). Data at kidney biopsy: creatinine was 3.13 mg/dL (0.6-14), eGFR was 20 ml/min/1.73 m2 (3-110), proteinuria was 5.1 g/24h (0.15-38.6), Bence-Jones proteinuria detected in 74% of patients. Clinical presentations: AKI (63.1%), Nephrotic syndrome (26.1%), General Practitioner (21.7%); Emergency Department (17.4%). The most frequent histological diagnosis was amyloidosis (32.7%), followed by cast nephropathy (19.2%). Renal Replacement Therapy was required in 41.3% patients. Treatment: 38 patients underwent chemotherapy (56.4% complete/very good hematologic response; 12.8% partial and 30.6% without response). Overall Survival at 24 months was 63.8% and it was reduced in patients with AKI at presentation (Fig. 1) and in patients without treatment response (Fig. 2). RFS was shorter in patients who presented with AKI and affected by Myeloma Cast. Early nephrological referral was associated with a better RFS (Fig. 3).

**Conclusion:** Haematological malignancies with renal involvement causing AKI have the worst prognosis. Kidney biopsy has a prognostic significance and early nephrological referral associated with haematological treatment response correlate with a better renal outcome. These data point to the central role of a multidisciplinary team aimed to the detection and treatment of renal damage due to hematologic malignancies.

![Figure 1: Overall Survival According to Clinical Presentation.](image1)

![Figure 2: Overall Survival According to Treatment Response.](image2)
A CASE REPORT OF MEMBRANOUS NEPHROPATHY SECONDARY TO SYPHILIS: A STEROID-RESPONSIVE DISEASE?

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Background and Aims: Membranous Nephropathy (MN) is among the most common forms of nephrotic syndrome in the adults. MN in adults is most often primary (75-80%) and caused by circulating autoantibodies against podocyte antigens being PLA2R the most important target. In the remaining 20-25% of cases, the MN lesion is associated with various disorders, including infections, autoimmune diseases, thyroiditis, malignancies, and the use of certain drugs. Syphilis is a chronic bacterial infection caused by Treponema Pallidum that can present in the primary, secondary or tertiary forms. Kidneys can be involved during either the secondary or the tertiary phase and the most frequent clinical presentation is nephrotic syndrome underlying membranous nephropathy. Here, we present the case of a 47-year-old man who developed rapidly progressive acute kidney injury, nephrotic syndrome and a blotchy diffuse macular rash secondary to Treponema Pallidum infection.

Method: Data review and collection of clinical records, kidney biopsy evaluation, treatment and outcomes description.

Results: A 47-year-old man presented to our hospital complaining about asthenia and dizziness. He reported recent use of both antinflammatory drugs and antibiotics to treat an anal fissure. His past medical history was notable for previous drug abuse and alcohol consumption. Physical examination highlighted peripheral edema and a diffuse macular rash. Serum analysis showed serum creatinine of 2.06 mg/dL, urea 84 mg/dL, haemoglobin 13.8 g/dL, albumin 4 g/dL and protein/creatinine ratio of 17741 mg/g; urinary dipstick was positive for haemoglobinuria and proteinuria. Urine collection revealed 22 g proteins/24h. Kidney ultrasound showed normal kidneys with a preserved cortico-medullary differentiation and thickness. In the next days kidney function worsened (serum creatinine 3 mg/dL and urea 100 mg/dL) and daily proteinuria reached a peak of 35 g/24h. A complete panel of antibodies was searched. IgG4 against PLA2R were negative. ANA, ENA and ANCA were absent, C3 and C4 were in the normal range. Serologic testing for HBV, HCV and HIV were negative. Empircic steroid therapy with prednisone 1 mg/kg/day was started obtaining a rapid improvement in terms of proteinuria and asthenia.

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and kidney function (Fig. 1), the cutaneous rash faded. Kidney biopsy was performed and demonstrated a membranous nephropathy. Serological testing for syphilis revealed positive TPHA (titer, 1:2560; normal value, <1:80) and a positive Veneral Disease Research Laboratory test (VDRL) (titer, 1:32; normal value, <1:2). The presentation suggested the diagnosis of anti-PLA2R negative membranous nephropathy secondary to systemic syphilis. Because of the serious clinical manifestation and the unknown duration of the infection we decided to treat the patient with Benzathine penicillin G 2.4 million units administered as three doses over one week intervals (Schön & Bertich, 2016). Oral steroid was maintained at a dose of 1mg/kg/body weight and desacalation started after 30 days. The proteinuria also improved with a reduction in the 24-hour collection from 30 g to 200 mg and serum creatinine went back to normal. Clinical course according to treatment phases are summarized in Fig. 1.

Conclusion: As far as we know, this is the first case of PLA2R negative membranous nephropathy secondary to syphilis. Although, antibiotic therapy is pivotal in syphilis treatment, our patient showed a fast improvement of kidney function, proteinuria and fading of the cutaneous erythema after steroid therapy and before starting antibiotic therapy. This suggested the possible role of steroids in treatment of secondary T. Pallidium infection complicated by anti-PLA2R negative membranous nephropathy. Further researches are needed to better define the possible role of steroids in the context of an infective but immune-complex mediated nephropathy.

#3121
THE EFFECTIVENESS OF A GLUTEN-FREE DIET IN PATIENTS WITH IGA NEPHROPATHY
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Background and Aims: Modern data from the world literature confirm the association of IgA nephropathy (IgAN) and celiac disease. The inclusion of a gluten-free diet (GFD) in the diet has a beneficial effect not only on gastrointestinal symptoms, but also reduces the clinical and laboratory activity of IgAN. The aim of this study was to evaluate the effect of a gluten-free diet on the course of IgAN using general clinical and immunological tests 6 months after the start of its use.

Methods: In patients with IgA nephropathy, with morphologically confirmed IgAN were included in the study. To detect a violation of gluten metabolism, screening determination of the level of IgA antibodies to tissue transglutaminase (Anti-TTG IgA) and IgA antibodies to deamidated gliadin peptides (Anti-DPG IgA) was performed. According to the results of the screening examination, a group of patients with the level of antibodies exceeding the reference values were formed (group 1, n = 13) and a group of patients in whose blood did not exceed the reference values, or were absent at all (group 2, n = 52). Patients of both groups were recommended GFD for a period of at least 6 months. The effectiveness of GFD was evaluated by the following indicators: protein in urine (g/l); red blood cells in urine (RBCs) (hp); daily proteinuria (g/day); blood creatinine (mmol/l), GFR calculated by the formula CKD-EPI (ml/min/1.73 m²) at the beginning of the study and 6 months after the inclusion of dietary recommendations. Statistical analysis of the data obtained was carried out using the statistical program SPSS Statistics 26.0 (IBM, USA). When comparing quantitative indicators, the distribution of which differed from normal in two related groups, the Wilcoxon criterion was used. Then the statistical hypothesis about the absence of differences and connections was rejected at p<0.05.

Results: among the examined patients there were 61 men (93.8%), 4 women (6.2%). The average age of men was 39.0±8.2 years, women - 34.7±9.7 years. The duration of the underlying disease at the time of inclusion in the study was 55.98 [40.67-71.28] months. 57 people (85.1%) received ACE inhibitors/sartans in therapeutic doses as the main therapy, 8 people (11.9%) did not receive drug therapy. It was possible to evaluate the effectiveness of GFD in patients from group 1 in 9 people. During the follow-up period 2 patients from group 1 showed progression of the disease to the End-Stage Renal Disease (GFR according to CKD-EPI <15 ml/min/1.73 m²), which required their exclusion from the study, in 2 more patients it was not possible to evaluate the effectiveness of GFD due to insufficient follow-up periods (less than 6 months.) GFD was also recommended to patients from group 2. Dietary restrictions were applied to patients with daily protein loss > 0.5 g/day and/or anti-TTG IgA and anti-DPG IgA levels in the reference values, thus it was possible to evaluate the effectiveness of GFD in patients of group 2 in 21 people. According to the results of the analysis, a statistically significant decrease in daily proteinuria (p = 0.028) and microscopic hematuria (p = 0.018) was revealed. After 6 months from the start of compliance with GFD, daily proteinuria decreased in 66.7%; microscopic hematuria – in 77.8% in group 1 patients. Among group 2 patients, a statistically significant decrease in microscopic hematuria (p = 0.05) was observed in 76.2% of those included in the study.

Conclusion: the inclusion of GFD in the diet of patients with IgAN is justified in patients with the presence of gluten antibodies in the blood serum, as it allows to significantly reduce the severity of proteinuria, microscopic hematuria in these patients. Screening examination of patients with IgAN for gluten metabolism disorders will expand therapeutic possibilities, and GFD can become part of a nephroprotective strategy.

#5339
TRANSTHYRETIN AMYLOIDOSIS WITH BIOPSY PROVEN RENAL INVOLVEMENT
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Background and Aims: Systemic amyloidosis is a cluster of disorders characterized by tissue deposition of amyloid (highly ordered fibrils composed of low molecular weight subunits of a variety of proteins). Transthyretin (TTR) amyloidosis (ATTR) is either an autosomal dominant inherited condition (ATTRv, where v stands for "variant") or a non hereditary disease due to misfolding of wild-type TTR (ATTRwt). ATTR is likely underdiagnosed due to its clinical variability and lack of specific symptoms or biomarkers. The first aim of the study is to emphasise the importance of suspecting ATTR when facing certain clinical manifestations in association with renal impairment and urinary abnormalities. Furthermore, renal biopsy provides crucial information for a correct diagnosis and treatment approach.

Method: We report 5 cases of biopsy-proven renal ATTR deposition in patients presenting with mild to moderate renal impairment and mild urinary abnormalities. The ATTRv precursor has been confirmed in kidney specimens by immunohistochemistry. Genotyping was carried out in every patient.

Results: The presence of amyloid was found in all patients, with different distribution (#1-3 pericapsular and vascular; #2 vascular; #4 mesangial, vascular, in tubular basement membrane and in the interstitium of cortex and medulla; #5 pericapsular, vascular and interstitial). On genetic analysis three patients were wild-type (#1-2-5), one carried the c.424G>A (p.Val142Ile) mutation (#3) and the last one the Val30Met mutation (#4).

Conclusion: Suspection of ATTR should be considered in patients with increase in serum creatinine, mild proteinuria and cardiac and peripheral nerve symptoms. This can be of utmost importance in elderly patients in whom a monoclonal gammapathy of undetermined significance can co-exist and drive a wrong diagnosis of primary light chain amyloidosis (AL), that could lead the clinician to undertake inappropriate treatments. Renal biopsy and genetic sequencing are both critical in diagnosing ATTR. Finally, we suggest distinguishing in the context of the ATTR deposition disease an ATTR nephropathy characterized by mesangial accumulation of amyloid, that impacts functional and urinary assessment, from isolated deposition in small vessels without specific clinical consequences, albeit critical for ATTR diagnosis.

#5163
RATIONAL USE OF ECULIZUMAB IN SECONDARY ATYPICAL HAEMOLYTIC UREMIC SYNDROME
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Background and Aims: Secondary atypical hemolytic uremic syndrome (secondary aHUS) is a heterogeneous group of thrombotic microangiopathies (TMA) associated with various underlying conditions. Unlike primary aHUS, there is still no hard evidence on the efficacy of complement blockade in treating secondary aHUS since the two main series in the literature that investigate this subject show discrepant results. Our work aims to reassess Eculizumab’s efficacy in treating secondary aHUS.

Method: Observational, retrospective, single-center study, in which we analyzed the hematological and renal evolution of 24 patients diagnosed with secondary aHUS who received treatment with Eculizumab compared with a control cohort of 14 patients who did not receive Eculizumab. Complete renal response was defined as the recovery of renal function before the event, partial renal response as a recovery of 50% of lost glomerular filtration rate, and hematological response as normalization of hemoglobin and platelets.

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Results: We found no statistically significant differences in baseline character-istics between the two groups. After a median of 5 doses of Eculizumab, the group of patients who received complement blockade presented a significant difference in renal response (complete in 47.8% of patients and partial in 17.4%) compared to the control cohort (complete response 14.3% and partial of 14.3%). Rates of hematological remission were similar in both groups (87% in the eculizumab cohort and 85.7% in the control cohort).

Conclusion: Rational and early use of Eculizumab in patients with secondary aHUS could be an effective and safe therapeutic option, guaranteeing better renal recovery compared to patients who do not receive complement blockade.

#5091 RITUXIMAB IN MANAGEMENT OF RELAPSING AND STEROID DEPENDANT C1Q NEPHROPATHY: A TALE OF THREE PATIENTS
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Background and Aims: C1q nephropathy is an immune glomerular disease in which dominant C1q electron-dense deposits are identified in the mesangium. It commonly presents with nephrotic syndrome, while nephritic syndrome or isolated haematuria are less common. Biopsy findings vary; from no glomerular lesion identified as in minimal change disease (MCD) to focal segmental glomerulosclerosis (FSGS) and immune-mediated proliferative glomerulonephritis. Steroids are the main therapeutic agents that have been tried.

Rituximab is an anti-CD20 human/mouse chimeric monoclonal antibody and one of the drugs used in managing C1q nephropathy. We present 3 cases of biopsy-proven C1q nephropathy that presented with nephrotic syndrome. They responded initially to steroids and achieved remission after treatment with rituximab.

Method: Case Scenarios: Case (1): A 30-year-old man had been diagnosed with steroid sensitive nephrotic syndrome since he was 18 months. Renal biopsy confirmed the diagnosis of C1q nephropathy, more in the spectrum of MCD. He was managed with steroids, and rituximab in 2011 and achieved remission for the last 7 years after 5 doses. His renal function had always remained normal. He presented to our department in 2020 with another relapse and heavy proteinuria (urine protein creatinine ratio (UPCR) was 1300 mg/mmol) but unchanged renal function. Repeat kidney biopsy showed C1q nephropathy in the spectrum of FSGS. He showed good response to oral steroids. On relapse while weaning steroids, Rituximab was considered. He had 2 doses of rituximab of 1 gram 2 weeks apart in July 2021. He achieved full remission over the last 2 years. Case (2): A 77-year-old female presented in 2020 with nephrotic syndrome (UPCR of 660 mg/mmol) and acute kidney injury (AKI) (creatinine 400 μmol/l). Her kidney biopsy showed C1q nephropathy with FSGS features. She was started on haemodialysis due to continuous kidney function deterioration. She recovered on steroid therapy to normal kidney function and negative proteinuria, but she relapsed with weaning steroids. So steroid dose was increased and tacrolimus was added. Her renal function remained intact. Following that she had another flare in May 2022 with mild kidney impairment and worse proteinuria (UPCR 500 mg/mmol) while she was on small dose steroid and tacrolimus. She was then started on rituximab. After 2 doses 1 gm 2 weeks apart she achieved remission and her kidney function normalised. She received 2 more doses of 1 gram rituximab 6 months apart with excellent response. She has been in complete remission since. Case (3): A 28-year-old male presented to our department in July 2020 with nephrotic syndrome (urine PCR > 900 mg/mmol) and preserved renal function. His kidney biopsy was initially reported as MCD and he was managed with oral steroids. He showed a good response with complete resolution of his proteinuria 3 weeks later and remained in remission for 2 years. However, in August 2022- he suffered a second severe relapse (UPCR 4000 mg/mmol) with preserved renal function. His kidney biopsy was therefore reevaluated and immunofluorescence was added which revealed C1q nephropathy. He had another course of steroids and was initiated on rituximab infusions. He showed full remission after 2 doses (1 gram IV 2 weeks apart) and is on ongoing 6 monthly infusions.

Results: Rituximab was effective in inducing remission in our patients with nephrotic syndrome due to C1q nephropathy. They were all steroid sensitive. It was effective in both steroid-sensitive and steroid-dependent cases. The first and second cases had biopsy findings in the spectrum of FSGS while the third case histological picture in the spectrum of MCD. They all achieved full resolution of their proteinuria and preserved their renal function finally.

Conclusion: Rituximab was effective in inducing remission in both steroid-responsive and steroid dependent relapsed patients with C1q nephropathy, despite differences in biopsy results. Kidney function was preserved. More solidified data, including multi-centre randomized controlled trials, are needed to establish clear guidelines for the position of rituximab in the management of the disease and the proper dose to use.
One of two main antigens are targeted in this condition, either proteinase 3 (PR3) or myeloperoxidase (MPO). Uncommonly, both antigens can be targeted in specific situations such as during levisamole use, propylthiouracil use, hydralazine use or infections. Herein, we illustrate a case of a patient who presented with progressively worsening kidney function in the setting of recent COVID booster.

**Method:** A 79 year old female with a history of hypertension, hyperlipidemia, acid reflux and hypothyroidism was admitted to our facility from her outpatient nephrologist due to abnormal labs. This was the first time the patient had seen a nephrologist, although she was told that her serum creatinine (Scr) was elevated to ~3 mg/dL three months earlier. At that time, she noted blood tinged urine as well as frothiness of urine that had since resolved. She also endorsed a raised erythematous rash that also resolved. She did mention that she had increasing fatigue over the past week prior to presentation along with weight loss over the past few months. She denied ear pain, sinus pain, epistaxis, hemoptysis or specific joint pain. She denied any kidney stones or NSAID use. She was a former smoker, having quit decades ago. She denied any current tobacco or illicit drug use, including cocaine as well as any herbal supplements or medications that were not otherwise prescribed to her by a medical provider. She did note recent COVID booster prior to being told of a Scr ~3 mg/dL. She had a repeat kidney function test one month prior to presentation, at which time she was told her Scr was 5 mg/dL. In our Emergency Department, Scr was elevated to 8.45 mg/dL with a BUN of 68 mg/dL. Computed tomography of the abdomen and pelvis ruled out any hydronephrosis or kidney stones. Urinalysis was revealing for 509 RBCs, 39 WBCs, and some granular casts. Spot urine protein to creatinine ratio was found to be elevated at 6925 mg/g. Serologies were pertinent for WBCs, casts as well as granular casts. Spot urine protein to creatinine ratio was found to be elevated at 6925 mg/g. Serologies were pertinent for a positive ANA as well as ANCA. Interestingly, both MPO and PR3 titres were elevated at 72 AU/mL and 391 AU/mL, respectively. Kidney biopsy was performed and revealed a pauci-immune glomerulonephritis with crescents along with mixed interstitial inflammatory infiltrate (Figure 1). The diagnosis of dual positive ANCA glomerulonephritis was made. Computed tomography of the chest revealed scattered ground glass opacities and subpleural nodules which was consistent with a vasculitis. She started treatment with Rituximab and steroids on Day 5 of hospitalization.

**Results:** Although evidence linking ANCA vasculitis to COVID infection and vaccine has been starting to develop, the association with dual positive ANCA is something that has been elusive. Having titres for both MPO and PR3 ANCA is uncommon and has traditionally been attributed to very few causes; as COVID infection and vaccination has been a fairly recent development, this has not historically been considered a cause to think of in such patients. In the case presentation above, our patient had no other identifiable risk factors for presenting with a dual positive ANCA vasculitis. She did endorse recent booster vaccination which was subsequently followed by elevated Scr and positive serologies.

**Conclusion:** Dual positive ANCA vasculitis is an uncommon finding and should trigger a high clinical suspicion for implicated drugs, infections as well as COVID vaccination.

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**MONOCLONAL GAMMOPATHY OF RENAL SIGNIFICANCE: A SINGLE CENTER EXPERIENCE**

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**Background and Aims:** Monoclonal gammopathy of renal significance is an organ-threatening manifestation of paraproteinemia. It can be secondary to the clonal proliferation of either plasma cells or mature B-lymphocytes. The underlying clonal disorder does not meet the current hematologic criteria for immediate myeloma-specific therapy. With the advent of routine use of light chain detection by immunofluorescence technique in tissue biopsy, more cases of monoclonal gammopathy of renal significance are being diagnosed but there remains a therapeutic uncertainty. Data regarding the prognosis and outcomes of the various clinical manifestations of monoclonal gammopathy of renal significance is limited due to its rarity and under diagnosis. MGRS if left untreated can lead to end-stage renal disease and premature death.

**Method:** This is a retrospective study conducted at the Institute of Nephro-urology, Bangalore by retrieving the data from the digital medical records of our institute. Demographic and clinical details of the patients diagnosed with monoclonal gammopathy of renal significance from 1st January 2018 to 31st October 2022 were collected. Myeloma related light chain cast nephropathy was excluded from the study. Follow-up data were collected using out patient data base, through telephone, and from the records at the cancer institute where the patient was referred post-diagnosis at our institute. The data collected was entered in excel and analyzed using SPSS software version 27.0.

**Results:** Fifty eight patients (n = 52) were diagnosed with the disease during the study period. MGRS contributed to 1.27% of all the renal biopsies conducted at our institute during the study period. The mean age of the study population was 52.1 with 95% CI [48.3 to 55.6] with a male: female ratio of 1.36:1 and 36.5% (n = 19) of study cohort aged above 60 years. Among clinical presentations CKD (n = 23) was the main clinical presentation followed by AKI, Nephrotic syndrome, Nephritic syndrome and RPGN as the other presentations. Dialysis requirement was noted in 35% at initial presentation. Most common histiopathological presentation was Amyloidosis (n = 15) followed by Light chain deposition disease LCDD (n = 14), monoclonal non-amyloid deposition disease NADD (n = 6), Light chain proximal tubulopathy LCPT (n = 5), Proliferative glomerulonephritis with monoclonal immunoglobulin deposition disease PGNMIDD (n = 9) and others (n = 3). The patient survival at the time of analysis was 22.7% and death censored renal survival was 80%.

**Conclusion:** MGRS contributed to 1.27% of all the renal biopsies conducted at our institute during the study period. Because of its variable clinical presentation, one needs high degree of clinical suspicion for early diagnosis. MGRS unlike MGUS carries significant morbidity and mortality.
Background and Aims: Development of SARS-CoV-2 vaccination has altered the natural course of the related infection and the pandemic. The present study aims to explore the frequency of adverse events in patients with glomerular diseases (GD).

Methods: Patients with biopsy-confirmed GD, who received at least one dose of the vaccine against SARS-CoV-2 were studied retrospectively. Patients who ended up in ESKD prior to vaccination were excluded. We recorded demographics, histopathological diagnosis, past medical history, immunosuppressive regimens which were given at diagnosis and thereafter, outcome of the GD and adverse events associated with the vaccine, both systemic and local. We also estimated the rate of GD relapse post vaccination in patients in remission of the primary diseases compared with patients who decided not to receive the vaccine.

Results: To date 280 patients with GD have been included in the study with a mean age of 47.6 (±17.8) years, of whom 111 (39.6%) are males. Patients received in total 3.0 (±0.9) vaccine doses with the mean time from the diagnostic kidney biopsy to the 1st dose being 76.5 (±61.5) months. 47.1% of the patients were on immunosuppressive therapy at the time of vaccination. 27.1% of the patients reported systemic side effects (fever, arthralgias, myalgias) and 50.7% reported local side effects (pain, swelling, itching, edema). Renal function and 24-hour proteinuria remained stable after vaccination. Among patients who were in remission of the GD at the time of vaccination 19 (8.2%) patients experienced a relapse of the primary disease after vaccination, versus 5% of patients not vaccinated (p = 0.99).

Conclusions: According to our findings the vaccine against SARS-CoV-2 appears safe for patients with GD with no significant impact in renal function or the probability for relapse.

#5946
MULTICENTER STUDY EVALUATING THE FREQUENCY OF ADVERSE EVENTS ASSOCIATED WITH THE SARS-COV2 VACCINATION AMONG PATIENTS WITH GLOMERULAR DISEASES
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Background and Aims: Development of SARS-CoV-2 vaccination has altered the natural course of the related infection and the pandemic. The present study aims to explore the frequency of adverse events in patients with glomerular diseases (GD).

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Conclusions: According to our findings the vaccine against SARS-CoV-2 appears safe for patients with GD with no significant impact in renal function or the probability for relapse.

#6517
CLINICOHISTOLOGICAL CHARACTERISTICS, THERAPEUTIC APPROACH AND RENAL OUTCOME IN PATIENTS WITH C3 GLOMERULOPATHY: A SINGLE-CENTER EXPERIENCE
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Background and Aims: C3 glomerulopathy has been identified as a distinct disease in the last decade but it has already been associated with a high burden of end stage renal disease (ESRD). Due to the rarity and heterogeneity of the disease, data regarding the prognosis and optimal treatment are still lacking. We aimed to describe the clinical and histological phenotype of patients with C3 glomerulopathy followed at our center, the treatment regimens applied and their long-term renal outcome.

Method: We conducted a retrospective medical chart review of 19 patients with C3 glomerulopathy followed at our center and we reported clinical, histological and therapeutic parameters as well as their long-term renal outcome.

Results: Median age of patients at the time of diagnosis was 23 years (IQR 28), median proteinuria 2.6 g/d (IQR 2.8) and median eGFR 63ml/min (IQR 63). 26% of patients (5/19) presented with an eGFR <30ml/min. Low serum C3 levels were reported in 11/19 patients (58%). A monoclonal paraprotein was detected in three patients and pathogenous mutations of CFH/CFI genes in 4 out of 10 patients who underwent genetic testing. 41% of patients (7/17) were treated with RAAS inhibitors only, while 59% (10/17) received immunosuppressive treatment. Immunosuppressive treatment consisted of different combinations of steroids with mycophenolic acid, cyclophosphamide, cyclosporine or rituximab and steroid monotherapy in one patient. Treatment data were not available for two patients. There was a significant difference in baseline proteinuria between patients treated with RAAS inhibitors only (median 1.5g/d, IQR 1.14) and those who were treated with immunosuppressants (median 3.95g/d, IQR 4.8) (p = 0.003). Remission (complete or partial) was achieved by 43% of patients at 6 months and by 50% at 12 months. Median follow up time was 45 months (IQR 66). Eight patients (42%) reached ESRD in a median time of 58.5 months (IQR 62.5) while other three patients (16%) ended up with a GFR decline >30%. Among patients with adverse renal outcome (ESRD, GFR decline >30%), 54.5% (6/11) had baseline proteinuria >3g/d, 73% (8/11) had low serum C3 and 54.5% (6/11) had interstitial fibrosis/tubular atrophy >25%, while the median percentage of glomerulosclerosis was 33% (IQR 58). On the contrary, in the group of patients with favorable renal outcome, baseline proteinuria >3g/d was reported in only 25% (2/8), low serum C3 in 37.5% (3/8), interstitial fibrosis/tubular atrophy >25% in 25% (2/8), while median glomerulosclerosis was only 8% (IQR 15). Attainment of complete remission was associated with favorable renal outcome (p = 0.001). Five of eight patients who reached ESRD underwent kidney transplantation from a living related donor. All of them received basiliximab,
mycopHENolic acid, tACROMLin and steroids. Recurrence of C3 glomerulopathy was observed in four of these patients and one of two of them.

Graft loss due to disease recurrence was observed in one patient.

Conclusion: The present case series of patients with C3 glomerulopathy highlights the great heterogeneity in the clinical phenotype, therapeutic approach and renal prognosis of the disease. It also underscores the importance of attainment of complete remission regarding the long-term renal survival. Large studies are needed in order to better define clinical and histological predictors of adverse renal outcome as well as the optimal treatment regimens.

#2663

KIDNEY INVOLVEMENT IN MYELODYSPLASTIC SYNDROMES

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Background and Aims: Myelodysplastic syndromes (MDS) are hematologic disorders characterized by ineffective and dysplastic hematopoiesis that can be associated with systemic inflammatory and autoimmune diseases. The objective of this study was to describe kidney involvement in MDS patients, their treatments, and outcomes.

Method: We conducted a French and American multicenter retrospective observational study in nine centers, identifying MDS patients with acute kidney injury (AKI), chronic kidney disease (CKD), and urine abnormalities.

Results: Seventeen patients (males n = 11, median age 76 [70-79]) developed a kidney disease 6 months [0-31] after the diagnosis of MDS. Median urinary protein to creatinine ratio was 1.93g/g [0.8-3.3], and median serum creatinine was 3.5mg/dL [1.5-4.7]. Twelve patients (70%) had AKI at presentation, and a kidney disease 6 months [0-31] after the diagnosis of MDS. Median urinary protein to creatinine ratio was 1.93g/g [0.8-3.3], and median serum creatinine was 3.5mg/dL [1.5-4.7].

Conclusion: The spectrum of kidney injuries associated with MDS is mostly represented by vasculitis, and especially ANCA vasculitis. A diagnosis of ANCA vasculitis in an elderly patient, or with a cutaneous manifestation, or without ANCA positivity, should lead to the search for a possible MDS.

#2730

MESENCHYMAL STEM CELLS FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMatosus WITH NEPHRITIS

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Background and Aims: Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease of unknown aetiology affecting various organs and tissues. In the last decade, alternative therapeutic methods for SLE refractory to immunosuppressive therapy have been actively studied. Of interest are the data of transplantation of mesenchymal stem cells (MSCs) that demonstrated immunomodulatory properties, as well as the ability to self-renewal and multi-lineage differentiation.

Objective: to evaluate the efficacy and safety of MSCs in patients with severe refractory SLE.

Method: The search was conducted on PubMed and Google Scholar platforms using the following strategy: “Systemic lupus erythematosus” plus “Mesenchymal stem cells”. All articles presented in these domains published before 01.12.2022 in the format of case reports, clinical studies, clinical trials, multicentre studies were analysed. The effectiveness of MSCs was evaluated using the systemic lupus erythematosus activity index SELENA-SLEDAI, renal functional parameters (daily proteinuria, creatinine, glomerular filtration rate (GFR), and serum albumin), immunological parameters (anti-nuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA)). The safety assessment included registration of various adverse events during and after transplantation.

Results: A total of 201 publications were retrieved for the period from 2000-2022, and 24 records about MSCs treatment in SLE patients met the above criteria and were included in the study. The analysed publications included data on the transplantation of MSCs obtained from various biological sources such as bone marrow, adipose tissue, and umbilical cord. In total, the results of MSCs transplantations in 806 patients were analysed. The average age of patients was 30.5±8.53 years old (from 12 to 62 years). The results obtained suggested that there was a significant decrease in the activity of SLE: 2.5-fold reduce in SELENA-SLEDAI score after 12 months (from 12.43±3.06 to 5.02±2.12). Anti-dsDNA titer dropped from 99.05±477.86 to 227.65±130.76. Some research also revealed decrease in ANA titer from 309.6±412.75 to 187.8±146.60. The improvement of kidney function was assessed by the 2.17-fold reduction of daily proteinuria from 2.48±0.66 to 1.14±0.56 g/l and an increase in GFR from 66.84±42.2 to 83.25±44.90 ml/min.

Conclusion: According to the analysis of currently available research data MSCs demonstrated a significant therapeutic effect in SLE with kidney injury: the decrease in the activity index SELENA-SLEDAI, the improvement in kidney function and the decrease in immunological indicators. According to the data from follow-up studies there were no serious adverse events, or tumor-related effects after MSCs transplantation in SLE patients.
the prognosis of this group of patients. Plasmic score have been shown to predict severe ADAMTS-13 deficiency; however, its role as a prognostic factor of CO in TMA-13n is unknown.

**Method:** We retrospectively evaluate the potential factors associated with the risk of CO. Patients diagnosed with TMA-13n (defined by microangiopathic anemia, thrombocytopenia, organ damage and ADAMTS-13 activity ≥ 10%) from January 2008 to May 2018 in our centre were included in the study.

**Results:** Forty-two consecutive patients were included. Mean (SD) age: 42 (20) years. Twenty-five (60%) were females. Mean (SD) ADAMTS-13 activity: 69 (24%). Twenty-six (62%) patients required dialysis at admission. Nineteen (45%) met CO (10 patients died). Higher age, lower lactate dehydrogenase, PLASMIC score values ≤ 4, neuroradiological damage and early eculizumab use [median (IQR): 4 (0-16) days from hospital admission: 5] were factors associated with the risk for developing CO. Only three factors were independently associated with CO mortality by logistic regression: early use of eculizumab (OR: 0.14; 95% CI: 0.02-0.94) and neuroradiological damage (OR: 6.67; 95% CI: 1.12-39.80) and PLASMIC score ≤ 4 (OR: 7.39; 95% CI: 1.18-46.11).

**Conclusion:** In TMA-13n patients, neuroradiological damage, low PLASMIC score and early use of eculizumab were independent prognostic factors of death and chronic renal replacement therapy requirements.

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**Abstracts**

**#3512 GLOMERULOPATHIES DURING PREGNANCY: A TEN-YEAR SINGLE CENTER EXPERIENCE**

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**Background and Aims:** Literature regarding pregnancy management and outcomes in women with glomerulopathies is still sparse. Specific guidelines for each glomerulopathy are still lacking which impairs a more homogeneous approach. The authors describe the multidisciplinary approach and the outcomes of pregnant women with primary and genetic glomerulopathies.

**Method:** Retrospective observational study in which the authors reviewed maternal, obstetric and perinatal outcomes in pregnant women with primary and genetic glomerulopathies surveilled at our nephro-obstetric clinic from 2011 to 2021.

**Results:** We evaluated 23 gestations in 20 patients (two pregnancies still ongoing). Mean age was 32.4 ± 5.4 years (18-41). 17 women were caucasian, 3 black African, 10/23 nulliparous and 5/20 had chronic hypertension. Mean baseline SCr was 0.8 ± 0.3mg/dl (0.5-1.8) and proteinuria was 1360 ± 2199.6 mg/day (150-8615), with 13/6/2 patients being on CKD stage 1/2/3, before pregnancy, respectively (unknown in 2 patients). The most frequent CKD etiologies were IgA nephropathy (6/20), Focal Segmental Glomerulosclerosis (FSGS; 3/20) and Membranous nephropathy (2/20). Exposure to teratogenic etiologies were IgA nephropathy (6/20), Focal Segmental Glomerulosclerosis (FSGS; 3/20) and Membranous nephropathy (2/20). Exposure to teratogenic

**Conclusion:** In our series, glomerulopathies with proteinuria or nephrotic syndrome were not associated with poor renal and perinatal outcome, with only one patient developing PE and renal function deterioration, probably associated to with CKD stage 3. In patients with nephrotic syndrome, immunosuppression with calcineurin inhibitor and low dose prednisone was associated with complete or partial remission in all patients.

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**#4323 A RARE CASE OF MEMBRANOUS NEPHROPATHY AS THE INITIAL PRESENTATION OF SJÖGREN SYNDROME**

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**Introduction:** Primary Sjögren’s syndrome (pSS) is an autoimmune disorder characterized by lymphocytic infiltrates in exocrine glands, most commonly manifesting as dry eyes and mouth. Even though extra glomerular involvement can occur in Sjögren, renal involvement is rare. It affects less than 10% of the patient population, with tubulointerstitial nephritis being the usual presentation. Glomerular involvement and, in particular, membranous nephropathy are not commonly encountered. We describe a rare case of membranous nephropathy as the initial presentation of Primary Sjögren’s syndrome.

**Case history:** A 21-year-old female with a history of sickle cell trait presented to our emergency department with one week history of anasarca. Vital signs were unremarkable, and the physical exam was significant for a 2+ pitting edema of bilateral upper and lower extremities. Initial investigation revealed acute kidney injury (Creatinine 2.9 mg/dl from normal baseline), nephrotic range proteinuria of 6 grams on 24-hour urine collection, and hypoalbuminemia (serum albumin 1.5 mg/dl). Immunological workup showed positive ANA (speckled), strongly positive anti-SSA, borderline elevated anti-SR, negative anti-PLA2R, negative cryoglobulins, negative anti-dsDNA, and negative anti-Smith antibody (Figure 1). Renal biopsy (Figure 2) revealed membranous nephropathy with acute tubular necrosis (ATN). PLA2R staining was negative. We attributed acute kidney injury to ATN and proteinuria to membranous nephropathy. Negative serologies and renal biopsy findings ruled out systemic Lupus. The patient was therefore diagnosed with membranous nephropathy secondary to pSS. The patient was started on Mycophenolate mofetil and steroid taper with an improvement of proteinuria and anasarca and currently follows at our clinic.

**Discussion:** Glomerular involvement is rare, and when involved, it is membranoproliferative glomerulonephritis (MPGN) associated with B-cell activation and positive cryoglobulins. Membranous nephropathy is rare with primary Sjögren syndrome. In our patient, a negative anti-PLA2R goes against primary membranous nephropathy. A negative anti-dsDNA and anti-Smith and biopsy findings essentially rule out Lupus nephritis, leaving Sjögren induced secondary membranous nephropathy as the most likely diagnosis. A literature search revealed few described cases of membranous nephropathy as the presenting feature of pSS with later development of sicca symptoms and progression of renal disease to MPGN. Interestingly, our patient had no sicca symptoms at the presentation time. Occult salivary gland involvement has been described in some of these patients; however, our patient deferred salivary gland biopsy. The management of renal disease in pSS has yet to be well described because of its rarity. Rituximab has shown the most benefit in patients with pSS who have positive cryoglobulins and associated MPGN. Steroids and mycophenolate mofetil (MMF) are other possible agents that can be tried. Given that experience, we started on steroids and MMF with an excellent response to treatment indicated by improvement in proteinuria.

**Conclusion:** This case adds to the limited available literature on membranous nephropathy as the initial manifestation of pSS. Although the European Alliance of Associations for Rheumatology (EULAR) criteria strongly emphasizes sicca symptoms and glandular involvement in pSS, the possibility of a small subset of pSS patients who present with early renal involvement with latent glandular findings needs to be recognized.
OLD BIOPSY IS ALWAYS GOLD, REVISITING MEMBRANOPROLIFERATIVE GN DIAGNOSIS IN A RENAL TRANSPLANT PATIENT
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Background and Aims: MPGN resulting from hepatitis C virus (HCV) infection typically shows granular deposition of immunoglobulin M (IgM), C3, and both kappa and lambda light chains. Immunoglobulin G (IgG) may or may not be present, and C1q is typically negative, the same pathology can be found in other viral infections. The recurrence rate post-transplantation is high, with 33% of immune-complex MPGN. Graft loss is even higher 65%, especially among patients with idiopathic MPGN. Treatment of a patient with significant proteinuria can be tricky, as no proven treatment is described yet, but plasmapheresis and induction with cyclophosphamide were described for heavy proteinuria >3.5 g/day.

Method: 79 year old female patient, known case of live unrelated renal transplantation in December 2013, primary renal disease is unknown. She had a history of equivocal hepatitis C virus antibodies, but Hepatitis C virus RNA was not detected. She is also known to have Type II Diabetes Mellitus and hypertension. The patient had baseline creatinine of 100-120 micromol/L. 24 hr urine protein was 0.8 g/Day but started rising quickly to reach a peak of 9.2 g/g seven months post-transplantation to nephrotic range proteinuria but her serum albumin level was always above 35 g/L. Serum protein electrophoresis showed no M band, a kappa/ Lambda ratio 1.21 within a normal range (0.260-1.65). Anti- nuclear antibody (ANA), P-ANCA, C-ANCA, and Double-stranded DNA all were negative. Complements were within normal range C3 1.39 g/L (0.79 -1.52), C4 0.44 g/L(0.17-0.57) rheumatoid factor and Anti- citrullinated peptide antibodies were negative. Hepatitis b Virus surface antigen and core antibodies were not reactive, HIV screening was negative. Urine analysis showed RBCs but no RBC casts. Renal biopsy showed mild mesangial expansion and mild l increase in mesangial cells and matrix. Some glomeruli show increased lobulation with increase in mesangial cells and matrix with segmental endocapillary proliferation There is double contour of the glomerular basement membrane with scattered spikes and holes within the basement membrane seen best with silver stain. There is mild increase in the thickness of glomerular basement membrane. There is focal mild lymphocytic infiltration. Tubulitis is not seen in the examined material. One Focal area of mild interstitial fibrosis. Sampled blood vessels are unremarkable. The stain for C4d is negative. Immunofluorescence showed granular capillary wall immunoreactivity to IgM (+2), C4 (+1), C1q (+1), and Lambda light chain (+2). The glomeruli show no immunoreactivity to IgG, IgA, C3, Kappa and fibrin. The glomeruli show (+) staining for albumin. Tubular protein reabsorption droplets showed immunoreactivity for albumin, IgG, IgM, C3, kappa and lambda light chains. Electron microscopy showed many subendothelial, and mesangial electron-dense deposits. The patient was on maintenance immunosuppression medications inform of mycophenolic acid 720 mg, cyclosporine; 250mg BID, and Prednisolone 5 mg daily.Revisiting the new classification of membranoproliferative glomerulonephritis is challenging in this patient, since there is the dominance of IgM deposition by immunofluorescence and C4 but not C3 makes it challenging, the negative monoclonal band in serum electrophoresis and negative autoimmune workup excludes immune complex mediate MPGN, leave idiopathic MPGN a possibility,
keeping in mind that hepatitis C virus infection was never confirmed. On the other hand, IF showed IgM with C4 subendothelial and mesangial dense deposits that excludes away the C4 glomerulopathy.

**Results:** Whether this is a recurrence of glomerular disease early on post-transplantation or denovo membranoproliferative disease, she responded well to the addition of losartan 100 mg daily, with a reduction of her urinary protein to less than 1 g/g: the patient never received treatment for the hepatitis C virus.

**Conclusion:** In our patient, it is difficult to conclude if the cause of MPGN is recurrence or denovo GN, especially with severe proteinuria that responded well to ACEi treatment. The pathological findings can be tricky.

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**REFERENCES**


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**HYPOCOMPLEMENTEMIA AT DIAGNOSIS OF ANCA-ASSOCIATED VASCULITIS IS ASSOCIATED WITH SEVERITY AND OUTCOMES**

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**Background and Aims:** A relationship between antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and complement has been shown, and complement has an important role in the pathogenesis of AAV [1]. Low serum complement levels (sC3) at diagnosis of AAV has been previously described although clinical characteristics and outcomes of AAV with hypocomplementemia still remain unclear [2]. The aim of this study was to investigate what proportion of patients with AAV have low sC3 at diagnosis, and whether they have different clinical and histological features or experience different outcomes compared to patients with normal sC3.

**Method:** A total of 93 patients with AAV diagnosed (81.3% Anti-MPO and 18.7% anti-PR3) were included in the study from 2000-2022. 12% of them had sC3 values below limit of normal range (i.e., <90 mg/dl). Patients were categorized according to sC3 levels into 2 groups, hypocomplementemic (G1; mean C3: 73.1mg/dl) and normocomplementemic (G2; mean C3: 123.3mg/dl).

**Conclusion:** Based on the Berden score and correlated with clinical features, main outcomes of interest included severity of acute kidney injury at diagnosis (AKI), histopathological patterns, end-stage kidney disease (ESKD) and death in the long term.

**REFERENCES**

assess the prognosis. The aim of this work was to evaluate the prognostic value of this anatomopathological classification.

**Method:** We conducted a single-center retrospective descriptive and analytical study of patients diagnosed with histologically confirmed GAA in our Nephrology Department during the period from 2016 to 2022.

**Results:** We collected 20 patients, median age 52 years (21-77 years). The sex ratio (M/F) was 0.8. Histological confirmation of GAA was based on renal biopsies in 100% of cases. Rapidly progressive glomerulonephritis was the nephrological presentation in 15 patients. One patient had no hematuria and one had no proteinuria and renal failure was present in all cases. Good Pasture syndrome was present in 7 cases. The Berden classification was applied to the renal biopsies: the focal form (2 cases), the cellular form (7 cases), the mixed form (7 cases) and the sclerotic form (4 cases). The evolution was marked by a partial remission for 11 patients. After an evolution of 1 year, end-stage renal failure (ESRD) was retained in 13 patients. The sclerotic form was not associated with a poor prognosis in our population (p = 0.642).

**Conclusion:** Of course, our sample size was small and in our population we found a predominance of the mixed and cellular forms compared to the sclerotic form, contrasting with poor therapy with a rapid evolution towards CKD.

**#650**

**MULTICENTER RETROSPECTIVE STUDY TO ASSESS THE CLINICAL PRESENTATION AND OUTCOME OF SARS-COV2 INFECTION IN PATIENTS WITH LUPUS NEPHRITIS**

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**Background and Aims:** The present study aims to describe the clinical presentation and outcome of SARS-CoV2 infection in patients with systemic lupus erythematosus (SLE) and renal involvement (LN).

**Method:** 82 patients with biopsy-proven LN were retrospectively studied. 56 (68.3%) had a positive test for SARS-CoV2 at some point during the follow-up time and were compared with 26 patients with SLE patients who had LN but were not infected with SARS-CoV2 in order to compare the impact of SARS-CoV2 infection in the outcome of LN. Patients who had reached end-stage kidney disease before infection were excluded. Biopsy data, treatment, outcome of LN, clinical presentation of SARS-CoV2 infection and outcome were recorded.

**Results:** The mean age of the patients was 33 (±12.7) years and 85.3% were females. In the histopathological diagnosis there was proliferative LN in 43 (76.8%) cases. All patients had received immunosuppressive therapy and 89.2% had achieved remission of LN. 66.1% of patients were treated with immunosuppressive agent at the time of diagnosis of the SARS-CoV2 infection. 96.4% of patients were tested due to symptoms while gradually all of the patients became symptomatic. 5 (9.01%) of patients required hospitalization mainly due to hypoxemia. 11 (19.6%) of patients received specific treatment for SARS-CoV2 infection, 91.6% of patients experienced complete recovery, 2 (3.57%) experienced prolonged symptomatology, and 1 (1.78%) died. 10.9% of patients with SARS-CoV2 infection, who were in remission before infection, experienced a relapse of LN in a mean time of 2.7 ± 2.1 months after the infection, while none of the patients without SARS-CoV2 infection relapsed in the same time period (p = 0.09).

**Conclusion:** SARS-CoV2 infection affects the morbidity of patients with SLE who have renal involvement and possibly the likelihood of relapse in those who have achieved remission prior to infection.

**#2691**

**GLOMERULAR LESIONS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME**

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**Background and Aims:** Antiphospholipid syndrome (APS) is a complex autoimmune systemic disease, characterized by the presence of circulating antibodies directed against anionic phospholipids and the protein bound to them (aPL), leading to recurrent thrombosis and/or obstetrical complications. Renal manifestation of antiphospholipid syndrome conform a wide spectrum of disease renal syndrome. APS nephropathy (APSN) is considered a renal small-vessels vasculopathy, that can present acutely or chronically. The aim of the study is to identify glomerular lesions in patients with APSN.

**Method:** We studied retrospectively 114 patients (51 male, 63 female; age between 19 and 58 years; duration of follow-up was between 2 and 16 years) fulfilling classification criteria for APS. Renal and extra-renal symptoms were analyzed. None of the patients developed SLE in follow up. 18 patients with evidence of renal involvement underwent renal biopsy. All cases had proteinuria and five of them presented nephrotic syndrome.

**Results:** Of 18 patients with kidney biopsy, 8 (44.4%) were male and 10 (55.6%) - female. Four of patients with renal biopsy had membranous glomerulonephritis, two had diffuse proliferative glomerulonephritis, 2 - mesangial C3 nephropathy, 2 - minimal change disease, 1- focal segmental glomerulosclerosis, the other seven had classic pathologic findings consistent with APSN. Chronic lesions with fibrous intimal hyperplasia being the most common. Thrombotic microangiopathy (TMA) in glomeruli was characterized by fibrin thrombi without inflammatory cells or immune complexes. Double contour of the glomerular basement membrane was associated with mesangiolysis and endothelial cell swelling in 5 patients with APSN. Electron microscopy confirmed subendothelial edema. Segmental glomerulosclerosis was observed in 4 patients. Tubulointerstitial was injured with interstitial fibrosis and tubular atrophy. Patients with APS and renal involvement were older (p < 0.05), had LA positive test (p < 0.005) and low complement levels (p < 0.05). Hypertension is present in all cases with APSN, reduced glomerular filtration rate – in 4. All cases had proteinuria and five of them presented with nephrotic syndrome. Microscopic hematuria is observed in 4 patients. The treatment of APSN includes standard anticoagulant treatment for APS, inhibitors of the angiotensin system in patients with hypertension and proteinuria, steroids, intravenous immunoglobulin, cyclophosphamide and azathioprine.

**Conclusion:** Of 18 patients with kidney biopsy, 8 (44.4%) were male and 10 (55.6%) - female. Four of patients with renal biopsy had membranous glomerulonephritis, two had diffuse proliferative glomerulonephritis, 2 - mesangial C3 nephropathy, 2 - minimal change disease, 1- focal segmental glomerulosclerosis, the other seven had classic pathologic findings consistent with APSN. Chronic lesions with fibrous intimal hyperplasia being the most common. Thrombotic microangiopathy (TMA) in glomeruli was characterized by fibrin thrombi without inflammatory cells or immune complexes. Double contour of the glomerular basement membrane was associated with mesangiolysis and endothelial cell swelling in 5 patients with APSN. Electron microscopy confirmed subendothelial edema. Segmental glomerulosclerosis was observed in 4 patients. Tubulointerstitial was injured with interstitial fibrosis and tubular atrophy. Patients with APS and renal involvement were older (p < 0.05), had LA positive test (p < 0.005) and low complement levels (p < 0.05). Hypertension is present in all cases with APSN, reduced glomerular filtration rate – in 4. All cases had proteinuria and five of them presented with nephrotic syndrome. Microscopic hematuria is observed in 4 patients. The treatment of APSN includes standard anticoagulant treatment for APS, inhibitors of the angiotensin system in patients with hypertension and proteinuria, steroids, intravenous immunoglobulin, cyclophosphamide and azathioprine.

**#2909**

**DOUBLE GLOMERULOPATHY OF THIN BASEMENT MEMBRANE DISEASE AND IGA NEPHROPATHY PRESENTING WITH NEPHROTIC SYNDROME IN AN ADULT WOMAN**

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**Background and Aims:** We report a case of a 44-year-old woman with no known comorbid conditions who, eventually was diagnosed to have simultaneous occurrence of IgA nephropathy and thin basement membrane disease atypically presenting with heavy proteinuria, hypoalbuminemia, bipedal edema, ascites, bilateral pleural effusion, and hemodynamic instability, but with a surprisingly normal light microscopic findings and an Oxford MEST score of 0 on renal biopsy who, clinically improved with immunosuppression and angiotensin II receptor blocker therapy. Physical exam revealed an
overweight female, with facial swelling, no rash, periorbital and a Grade II "p" bidental pitting edema. The presence of decreased breath sounds and dullness on percussion on both lower lung fields were also observed. Shifting dullness and fluid wave on abdominal exam. The patient was afebrile, no desaturation at room air and a palpatory blood pressure of 70 mmHg. Secondary causes of glomerulonephritis such as Hepatitis B and Hepatitis C infection were ruled out. Antinuclear antibody (ANA) test, compliment (C3 and C4) with anti-dsDNA determination to rule out SLE were unremarkable as well. Serum creatinine was elevated at 2.63 with estimated GFR of 22 mL/min. Further work-up with 24-hour total urine protein was 22,026.2 grams/day. The patient underwent percutaneous kidney biopsy which showed IgA Nephropathy with a MEST C score of 0 with simultaneous occurrence of thin basement membrane disease.

Method/Treatment: Pulse steroid therapy was started with Methylprednisone 1 gram intravenous infusion once daily for 3 days followed with Prednisone (1mg/kg/day) 60 mg a day and a low-dose of Angiotensin receptor blocker, Candesartan, 4mg once daily for the proteinuria.

Results: After 8 weeks of corticosteroid and ARB therapy, patient was seen at the clinic with resolution of bidental edema, no demonstrable ascites and clear breath sounds on chest and lungs auscultation. Blood pressure was 130/80 with no proteinuria on dipstick, random urine protein: creatinine ratio (UPCR)
of 0.07, creatinine of 0.97 mg/dl and BUN of 17 mg/dl. Prednisone was then reduced with the goal to taper the dose for a period of 6 months. 

**Conclusion/Significance:** Both IgA nephropathy and thin basement membrane disease usually present with hematuria, hypertension, and varying degrees of proteinuria. However, nephrotic syndrome as its presentation has not been well characterized to date, and whether this adds to the mortality is not yet established. Although the most widely accepted system, the Oxford MEST-C scores is utilized in predicting renal outcomes, its role in double glomerulopathies has not been validated. Even though many investigators have indicated that the presence of heavy proteinuria at the initial evaluations was almost always associated with progressive renal failure and that there is no effective medical treatment aside from supportive care, in this study, a trial of immunosuppression yielded improved clinical outcomes.
#3564

**DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF INTERLEUKIN-6 IN LUPUS NEPHRITIS**

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**Background and Aims:** Lupus nephritis is a frequent and potentially serious complication of SLE. The present study is aimed to evaluate the usefulness of urinary IL-6 as a non-invasive diagnostic & prognostic biomarkers of disease activity in LN.

**Method:** The study was done in IMS and Sum hospital, Bhubaneswar, India from January, 2018 to July 2022. The study included 20 healthy controls and 32 patients of SLE diagnosed based of Systemic Lupus International Collaborating Clinic (SLICC) criteria, who presented with renal involvement. The exclusion criteria was inability to obtain informed consent and SLE patients without renal involvement. Urinary IL-6 levels were assessed in patients before initiation of therapy and in controls by quantitative sandwich EASIA technique using human IL-6 EASIA kit (DIA Source Belgium). All patients underwent ultrasound guided renal biopsy and the results were classified according to the ISN/RPS classification of LN. Treatment was started in all patients according to class of LN as per KDIGO guidelines. Urinary IL-6 levels were again assessed in all patients after 6 months of induction phase treatment.

**Results:** In our 32 patients, female to male ratio was 7:1 with a mean age of 28.68 ± 9.28 years. In our study, ANA was positive in 96.8%, anti-dsDNA Ab in 78%, C3 was low in 78% & C4 was low in 72% of LN patients. Based on renal biopsy findings, there were 2 cases of Class II LN, 6 cases of Class III LN, 19 cases of Class IV LN and 5 cases of Class V LN. In our study, patients with LN have significantly higher urinary IL-6 levels (301.58 ± 483.96 pg/ml) as compared to 20 healthy controls (4.7 ± 2.282 pg/ml) with a p-value of 0.001. The mean urinary IL-6 levels in different ISN/RPS classes of LN patients based on renal biopsy showed a statistically significant difference between different classes (p-value = 0.005). Highest values of urinary IL-6 (473.126 ± 580.90 pg/ml) was seen in Class-IV LN which is most active form of LN and lowest values (28.28 ± 7.30pg/ml) were seen in Class-IILN. In our study, a significant correlation was found between serum creatinine & presence of active urinary sediment with urinary IL-6 levels but there was no correlation between 24 hour urinary protein with urinary IL-6 levels in patients of LN (p = 0.799). In our study 2 patients (6.25%) died, 3 patients (9.37%) lost follow up, 16 patients (50%) achieved complete remission, 8 patients (25%) achieved partial remission and 3 patients (9.37%) did not show any improvement after 6 months treatment. Urinary IL-6 levels were near normal among 12 patients (75%) out of 16 patients who achieved remission after 6 months of induction treatment (p-value = 0.001). Urinary IL-6 levels remained elevated in all 8 patients (100%) who achieved partial remission (p-value = 0.028, and also remained elevated in all 3 patients who had no remission at all (p-value = 0.109).

**Conclusion:** Urinary IL-6 may provide a simple non-invasive potential biomarker of disease activity of renal involvement in patients with SLE and may be used to monitor therapy.

**Table 1: Urinary IL-6 levels in controls and Patients with Lupus Nephritis.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Range</th>
<th>Mean ± SD</th>
<th>Z-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 20)</td>
<td>2.03-9.41</td>
<td>4.707 ± 2.282</td>
<td>6.021</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LN Patients (n = 32)</td>
<td>14.23-2478</td>
<td>301.582 ± 483.944</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Table 2: Urinary IL-6 after 6 months induction treatment in CR/PR/NR groups of Patients with LN.**

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Total (n = 27)</th>
<th>Urinary IL-6 before start of treatment (Mean±SD) (pg/ml)</th>
<th>Urinary IL-6 after 6 months of Induction treatment (Mean±SD) (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with CR</td>
<td>(n = 16)</td>
<td>101.152±77.546</td>
<td>10.73±2.778</td>
</tr>
<tr>
<td>Patients with PR</td>
<td>(n = 8)</td>
<td>341.213±218.677</td>
<td>45.33±14.065</td>
</tr>
<tr>
<td>Patients with NR</td>
<td>(n = 3)</td>
<td>1528.666±822.152</td>
<td>854.67±306.523</td>
</tr>
</tbody>
</table>

**#3041 DNAJB9 POSITIVE PRIMARY FIBRILLARY GLOMERULONEPHRITIS: TREATMENT WITH CORTICOSTEROID PULSES EXPERIENCE**

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**Background and Aims:** Fibrillar glomerulonephritis (FGN) is a rare histological pattern. Electron microscopy is needed for diagnostic confirmation where predominantly mesangial fibrils are observed. To support the diagnosis, DNAJB9 is a biomarker that is 100% sensitive and 100% specific for FGN. To date, there is no defined therapeutic approach. Various immunosuppressants have been implemented to treat FGN showing poor renal response and approximately 50% progression to chronic kidney disease.

**Method:** Ambispective observational study. A protocol based on a bibliographic review was developed. The protocol included an induction therapy with methylprednisolone pulses (MTP), 300 mg a day for three days. Followed by oral prednisone at a dose of one mg/kg with an individual titration period considering the clinical evolution. Demographic, clinical, and pathological variables were extracted from the electronic health record.

**Results:** Case 1. Seventy-eight-year-old female. History of arterial hypertension (HT) treated with an angiotensin-converting enzyme inhibitor (ACEI). She debuted with a nephrotic syndrome characterized by proteinuria of 15 grams/day, hyperalbuminemia, and altered kidney function with creatinine (Cr) of 2.7 mg/dL. Secondary causes were rule out. The kidney biopsy showed mesangial expansion with mesangial deposition of IgG and C3 on the immunofluorescence. Congo red was negative. Positivity for DNAJB9 was observed. The electron microscopy (EM) showed 20-nanometer fibrils in the mesangium. The patient was initiated on the treatment protocol with a subsequent reduction of prednisone over a period of 24 weeks. Complete remission, defined as proteinuria <0.5g/day and reduction >50% of Cr was achieved after 20 weeks of treatment. Case 2. Forty-seven-year-old female with a history of hypertension treated with ACEI. The patient presented with proteinuria 3.5g/d with a normal kidney function. Secondary causes were rule out. The kidney biopsy showed mesangial thickening with IgG, C3, C1q, Kappa, and lambda positivity on immunofluorescence. Congo red was negative. DNAJB9 was positive. An electron microscopy study showed randomly arranged mesangial fibrils. The treatment protocol was started. Prednisone was titrated over a period of 20 weeks. Partial remission was observed, defined by >50% reduction of proteinuria. Kidney function remained preserved.

**Conclusion:** Induction treatment based on steroid pulses followed by prednisone titration in patients with FGN with predominantly mesangial remission was associated with a substantial reduction of proteinuria and stabilization of kidney function.

**#5891 REPEAT RENAL BIOPSIES IN ADULT LUPUS NEPHRITIS PATIENTS**

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**Background and Aims:** The role of repeat renal biopsy in lupus nephritis (LN) to guide treatment or predict prognosis has been controversial. The objective of this work is to evaluate the causes were requiring the use of a second renal biopsy, as well as to describe the histological results and the therapeutic management according to the results.

**Method:** This is a descriptive retrospective study, covering 450 renal biopsy performed between January 1, 2020 and December 31, 2022 at the nephrology department of the Casablanca University Hospital. The patients were selected from the kidney biopsy register.

**Results:** Thirty patients followed for lupus nephritis had benefited from a 2nd renal biopsy. The average age of our patients was 36.4 years with a sex ratio of 0.8. The average time from first to second biopsy was 2.1 years. The indications for a second renal biopsy was included a suspected flare (76.6%), of which had worsening proteinuria with or without rising serum creatinine (90%), or lack of treatment response (23.4%). Twenty-two patients (73.3%) had proliferative class on their first renal biopsy. When comparing first and second renal biopsy, 26 patients (86.6%) switched histological classes. When categorized as proliferative versus non-proliferative, 21 (95.4%) patients with proliferative class on the first biopsy remained similar on the second biopsy. The mean chronicity index (CI) was significantly different for 10 consecutive biopsies with worsening CI noted with increased number of renal flares. 11 patients (36.6%) required intensification in immunosuppressive therapy after the second renal biopsy whereas 3 patients (10%) experienced a reduction in immunosuppression. 16 patients (53.3%) did not experience any change in immunosuppression.

**Conclusion:** A 2nd renal biopsy was justified in most cases, making it possible to establish a precise diagnosis, to identify the evolution of the histological lesions, and to guide the therapeutic management.

**#6260 PREDICTING KIDNEY FUNCTION AND END-STAGE KIDNEY DISEASE IN ANCA-ASSOCIATED VASCULITIS USING ANCA, C-REACTIVE PROTEIN AND C3**

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**Background and Aims:** Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are systemic autoimmune diseases that involve small- and medium-sized blood vessels. AAV compromises the overall survival of patients, and its kidney involvement can lead to end-stage kidney disease (ESKD). Our aim was to determine whether the serum C3, C-reactive protein (CRP) and ANCA levels could predict kidney survival.

**Method:** We retrospectively reviewed patients with AAV and kidney involvement (n = 62) from 2006 to 2022. Demographic, clinical and laboratory data were collected. Patients’ ANCA title were measured by ELISA, and Glomerular Filtration Rate (GFR) was estimate by CKD-EPI equation. ANCA, C3 and CRP were measure at diagnosis, remission, and last follow-up. ANCA was analyzed as continuous and categorical variable. We analyzed factors associated with dialysis dependency at diagnosis and evolution to ESKD. Multivariable adjusted Cox regression analysis was performed for assessing predictive variables associated with dialysis outcome.

**Results:** The cohort included 62 total patients, with median age of 69 (63-77) years old, 44% were female, 35.5% (n = 22) presented with alveolar haemorrhage, 82.3% (n = 51) were MPO-ANCA+ and 4 patients had concomitant anti-GBM+. At admission, the median ANCA title was 80.5 UI/mL (36.75-112.25), C3 was 108.5 mg/dL (90-130.25) and CRP 7.5 mg/dL (2.14-14.34). The GFR was 11.7±11.6 at admission and 24% of patients required dialysis at admission (n = 15). At 3 months 30% (n = 19) required dialysis, 10% at 6 months (n = 6) and 5% at 1 year (n = 3). The median time until dialysis was 488.98 (0-5702) days. Twenty (32.3%) patients died during the study period. The title of ANCA at admission, as categorical variable, did not associate with requirement of kidney replacement therapy during follow-up (p = 0.523). Considering C3 and CRP, only low C3 at last follow-up correlates with ESKD (p = 0.028). Median C3 at last follow-up was 91.5 mg/dL (79.5-107) in ESKD patients and 114.5 mg/dL (92-142.75) in patients that do not require dialysis. In a multivariate analysis, including age and gender, C3 levels at last follow-up lost significance to predict time until ESKD (p = 0.083, model p = 0.005). Initial GFR was not correlated with ANCA title at admission (r = 0.220, p = 0.205) nor as a categorical variable (p = 0.592). At remission, GFR was not correlated with ANCA title (r = 0.383, p = 0.349). Considering factors associated with the need for dialysis at admission, only CRP levels at admission were significantly significant.
higher (p = 0.035) in those who required dialysis. ANCA title and C3 at admission did not correlate with dialysis at admission (p = 0.875, p = 0.702). In multivariate analysis, including age and gender, CRP maintain its significance (p = 0.036, model p = 0.044).

Conclusion: C3 and CRP levels have been studied as possible factors predicting kidney survival, however, results are not consistent. CRP is a marker of inflammation and C3 represents complement activity, these serological markers could be important to identify patients at risk for ESKD. In our study CRP levels seems to be related to dialysis requirement at admission. These patients should be followed more closely and carefully to improve kidney survival.

#6470

PATIENT SURVIVAL IN AN ASSOCIATED VASCULITIS COHORT – DATA FROM A REFERRER CENTER

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Background and Aims: Patients with ANCA associated vasculitis (AAV) have variable survival rates depending on disease activity, complications and sometimes the choice of treatment. Still today there are a lot of differences between various cohorts regardless of similarities in clinical presentation, serology or histology. Understanding risk factors for various outcomes in cohorts from different geographical areas might help build better and more uniform prediction models. We present data on patient survival from our referrer center.

Method: This study included 106 consecutive AAV patients with biopsy proven renal involvement in the period from 2007-2017. We analyzed clinical, laboratory and pathohistological data as predictors for death of the patients. Survival univariate analysis was performed using Kaplan-Meier method and log-rank (Mantel-Cox) test. Variables that had p<0.1 in univariate analysis were alongside age and gender included in multivariate Cox proportional hazard model.

Results: The study included 106 AAV patients with renal involvement: 66 (61.1%) MPA, 20 (18.5%) GPA, 20 (18.5%) RLV. There were 14 (13%) PR3-ANCA positive patients, 57 (52.8%) MPO ANCA positive, 5 (4.6%) PR3-ANCA+MPO-ANCA and 32 (29.6%) ANCA negative patients. Average SCr was 316.5 μmol/l (IQR 207.0-548.5), 24-hour proteinuria median was 1,7g/24h (IQR 0.8-2.8). Histologically (Berden classification) 43 (39.8%) patients had crescentic, 19 (17.6%) focal, 34 (31.5%) mixed and 12 (11.1%) sclerotic class. Follow up time was 1 to 127 months with median 21 months (IQR = 7 - 44) and medium follow up time of 28.6 months (SD = 26.6). All the patients recieved the same induction treatment (cyclophosphamide and glucocorticoids +/- acute haemodialysis and plasma exchange treatment) and remission maintenance treatment (azathioprine). During the follow up 21 patient (19.8%) died. Out of those 13 were females. Main causes of death were either infections or cardiovascular diseases. In follow up period patient survival was 83.9,81.2,79-74,7% at 12-24-36-60 months. There were no differences in survival rates between clinical, histological or serological phenotypes. In univariate analysis significant predictors for death of patients were: age (>68 years; p = 0.002), anaemia (Haemoglobin <96 g/l; p = 0.001), increased CRP levels (CRP > 63mg/l; p = 0.001), lower serum C3 levels (p = 0.001), BVAS > 18 (p = 0.003) and the need for dialysis (p = 0.06). In multivariate analysis however significant predictors for the death of patients were age (HR = 1.059, 95% CI = 1.001-1.120; p = 0.046), anaemia (HR = 0.952, 95% CI = 0.908-0.998; p = 0.040) and BVAS (HR = 1.093, 95% CI = 1.030-1.159; p = 0.003).

Interestingly in additional analysis PLEX was, alongside acute haemodialysis, significant predictor in combined ESRD/death outcome (as well as for ESRD and relapse rate) but not for death alone.

Conclusion: In our data disease activity as defined by BVAS and anaemia alongside the patient age are predictors for the patient survival. Anaemia is not included either in BVAS or in other disease activity scores or prediction models. Considering its potential impact on multiple organ functions perhaps anaemia levels should be included either in BVAS or perhaps in VDI though anaemia itself is mostly not autoimmune phenomenon in AAV patients. Also in our cohort PLEX wasn’t a significant predictor for patient survival.

#6949

MPO ANCA-ASSOCIATED VASCULITIS IN A PATIENT WITH A HISTORY OF METHAMPHETAMINE ABUSE

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Background and Aims: Methamphetamines cause kidney damage by different mechanisms. The most common is the tubular lesion associated with myoglobinuria secondary to rhabdomyolysis. Other renal effects include prerenal azotemia, acute tubular necrosis, malignant hypertension, and necrotizing vasculitis have been reported. It is important to consider this drug as a possible cause of glomerulonephritis.

Method: We present the case report of a patient with suspected MPO ANCA-associated vasculitis from methamphetamines.

Results: A 24-year-old male, he was admitted to nephrology due to hematuria and proteinuria accompanied by serum creatinine elevation (2.5 mg/dl). He reported inhaled methamphetamine abuse since the age of 14, smoking and occasional ethylism. His symptoms began in October 2022 with asthenia and anemia, accompanied by generalized pallor and edema in both malleoli. At admission with normal blood pressure (112/70 mmHg), Laboratory tests revealed: leukocytes 6.35 thousand/UL, hemoglobin 7.7 g/dl, platelets 698,000 thousand/UL, urea 70.81 mg/dl, sodium 137 mmol/L, potassium 4.72 mmol/L, albumin 3.85 g/dl, urine test with proteinuria 25 mg/dl, hemoglobinuria 250 eri/microl. Leukocytes 15-20 field and countless erythrocytes, albuminuria 450.87 mg/day, globular sedimentation rate 18 mm/hr, reactive protein C 37 mg/L. Complement levels were normal, negative serologies for hepatitis B, C, human immunodeficiency viruses, antinuclear antibodies, double-stranded anti DNA and anti-proteinase 3, but was positive for IgG anti myeloperoxidase (anti-MPO) 33.6 U/ml. Urinary sediment showed the presence of dysmorphic erythrocytes, as well as abundant erytrocyte and granular casts. Ultrasound-guided renal biopsy was performed; light microscopy reported 21 glomeruli, 6 globally sclerosed, 4 with irregular segmental sclerosis, 4 with destruction and granuloma formation. Immunofluorescence showed traces of mesangial IgM, the rest negative for IgG, IgA, C3, C1q, fibrinogen, kappa and lambda. The patient received 3 pulses of methylprednisolone 300 mg followed by oral prednisone and rituximab. Baseline creatinine decreased to 1.88 mg/dl.

Conclusion: Inhaled methamphetamine is commonly used in young people, it is important to consider this drug as a possible cause of crescentic and necrotizing glomerulonephritis.
Urinary sediment shows erythrocyte cast, light microscopy 40x

Urinary sediment shows granular cast, light microscopy 40x
KIDNEY INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS
Daniela Valentinova Monova1, Todor Todorov2 and Simeon Monov2
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Background and Aims: In rheumatoid arthritis (RA) kidney is commonly affected organ with clinical presentation characterized by proteinuria and microalbuminuria, followed by chronic renal failure. RA is associated with reduced kidney function, possibly due to chronic inflammation or the use of nephrotoxic therapies. Renal diseases occurring in patients with RA may have a variable clinicopathological picture. Little is known about the effects of using the novel biological agents on the risk of kidney diseases.

The aim of this study was to determine the relationship between effect of therapy and kidney involvement in patients with RA and evaluated the histopathological findings and associated clinical manifestation.

Method: In this retrospective study 275 patients with diagnosis of RA were included. In 48 patients renal biopsy was performed. The patients were divided in three groups according to changes in management of RA: 1991-2001, 2002-2011 and 2012-2022 year. Data of demographic characteristics, clinical symptoms and pathological diagnosis were extracted from medical records and pathological reports.

Results: In our study amyloidosis was the most common histologic pattern, followed by chronic glomerulonephritis (GN) and tubulointerstitial nephritis. Renal amyloidosis was diagnosed in 13 patients, membranous GN – in 9, mesangio proliferative GN – in 7 patients, focal segmental necrotizing GN – in 5, focal segmental sclerosis – in 4, minimal change disease – in 3, tubulointerstitial nephritis – in 7 patients. Between 1991 and 2001 year the most common clinical manifestation was nephrotic syndrome and the most common histopathological findings – renal amyloidosis, followed by...
membranous GN and focal segmental necrotizing GN. The membranous GN was the leading cause of kidney disease between 2002–2011 years and focal segmental sclerosis – between 2012–2022. In our study 68 patients had a decrease of glomerular filtration rate (GFR) < 60 mL/min/m². No kidney biopsies were performed in these cases because no urine abnormalities were detected. We found that age, duration of the disease, arterial hypertension, C-reactive protein were significant risk factors for disease, arterial hypertension, C-reactive protein were significant risk factors for

Conclusion: In all patients with RA, renal function should be monitored and in the case of pathologic results, renal biopsy should be performed. In RA patients with renal disorder, suspected causal drug should be removed from the treatment and specific immunosuppressive therapy initiated. Improved pain management associated with biologic treatment may help to reduce the need for potentially nephrotoxic anti-inflammatory agents such as NSAIDs and certain types of non-biologic DMARDs, which could consequently reduce the risk of drug-induced nephrotoxicity and thereby contribute to the lower risk of renal diseases.

#6227

SPONTANEOUS REMISSION OF MEMBRANOUS VARIANT OF PGNMID WITH MONOCLONAL IgG2κ

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Background and Aims: The clinical significance of the morphological patterns of glomerular injury and each IgG subclass in proliferative glomerulonephritis (GN) with monoclonal immunoglobulin deposits (PGNMID) is not well understood. Literature suggests that PGNMID with certain histological features such as membranous or mesangio-proliferative features or non-IgG3 subclass staining may be associated with a more favourable renal prognosis. We present a patient with membranous variant of PGNMID with monoclonal IgG2κ who had spontaneous remission without recurrence over a 2-year follow-up.

Method: Not applicable

Results: A 62-year-old Malay gentleman presented with new onset nephrotic range proteinuria, on a background of type 2 diabetes mellitus with diabetic duration of 5 years, hypertension and hyperlipidaemia. He was mildly hypertensive (blood pressure 148/87) and non-edematous at presentation. Investigations revealed preserved kidney function [serum creatinine (sCr) 66μmol/L], bland urinalysis, and 24-hour urinary total protein (UPT) of 3.74g/day. Serum albumin (sAlb) was 35g/L. Serum complements were not low. Autoimmune markers inclusive of anti-double stranded DNA antibodies, anti-neutrophil cytoplasmic antibodies, and anti-phospholipase A2 receptor (PLA2R) antibodies were negative. Viral serologies were also unremarkable. No monoclonal band was detected on serum electrophoresis, while serum immunofixation was not performed. Kidneys were normal sized. Renal biopsy performed demonstrated 28 glomeruli, of which only 1 was globally sclerosed. Glomeruli capillary walls were diffusely thickened by vacuolations. Capillary loops were mostly single contoured although occasional focal double contouring was seen. Masson trichome stain revealed fuchsinophilic subepithelial immune deposits while periodic acid methenamine silver stain showed argyrophilic basement membrane spikes. Variable mesangial expansion and hypercellularity was observed, as well as mesangiolysis. Focal leucocyte margination was present, but significant endocapillary proliferation was not seen. There were no Kimmelstiel-Wilson lesions. Tubular atrophy with interstitial fibrosis was overall mild (10% of parenchymal area) and there were no tubulointerstitial infiltrates. Immunofluorescence showed granular staining of IgG (1-2+), C3 (2-3+) along glomerular capillary walls, as well as presence of kappa light chain restriction (k 1-2+; λ negative in glomeruli). Immunostaining for PLA2R was negative. IgG subclass analysis performed in view of kappa light chain restriction revealed isolated deposition of IgG2κ. Electron microscopy was not available. Overall findings were most consistent with membranous variant of PGNMID with monoclonal IgG2κ. Age-appropriate and symptom-directed malignancy screening did not reveal significant abnormalities. Given that the patient was minimally symptomatic, a trial of conservative therapy was initiated with optimized non-immunosuppressive anti-proteinuric therapy using renin-angiotensin-aldosterone and sodium-glucose co-transporter-2 inhibitors. Gradual spontaneous remission was observed without recurrence over 2 years of follow-up (sCr 77μmol/L; sAlb 40g/L; 24-hour UPT 0.22g/day).

Conclusion: Our case adds to the literature that a membranous variant of PGNMID with monoclonal IgG2κ may be associated with better renal outcomes. Despite the lack of proliferative changes, it is possible that membranous variants may share similar underlying disease mechanisms as the other proliferative variants. Large international registries to allow the correlation of morphological features and IgG subclasses with clinical outcomes are required to confirm our observation.

#2885

DYNAMICS OF URINARY SYNDROME IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS DEPENDING ON THE USE OF ANTICOAGULANT

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Background and Aims: to study the dynamics of urinary syndrome in patients with chronic glomerulonephritis (CGN) against the background of the use of rivaroxaban.

Method: 108 patients with chronic glomerulonephritis (CGN), on the background of 3-month basic therapy with the inclusion of anti-coagulant rivaroxaban 55 patients and without anti-coagulant 53 patient. Initially and after 3 months, the composition of the urinary sediment was assessed.

Results: Patients with CGN had significant proteinuria (3.2±0.12g/l versus 0.01±0.004 control group (CG), p<0.001), hematuria (42.58±2.10 erythrocytes in the field of vision, against 0.75±0.25 cells in the field of vision, p<0.001), leukocyturia (38.25±0.80 leukocytes in the field of vision, against 1.70±0.24 cells in the field of view in CG, p<0.001) and cylindruria (38.11±1.04 cylinders in the field of view, versus 0.10±0.07 cylinders in the field of view in CG, p<0.001). Albuminuria contributed to an increase in the specific gravity of urine (1021.64±0.44 g/l versus 1017.45±0.65g/l in CG, p<0.001). By the end of the hospitalization period, there was a significant improvement in urinary syndrome: the relative dynamics of urinary syndrome indicators was more than 30%. Thus, the degree of proteinuria decreased to 1.98±0.10 g/l (p<0.001 the reliability of the difference with the initial data), hematuria – to 26.38±1.43 cells in the field of vision (p<0.001), leukocyturia – to 22.04±0.88 cells in the field of vision (p<0.001), cylindruria – to 25.45±0.79 cylinders in the field of view (p<0.001). Against the background of a decrease in proteinuria and diuretic therapy, there was a decrease in the specific density of urine by 0.73% (up to 1014.15 ± 0.45g/L, reliability with baseline data - p<0.001).

Conclusion: Rivaroxaban is an effective oral anticoagulant, the long – term use of which as part of the basic therapy of patients with CGN is safe, well tolerated and pathogenetically justified. The inclusion of rivaroxaban in the basic therapy of patients with CGN is associated with the achievement of more favorable values of proteinuria, hematuria and leukocyturia by the end of the 3rd month of therapy.

#3412

THE THROMBOTIC EVENTS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: A RETROSPECTIVE COHORT STUDY AND MENDELIAN RANDOMIZATION ANALYSIS

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Background and Aims: Thrombotic event in ANCA-associated vasculitis (AAV) was prevalent but not clarified in the causal relationship between AAV and thrombotic events. We tried to identify the clinical characteristics and risk factors of thrombotic events in a large sample-size retrospective cohort and investigate the causal relationship by Mendelian randomization (MR) analysis.

Method: In this retrospective, observational study, all hospitalized AAV patients were included in a single-center tertiary hospital in China from Jan 2013 to April 2022. Clinical data were collected for multivariate regression analysis to determine the risk factors of thrombotic events. As for MR analysis, we selected single nucleotide polymorphisms (SNPs) related to AAV from published genome-wide association studies. The outcome data containing deep vein thrombosis (DVT) and pulmonary embolism (PE) were extracted from the UK biobank. The inverse variance weighted (IVW) method and weighted median (WM) were performed in MR analysis.

Results: A total of 1203 primary AAV patients were enrolled, with 11.3% developing thrombotic events, with the average age of 49 (ranging from 43.75 to 59.75), and males occupied 36.3%. AAV patients with thrombosis were older (>65 years, 44.9% vs. 29.9%, P<0.001) and with more commodities

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like chronic kidney disease (CKD, 22.8%) or artery disease (CAD, 11.8%). The thrombotic incidences were more common in eosinophilic granulomatosis with polyangiitis (EGPA, 19.5%), with prolonged hospitalization without significant difference in hospital mortality. Multivariate regression suggested that age over 65 years (OR = 1.574, P = 0.029), EGPA (OR = 3.686, P = 0.029), elevated D-dimer (>2 mg/L, OR = 7.119, P < 0.001), and end-stage renal disease (ESRD) status were associated with thrombosis events in patients with AAV. In addition, MR analysis showed that EGPA could increase the risk of developing DVT and PE (OR = 1.0038, 95% CI = 1.0035-1.0041, P = 0.009).

Conclusion: Thrombotic events were not rare in Chinese patients with AAV with independent risk factors such as highly elevated D-dimer and EGPA, which served as a causal risk factor for DVT and PE.

#6333
LARGE B CELL RENAL INFILTRATION IN A PATIENT WITH WALDESTRÖM MACROGLOBULINEMIA: A CASE REPORT
Federica Allegretta1, Campolo Gesualdo2, Olivieri Antonella1, Sarah Ercoletti1, Marco Allinovi3, Leonardo Caroti3, Giulia Antognoli3, Raffaella Santi4, Luca Novelli4 and Fiammetta Ravaglia2

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Background and Aims: Waldeström Macroglobulinemia (WM) is a clinicopathologic entity demonstrating lymphoplasmacytic lymphoma (LPL) in the bone marrow with an IgM monoclonal gammopathy in the blood. Only 15% of patients with WM may develop a renal insufficiency due to either glomerular or tubulointerstitial pathologies. Most common findings include deposits of IgM in the glomerular basement membrane and infiltration of lymphocytes or plasmacytoid cells; light chain cast nephropathy; nephrotic syndrome led by AL amyloid deposition; immune-mediated glomerulonephritis (typically due to IgM deposition or cryoglobulinemia) and non-amyloid nephrotic syndrome (minimal change-like). Moreover, WM may evolve in hematological malignancies with renal localization. Therefore, a renal biopsy may be needed in patients who have recent unexplained renal dysfunction.

Method: A 72-year-old male with a history of WM is referred to our nephrology center for declining renal function. He had been diagnosed with Waldemström Macroglobulinemia IgM Kappa 4 years prior to presentation, at onset serum protein electrophoresis showed an M spike of 4900. After diagnosis confirmation, he underwent treatment with 6 cycles of rituximab and bendamustine resulting in a complete response and M spike at serum protein electrophoresis lowering to 23. At WM diagnosis his renal function was normal, he had no proteinuria nor urinary Bence-Jones. His medical background also included hypertension and diabetes mellitus type 2, both in good pharmacologic control and Sars-Cov2 infection. Two years later, we witnessed to progressive presentation of anemia, fatigue and cough along with hepatomegaly, axillary lymphomegaly, pulmonary basal thickenings and IgM levels elevation. Serum creatinine was 1.47 mg/dl, proteinuria 1.75 g/die, no urinary Bence-Jones proteinuria. A renal ultrasound showed poor corticomedullary differentiation in both kidneys and a left kidney slightly bigger than the other one. Respiratory symptoms and pulmonary thickenings persisted after antibiotics therapy, also cytology and culturing exams performed on broncho-alveolar lavage resulted negative. To exclude a possible relapse of WM, a BOM and a lymphnodal mass biopsy were performed. Both exams showed no disease progression. Due to lack of WM progression, the patient is referred to renal biopsy execution.

Results: Renal biopsy showed morpho-phenotypic findings for localization of mainly large B peripheral cells, partial plasmocytic differentiation and high proliferation levels. Further exams revealed a double monoclonal component IgM Kappa with normal Kappa/Lambda, also a total Body TC was performed, and it evidenced a possible renal and pulmonary lymphoproliferative disease involvement. In the figure an image of the patient’s renal biopsy showing IgM immunofluorescence. Our patient is still fulfilling all the supplementary analysis needed to evaluate the best therapeutic strategies. We also reviewed all renal biopsies performed in our center in patients with hematological diseases in the last 10 years and a neoplastic renal infiltration was documented in just 6 cases out of 650 biopsies.

Conclusion: Although lymphomatous infiltration of the kidney in WM is a rare event, it should be considered in patients presenting with abnormal renal function. It is important during follow-up to monitor kidney function in patients with plasma cell dyscrasias, even if patients appear to have stable lymphoproliferative disease.

Figure 1: Renal biopsy - IgM immunofluorescence.
Background and Aims: Henoch - Schönlein purpura (HSP) is an immunemediated small-vessel vasculitis that manifests as non—thrombocytopenic purpura, arthritis or arthralgia, abdominal pain and/or kidney involvement. HSP nephritis can presented as micro- or macroscopic hematuria, proteinuria, nephrotic or nephritic syndrome, as well as acute renal failure. The aim of the study is to identify risk factors associated with unfavorable outcomes in patients with HSP nephritis.

Method: This retrospective study enrolled 68 patients with HSP nephritis. Renal and extra-renal symptoms were analyzed. A diagnosis of HSP nephritis was made when hematuria and/or proteinuria, and/or renal failure was associated with a palpable purpuric eruption or abdominal or joint pains (at least two of these three clinical signs) and predominant mesangial IgA immune deposits, confirmed by renal biopsy. The patients were subdivided into five classes according to the renal manifestation at onset of disease: 1) micro- or macroscopic hematuria; 2) mild proteinuria (<1 g/L); 3) acute nephritic syndrome, defined as moderate proteinuria, hematuria, increased serum creatinine and/or hypertension; 4) nephrotic syndrome; 5) mixed nephritic-nephrotic syndrome.

Results: Of 68 patients with HSP nephritis, diagnosed by kidney biopsy, 41 (60,29%) were male and 27 (39,71%) - female. Age of onset was between 18 and 66 years (mean 37,28 ± 9,34). Duration of follow-up was between 2 and 28 years. 29 patients had histories of infection preceding presentation. At onset all patients had palpable purpura and urinary abnormalities (only hematuria - in 16,18%; mild proteinuria ± hematuria - in 44,12%; moderate or severe proteinuria and hematuria – in 39,70%). Arthralgias were present in 49 patients (72,06%), gastrointestinal involvement – in 32 patients (47,05%). Renal function was impaired in 26,47% of patients, and 51,47% were hypertensive. Mesangial hypercellularity lesions were found in most patients (97,06%), endocapillary proliferation – in 20,58%, segmental sclerosis – in 32,35%, tubular atrophy/interstitial fibrosis – in 38,23%. Corticosteroids and cyclophosphamide were prescribed in patients who presented with severe infection, active malignancy, those with prior explosion seen at Kasturba Hospital and Medical College, Manipal. Exclusion: Patients with active/recent infection, active malignancy, those with prior explosion to immunosuppression. Outcome measures, 1. To detect correlation if any, between peripheral blood lymphocyte subset and clinical remission achieved at six months. 2. To determine correlation if any, between peripheral blood lymphocyte subset and clinical remission achieved following immunosuppressive regimens at the end of six months of initial intensive treatment phase.

Results: 22 patients were taken for study. Relationship between SLEDAI score, lymphocyte subset characters, and clinical outcome given in Table 1 and 2. There was good correlation between lymphocyte subset characters, inflammatory markers and SLEDAI score, indicating ability of lymphocyte subset characters to characterize the severity of lupus nephritis. We found significant difference in lymphocyte subset characters between baseline and at the end of 6 months treatment. But there was no significant correlation for remission attainment with lymphocyte subset characters and SLEDAI score.

Conclusion: 1. Correlation found between peripheral blood lymphocyte subset, serum inflammatory markers and disease activity score at presentation and 6 months of treatment of lupus nephritis. 2. Peripheral blood Lymphocyte subset analysis was not found useful in predicting clinical outcome in lupus nephritis at the end of 6 months of intensive treatment.
Background and Aims: Impaired renal function is one of the most relevant factors associated to crescentic glomerulonephritis (CGN) prognosis. However, renal remission has not yet been defined and clinicians are required to use systemic scores (such as BVAS) to predict severity. In this retrospective study, we aim to describe the associated factors to long-term chronic dialysis incidence and survival in CGN.

Method: We included all biopsy-proven CGN of our center between 2004 and 2022. At baseline, demographics, treatments, and comorbidities were collected. Renal function was assessed by glomerular filtration rate (GFR) using CKD-EPI equation, quantification of proteinuria and demonstration of hematuria. During follow-up (median 1486, interquartile range [25-3082] days) renal and vital status was evaluated. Factors associated to dialysis requirement were assessed using Cox regression models. A combined endpoint of death and dialysis was established. Factors associated to the combined endpoint were assessed.

Results: We included 47 CGN (77% female, 67±15 years). Of them, 35 (75%) presented positive ANCA antibodies, 8 (17%) ANCA and GBM antibodies and one (2%) presented negative autoimmunity. Induction treatment was based on prednisone and cyclophosphamide in 43 patients (91%), prednisone and rituximab in 3 (6%) and prednisone alone in one (2%). At admission, median CKD-EPI was 11 (11-21) ml/min/1.73 m², proteinuria was 1030 (552-1872) mg/g and 43 (91%) patients presented hematuria. Nineteen patients (40%) required dialysis at admission. Following the definition of KDIGO guidelines for renal remission, 28 (64%) patients achieve it at 6 months.

During follow-up, fifteen patients (36%) started chronic dialysis. Factors associated to chronic dialysis were the type on CGN (dual ANCA and GBM and GBM (+) vs ANCA (+), p = 0.003), CKD-EPI at admission (p = 0.001), AKIN (p = 0.050), requirement of dialysis at admission (p<0.001), percentage of crescents (p = 0.037), proteinuria at admission (p = 0.046) and remission after induction treatment (p<0.001). Twenty-four patients (53%) died or needed dialysis during follow-up. Factors associated to this combined endpoint were CKD-EPI at admission (p = 0.017), type on CGN (dual ANCA and GBM vs others, p = 0.003) (Figure 1), debut in dialysis (p<0.001), remission after induction treatment (p<0.001). An adjusted Cox regression model demonstrated that the need for dialysis or death during follow-up was independently associated to not achieving remission after induction (i.e. 6 months) (HR 8.78, 95%CI [2.88-26.7], p<0.001) and requirement of dialysis at debut (HR 3.96, 95%CI [1.15-13.6], p = 0.029).

Conclusion: The requirement of dialysis at debut and not achieving remission after induction are independent predictors of death or need for chronic dialysis in CGN.

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### #4360

**FACTORS ASSOCIATED TO RENAL REMISSION IN CRESCENTIC GLOMERULONEPHRITIS**

Loreto Mariscal de Gante Sánchez1, Cristina Morales2, Yohana Gil Giraldo1, María Alejandra Cortiñas Aranzábal1, Pablo Ruano1 and Borja Quiroga1

1Hospital de La Princesa, Madrid, Spain and 2San Pablo CEU University - Faculty of Medicine, Alcorcón, Spain

**Background and Aims:** Impaired renal function is one of the most relevant factors associated to crescentic glomerulonephritis (CGN) prognosis. However, renal remission has not yet been defined and clinicians are required to use systemic scores (such as BVAS) to predict severity. In this retrospective study, we aim to describe the associated factors to long-term chronic dialysis incidence and survival in CGN.

**Method:** We included all biopsy-proven CGN of our center between 2004 and 2022. At baseline, demographics, treatments, and comorbidities were collected. Renal function was assessed by glomerular filtration rate (GFR) using CKD-EPI equation, quantification of proteinuria and demonstration of hematuria. During follow-up (median 1486, interquartile range [25-3082] days) renal and vital status was evaluated. Factors associated to dialysis requirement were assessed using Cox regression models. A combined endpoint of death and dialysis was established. Factors associated to the combined endpoint were assessed.

**Results:** We included 47 CGN (77% female, 67±15 years). Of them, 35 (75%) presented positive ANCA antibodies, 8 (17%) ANCA and GBM antibodies and one (2%) presented negative autoimmunity. Induction treatment was based on prednisone and cyclophosphamide in 43 patients (91%), prednisone and rituximab in 3 (6%) and prednisone alone in one (2%). At admission, median CKD-EPI was 11 (11-21) ml/min/1.73 m², proteinuria was 1030 (552-1872) mg/g and 43 (91%) patients presented hematuria. Nineteen patients (40%) required dialysis at admission. Following the definition of KDIGO guidelines for renal remission, 28 (64%) patients achieve it at 6 months.

During follow-up, fifteen patients (36%) started chronic dialysis. Factors associated to chronic dialysis were the type on CGN (dual ANCA and GBM and GBM (+) vs ANCA (+), p = 0.003), CKD-EPI at admission (p = 0.001), AKIN (p = 0.050), requirement of dialysis at admission (p<0.001), percentage of crescents (p = 0.037), proteinuria at admission (p = 0.046) and remission after induction treatment (p<0.001). Twenty-four patients (53%) died or needed dialysis during follow-up. Factors associated to this combined endpoint were CKD-EPI at admission (p = 0.017), type on CGN (dual ANCA and GBM vs others, p = 0.003) (Figure 1), debut in dialysis (p<0.001), remission after induction treatment (p<0.001). An adjusted Cox regression model demonstrated that the need for dialysis or death during follow-up was independently associated to not achieving remission after induction (i.e. 6 months) (HR 8.78, 95%CI [2.88-26.7], p<0.001) and requirement of dialysis at debut (HR 3.96, 95%CI [1.15-13.6], p = 0.029).

**Conclusion:** The requirement of dialysis at debut and not achieving remission after induction are independent predictors of death or need for chronic dialysis in CGN.

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Figure 1: Survival plot for combined endpoint regarding serology.
Background and Aims: Belimumab (BLM) has been approved for the treatment of active systemic lupus erythematosus (SLE) and active lupus nephritis (LN). Multitarget therapy (MT) consisting of tacrolimus (FK506), mycophenolate mofetil (MMF), and steroid has been proved that can provide good curative effect as induction therapy for LN. Because of the limitations of BLM’s phase III clinical trails, the exact curative effect in severe active LN of BLM is not clear yet. To assess the safety and generate preliminary efficacy data on MT followed by BLM for severe active Chinese LN patients, a case series were investigated.

Method: Six patients with severe active LN were reported. Among the 6 patients, 2 were treated with MT followed by BLM infusions, 2 were treated with MMF / (FK506) followed by BLM infusions, and 2 were treated with MT. BLM was given 10 mg/kg every 2 weeks for 3 times, then every 4 weeks till Week 24. Primary renal response index, SLEDAI, and safety data were analyzed.

Results: The patients affected by LN ISN/RNP Class III/IV±V with high disease activity are 3 de no LN and 3 refractory LN (each regimen included 1 de no LN and 1 refractory LN). At baseline, the SLEDAI score were 15,20,17,16,15,15 respectively. 4 of the 6 patients (case 1, case 2, case 3, and case 5) accepted intravenous (IV) methylprednisolone, followed by MT/MMF/FK506 after admission. The initial oral prednisone was 30-45 mg/day. Within 2 weeks of starting treatment, IV BLM was introduced. At Week 24, the SLEDAI score decreased to 2,8,8,10,8,10 respectively. 2 patients accepted BLM and MT achieved complete renal remission, and the other 4 patients achieved partial renal remission (Fig. 1). MT and BLM therapy reduced SLEDAI more rapidly than MMF/FK 506 +BLM or MT (Fig. 2). Prednisone was reduced to 10-15 mg/d. No adverse events occurred.

Conclusion: The addition of BLM to basic immunosuppressants was effective and safe for severe active LN. The BLM and MT regimen seems to lead a faster and more pronounced remission. Further prospective clinical studies with larger samples are needed to evaluate the benefits of belimumab combined with MT in severe active LN.
Figure 2: The details of the 6 patients’ Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). The graph shows the patients’ overall scores along with the SLEDAI components with their respective weights during the treatment. 0 week is the time to start the belimumab in cases 1-4 and is the time to start therapy in cases 5-6. Case 1 and Case 2 accepted belimumab and multitarget therapy. Case 3 accepted belimumab and mycophenolate mofetil. Case 4 accepted belimumab and tacrolimus. Case 5 and Case 6 accepted multitarget therapy.

#5710
CHARACTERIZATION OF RESPONSE TO TREATMENT WITH RITUXIMAB IN PATIENTS WITH PRIMARY GLOMERULOPATIES
Roxana Bury¹, Maria Larrosa García², Bruno Montoro³, Sheila Bermejo García¹, Ander Vergara¹, Marina López¹, María José Soler Romeo¹, Anguita Danae², Sanz María¹, Martínez Monica¹ and Irene Agraz Pamplona¹

¹Vall D Hebron University Hospital, Nephrology, Barcelona, Spain, ²Vall D Hebron University Hospital, Pharmacy, Barcelona, Spain and ³Vall D Hebron University Hospital, Immunology, Barcelona, Spain

Background and Aims: Rituximab (RTX) is an anti-CD20 monoclonal antibody used in renal diseases with glomerular involvement, which usually present with proteinuria. The doses used in this pathologies are extrapolated from other diseases such as rheumatoid arthritis, but the optimal regimen in this population has not been well defined.

Objective: To describe the behavior of RITUXIMAB in patients with primary glomerulopathies in whom its use is indicated.

Method: Descriptive low-intervention single-center clinical trial approved by the Spanish Medicines Agency (NEFRX, EUDRACT 2020-000484-23). Patients treated with rituximab were included according to medical criteria, prior approval by the Pharmacy Commission. The regimen used was 1g every 15 days, or only 1gr dose with premedication according to clinical practice guidelines. 24-hour blood and urine samples were collected on days 1 (post-rituximab), 7, 15 (pre and post-rituximab), 28, and 45. Serum rituximab was determined using ELISA (Lisa-Traker®, TheraTrak®). Clinical and pharmacokinetic data analyzes were performed considering a single compartment model by non-linear regression with Winnolin® to obtain clearance (Cl), half-life (t1/2), maximum concentration (Cmax) and volume of distribution (Vd). Some quantitative results are expressed as mean ± standard deviation. Linear regression was used to establish correlations.

Results: The results of 5 patients were analyzed, 2 women and 3 men, with a mean age of 68.8 ± 17.02 years of 72 years and a diagnosis of membranous GN (3), ANCA MPO GN (1), focal and segmental GN (1). Renal function CKD EPI: GFR between 45- 60 ml/min N=2 GFR >60 ml/min N=3. According to clinical practice guidelines, patients received 1g doses, 2/5 patients received a second dose on day 15. The evaluation parameters were: proteinuria, CD19+ lymphocyte depletion, Antibodies titers and histological characteristics as appropriate. Levels of rituximab in urine samples after the rituximab administration (15, 30, 180, 365 days after) were determined. All the patients presented proteinuria, with a mean of 11 ± 14.6 g in 24 h urine.

Mean Rituximab clearance was 0.676 ± 0.431 ml/h/kg, distribution volume was 222.35 ± 140.52 mL/Kg and Cmax 69.66 ± 26.14 mcg/mL and t1/2 269.66 ± 229.71 h (11 days approximately). There is a correlation between proteinuria and rituximab half-life (p = 0.077), as well as between proteinuria and clearance creatinine (p = 0.975) suggesting that half-life of rituximab is lower if proteinuria increases (Fig. 1). All presented lymphocyte depletion of CD 19 at 45 days. However, those with more proteinuria >2.5 g (N = 3) in those 45 days, after 6 months of exposure to RTX, progressive repopulation of CD19 was observed, which persisted in the year of follow-up.

Conclusion: In patients with high proteinuria, rituximab has a t1/2 lower than the 21–28 days described in the data sheet, which may suggest that patients with nephrotic syndrome may require higher doses to ensure the effectiveness of treatment with rituximab. Repopulation of CD19 in 45 days could be a reliable indicator of non-response in patients with nephrotic proteinuria.
NEW ONSET OR RECURRENT GLOMERULONEPHRITIS FOLLOWING SARS-CoV2 VACCINATION: A MULTICENTER EXPERIENCE

Chiara Rimoldi1, Marica Gilberti2, Loreto Gesualdo2, Giulia Sossai1, Renato Alberto Sinico4, Elisa Giglio5, Marta Calatroni6, Davide Raimondo7, Beniamina Gallelli1, Lucia Del Vecchio1 and Sara Visca1

1Sant’Anna Hospital, ASST Lariana, San Fermo della Battaglia (CO), Italy, 2University of Bari Aldo Moro, Bari, Italy, 3Careggi University Hospital, Florence, Italy, Nephrology, Dialysis and Transplantation Unit, Florence, Italy, 4University of Milano-Bicocca, Department of Medicine and Surgery, Monza, Italy, 5Azienda Sanitaria Provinciale di Ragusa, Nephrology and Dialysis., Ragusa, Italy, 6IRCCS Humanitas Research Hospital, Nephrology and Dialysis Unit, Rozzano (Milan), Italy and 7Uboldo Hospital, ASST Melegnano and Martesana, Nephrology and Dialysis, Cernusco sul Naviglio, Milan, Italy

Background and Aims: In general, vaccination is a well-known trigger for the onset or recurrence of glomerulonephritis or more in general autoimmune disease. Starting from the beginning of 2021 millions of people worldwide have received a vaccination of SARS-CoV2. Over the months, several cases of glomerulonephritis with a clear temporal association with the vaccine have been described [1,2].

Method: To better understand the characteristics, pattern of presentation, temporal and qualitative association with SARS-CoV2 vaccination and outcome, we designed a retrospective, multicenter, nationwide study aimed at collecting information on new onset or recurrence of primary or secondary vaccination following SARS-CoV2 infection. We present the preliminary findings from the first seven participating centers that completed data collection. For inclusion patients needed to be ≥16 years, have either a biopsy-proven glomerulonephritis or gross haematuria without urological explanation in close relationship with the vaccine. For outcome definition, partial remission was proteinuria > 300 mg/day, complete remission proteinuria 300–3500 g/day.

Results: We report 57 cases (M/F 22/35, mean age 48.59±18.99 years, median follow-up of 11.8 months (min 1.1, max 22.5). Of these, 25 (44%) were new onset glomerulonephritis, the remaining 32 (56%) were recurrence of already known cases (1/3 in complete remission, 2/3 in partial remission). Table 1 summarises the diagnosis new-onset or recurrent glomerulonephritis. 37 (65%) were primary glomerulonephritis, the other 20 (35%) kidney involvement of systemic diseases. The most frequent diagnosis was IgA nephropathy (IgAN, n = 17, 30%), followed by lupus nephritis (n = 9, 16%) and membranous nephropathy (n = 7, 12%). Compared to recurrence, patients with new-onset glomerulonephritis had a higher prevalence of minimal change disease (4 vs 1 case), Henoch Shoenlein purpura (3 vs 0) and FSGS (2 vs 0). Conversely, in patients with recurrence, we observed a higher rate of IgAN (14 vs 3), microscopic polyangiitis (5 vs 1) and lupus nephritis (7 vs 2). Most of the cases occurred following an mRNA vaccine (n = 42, 90%). The median time of onset was of 18 days. The onset was related more to the second dose of vaccine (n = 27, 47.4%), followed by the first dose (n = 14, 25%) and then the third dose (n = 12, 21.1%), with an imbalance between new-onset vs recurrence (C2, 11.18; p = 0.011) Fig.1). The information is missing in 4 cases. Most of the patients presented with nephrotic proteinuria (n = 24, 42%). Following treatment, 15 (26.3%) patients obtained partial remission, 18 (31.6%) had complete remission and the remaining 21 (36.8%) had no response. The information is missing for 3 patients.

Conclusion: Following SARS-CoV2 vaccine, de novo or recurrent glomerulonephritis can occur. The majority of the cases were related to mRNA vaccines. However, the vaccine policy in Italy could have influenced this finding.

REFERENCES
Table 1: Main diagnosis of new-onset or recurrent GN.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>De novo GN N (%)</th>
<th>Recurrence N (%)</th>
<th>Overall N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA nephropathy</td>
<td>3 (5.3)</td>
<td>14 (24.6)</td>
<td>17 (29.8)</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>2 (3.5)</td>
<td>7 (12.3)</td>
<td>9 (15.8)</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
<td>4 (7.0)</td>
<td>3 (5.3)</td>
<td>7 (12.3)</td>
</tr>
<tr>
<td>Microscopic polyangiitis</td>
<td>1 (1.8)</td>
<td>5 (8.8)</td>
<td>6 (10.6)</td>
</tr>
<tr>
<td>Minimal change disease</td>
<td>4 (7.0)</td>
<td>1 (1.8)</td>
<td>5 (8.8)</td>
</tr>
<tr>
<td>Henoch Shoenlein purpura</td>
<td>3 (5.3)</td>
<td>0 (0)</td>
<td>3 (5.3)</td>
</tr>
<tr>
<td>Gross Haematuria</td>
<td>2 (3.5)</td>
<td>0 (0)</td>
<td>2 (3.5)</td>
</tr>
<tr>
<td>FSGS</td>
<td>2 (3.5)</td>
<td>0 (0)</td>
<td>2 (3.5)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (8.8)</td>
<td>1 (1.8)</td>
<td>6 (10.6)</td>
</tr>
<tr>
<td>Total</td>
<td>25 (43.9)</td>
<td>32 (56.1)</td>
<td>57 (100)</td>
</tr>
</tbody>
</table>

Figure 1: Temporal association between vaccine dose and new-onset (Blue bar) or recurrent glomerulonephritis (orange bar).

UTILITY OF REPEAT KIDNEY BIOPSY IN LUPUS NEPHRITIS PATIENTS: A SINGLE CENTRE EXPERIENCE
Alexandra Vornicu, Bogdan Obrisca, Alexandru Procop, Vlad Herlea, George Terinte-Balcan, Mihaela Gherghiceanu, Nicu Caceaune and Gener Ismail

Background and Aims: Given the accumulating evidence of discrepancies between the clinical features and histological lesions in lupus nephritis patients, there is an increasing need for a histology-guided approach in order to optimise the management of these patients.

Method: 13 adult patients with a diagnosis of systemic lupus erythematosus and biopsy-proven lupus nephritis, followed up in the Nephrology Department of Fundeni Clinical Institute in Bucharest, Romania from 2015 to 2022, which had undergone a repeat per-protocol biopsy at 6 months were included in this retrospective, single-centre study. The objectives of the study were to determine the evolution of the clinical and histological parameters at first and at 6-months repeat-biopsy, their possible associations and their relationship with the primary efficacy renal response (PERR) at 12 months. The National Institutes of Health activity index (AI) and chronicity index (CI) scores were assessed in all biopsies. PERR was defined as proteinuria ≤ 0.7 g/24 h and eGFR ≥ 60 ml/min/1.73 m².

Results: The median (IQR) follow-up was 20 (13.5-34) months. 53.8% were class IV lupus nephritis at the first biopsy. Repeat biopsies were performed after a median time (IQR) of 6 (6-9) months. The majority of the patients received cyclophosphamide and corticosteroids as induction regimen (69.2%) and mycophenolate mofetil and corticosteroids as maintenance regimen (92.3%). PERR was achieved in 61.5% of cases at 12 months. Proteinuria (g/24 h) decreased from the median value (IQR) of 2.3 (1.55-4.3) to 0.4 (0.2-3.1) at biopsy 2 (p 0.02), hematuria (red blood cells/μl) decreased from 33 (11.5-178.5) to 10 (1.75-62) at biopsy 2 (p 0.017) and serum creatinine decreased from 1.18 (0.81-1.48) to 0.9 (0.73-1.07) at biopsy 2 (p <0.001). Serum C3 (mg/dl) increased from 56 (41-76.5) to 103 (84-126) (p <0.001), whereas serum C4 (mg/dl) increased from 10 (4-19) to 22 (11-31) (p <0.001). AI scores decreased from 10 (8.5-13.5) to 3 (2.5-7) (p <0.001) and CI scores increased from 2 (2-3) to 3 (3-5.5) (p <0.001). At repeat biopsy, CI increased in 8 patients (61.5%). Its increase was not predicted by baseline or at the moment of repeat biopsy values of activity and chronicity indices, renal function, hematuria, proteinuria and complement fractions. The type of induction regimen used did not protect against CI increase (p 0.506). The baseline value – median (IQR) of AI (9 (6.5-14.5) vs 10.5 (9-13.75), p 0.596), CI (2 (1.5-2.5) vs 3 (2-4.5), p 0.127), serum creatinine (mg/dl)(1.18 (0.96-1.66) vs 1.03 (0.75-1.36), p 0.316), hematuria (red blood cells/μl) (78 (10.9-1086) vs 29 (7.25-111.5), p 0.622) and complement fractions C3 (mg/dl) (74 (40-104) vs 48.5 (41-71.5), p 0.33) and C4 (mg/dl) (18 (6-23.5) vs 8 (3-15.75), p 0.36) were not associated with the PERR at 12 months. The median value (IQR) of AI (3 (2.9-3.5) vs 3.5 (2.25-7), p 0.943) and CI (3 (2.5-5) vs 5 (3-5.5), p 0.42), hematuria (red blood cells/μl) (26 (2.25-85.5) vs 6.5 (1.4-48.25), p 0.35) and serum creatinine (mg/dl) (1.18 (0.89-1.12) vs 0.77 (0.7-0.9), p 0.13) at the second biopsy were also not associated with the PERR at 12 months. Proteinuria at baseline (g/24 h) (4.6 (2.37-8.1) vs 1.85 (1.16-2.6), p 0.019) and proteinuria at repeat biopsy (g/24 h) (4.6 (1.45-6.1) vs 0.23 (0.17-0.36), p 0.002) were associated with PERR at 12 months. Lower complement fraction C3 at the second biopsy (mg/dl) (123 (104-142) vs 88.5 (74.75-106.5), p 0.036) was associated with the PERR at 12 months and lower serum C4 at the second biopsy (mg/dl) (26 (21-34.5) vs 16 (7-29), p 0.082), had a trend to associate with the PERR at 12 months.
Conclusion: At the second biopsy, the chronicity index increase was not predicted by baseline or at the moment of repeat biopsy values of activity and chronicity indices, renal function, hematuria, proteinuria or the values of complement fractions. The type of induction regimen used did not protect against chronicity index increase. Proteinuria at baseline and at repeat biopsy was associated with PERR at 12 months. Lower complement fraction C3 at the second biopsy was associated with the PERR at 12 months and lower serum C4 at the second biopsy had a trend to associate with the PERR at 12 months.

ROLE OF THERAPEUTIC PLASMATHERAPY IN PAUCI-IMMUNE VASCULITIS – A SINGLE CENTRE EXPERIENCE

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Background and Aims: The indication for plasmapheresis (PLF) in pauci-immune vasculitis (PIV) is controversial. This study aimed to characterize the population and renal outcome of patients with PIV undergoing PLF in a hospital in the north of Portugal.

Method: We conduct a retrospective cohort study of patients followed by a multidisciplinary team, from diagnosis to death or May/22. Two groups were defined: patients undergoing PLF (group A, GA) and not undergoing PLF (group B, GB). Demographic variables, comorbidities, serological subtype, clinical presentation, histological classification and therapeutic were evaluated. Recorded outcomes were death and ESRD (end-stage renal disease) (eGFR<15 ml/min per 1.73 m², dialysis, or transplantation). Renal survival was estimated using the Kaplan-Meier analysis and differences between curves were evaluated using the log-rank test.

Results: A total of 72 patients, 26 (36.1%) in group A and 46 (63.9%) in group B were included. In both groups the most frequent serotype was myeloperoxidase (MPO) (n = 23, GA; n = 38, GB). In both groups, most patients were male (61.5% in GA and 56.5% in GB), with a mean age at admission of 64 (SD±11.5) and 66.5 years (SD±12.2) in GA and GB, respectively (p = 0.362). Most GA patients had pulmonary and renal involvement on admission (80.7%, n = 21), versus GB (36.9%, n = 17), p<0.05. Mean serum creatinine was superior in GA (7.64 mg/dl, SD ±2.75) versus GB (3.82 mg/dl, SD±2.95), p<0.05. Twenty patients from GA (76.9%) and 7 from GB (15.2%) required dialysis upon admission, p<0.05. In both groups, almost all patients underwent immunosuppression with cyclophosphamide (mean cumulative dose of 4.4 grams (SD ± 2.6) and 5.9 grams (SD ± 2.7), in GA and GB, respectively) and azathioprine in the maintenance phase, with a rapid corticosteroid weaning scheme in both phases. Median follow-up time (months) of GA and GB was 11 (IQR [4.8-37.5]) and 58.5 (IQR [14.5-92]) months. Regarding renal prognosis, 9 of 20 patients in GA and 3 of 7 patients in GB who needed dialysis on admission, partial recovery of renal function (p = 1.00). About 37% (n = 17) of patients of GB and 73% (n = 19) of patients of GA reached the composite renal outcome, with a median time of 0 (IQR 0 - 21.8) and 38.5 months (IQR 5.3-92), respectively. GA showed worse renal survival, with a mean of 30.9 months vs. 116.5 months in GB, p = 0.01. Renal survival at 2 years was 68.7% in GB and 24% at GA. Patients in both groups with admission serum creatinine ≥ 5.7 mg/dl had similar renal survival (GA 39.9 and GB 32 months, p = 0.714). Regarding the histological classification, 91.7% and 38.9% in GA and GB belonged to the crescentic class, (p = 0.009). Renal survival in the subgroup of patients with crescentic class was worse in GA (16.6±10.2 vs 83.3±16.1, p = 0.015). The analysis of the Renal Risk Score showed no statistically significant difference between the groups, and between patients with crescentic class in both groups, p = 0.274. Mortality and hospitalization rate due to infection were similar in both groups (p>0.05).

Conclusion: Patients undergoing PLF had a worse renal outcome, consistent with the higher proportion of patients with severe azotemia and requiring dialysis at admission, in a sample that was mostly ANCA MPO. As described in the literature, the experience of our centre did not demonstrate benefit in the addition of PLF, despite the limitations inherent to an observational, retrospective study and the modest sample size. A better knowledge of etiopathogenesis is essential for the optimization of the therapeutic strategy, together with the implementation of measures that allow timely referral, an early diagnosis and consequent improvement of renal prognosis.
**Results:** A total of 1227 VTE cases were identified in the hospitalized NS population and the detection rate was 1.56%. Detection rate of VTE varied significantly in patients with different pathologic types of NS. Patients with membranous nephropathy (MN) had a significantly increased risk of VTE [Odds ratio [OR] 2.11 [95% confidence interval (CI) 1.12–4.36]]. While patients with focal segmental glomerulosclerosis (FSGS) did not show a significant high risk [OR 0.93 (95% CI 0.29–2.60)] compared with minimal change disease. We also found that male [OR 1.44 (95% CI 1.15–1.80)], age [OR 1.09 (95% CI 1.02–1.17)], anemia [OR 1.50 (95% CI 1.15–1.95)], cerebral bleeding [OR 3.23 (95% CI 1.69–6.10)], respiratory tract infection [OR 2.05 (95% CI 1.60–2.63)], respiratory failure [OR 2.24 (95% CI 1.42–3.53)], use of proton pump inhibitors (PPIs) [OR 2.19 (95% CI 1.54–3.12)], use of glucocorticoids [OR 1.46 (95% CI 1.03–2.09)] and immunosuppressants [OR 1.48 (95% CI 1.14–1.93)], orthopedic operations [OR 1.97 (95% CI 1.22–3.18)], high-level D-dimer (>0.55 mg/L) [OR 2.62 (95% CI 1.87–3.65)] were associated with increased risk of VTE detection. While 24-hour urine protein quantification >10 g/d [OR 1.24 (95% CI 0.90–1.70)] showed little significant correlation with VTE. Hypertension [OR 0.74 (95% CI 0.58–0.95)] and the use of diuretics [OR 0.72 (95% CI 0.53–0.97)] were found to have a negative correlation with VTE detection.

**Conclusion:** The detection rate of VTE among patients with NS during hospitalization was 1.56%. Male, age, MN, anemia, cerebral bleeding, respiratory tract infection, respiratory failure, and use of PPIs, glucocorticoids and immunosuppressants, high D-dimer concentration were associated with VTE detection in NS. While 24-hour proteinuria did not show a significant association with VTE identification.

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**Table 1: Association between pathologic types of nephrotic syndrome and venous thrombosis detection among patients with pathologic diagnosis.**

<table>
<thead>
<tr>
<th>Pathological Types</th>
<th>VTE events/ Total (Rate, %)</th>
<th>Reference OR</th>
<th>Reference 95%CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCD 11/1861 (0.59)</td>
<td>2.11 (1.12, 4.36)</td>
<td>0.030</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MN 70/5017 (1.40)</td>
<td>0.93 (0.29, 2.60)</td>
<td>0.895</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSGS 5/886 (0.56)</td>
<td>1.02 (0.15, 3.92)</td>
<td>0.984</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others 2/336 (0.60)</td>
<td>1.02 (0.15, 3.92)</td>
<td>0.984</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** MN: membranous nephropathy; MCD: minimal change disease; FSGS: focal segmental glomerulosclerosis.

1 Adjusted for sex, age, chronic comorbidities (anemia, AF: atrial fibrillation, CHD: coronary heart disease, CKD: chronic kidney disease, CHF: congestive heart failure, CTD: connective tissue disease, diabetes, hypertension, VHD: valvular heart disease, malignant tumor), Albumin.
Table 1: Various features and outcomes of all patients (n = 74).

<table>
<thead>
<tr>
<th>Characteristics at baseline</th>
<th>n (%)</th>
<th>Median (IQR)</th>
</tr>
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<tbody>
<tr>
<td>Sex (male)</td>
<td>39 (52.7)</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>34 (24-46)</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.3 (0.7-2.1)</td>
<td></td>
</tr>
<tr>
<td>eGFR (ml/min/1.73 m²)</td>
<td>58.9 (30.9-119.7)</td>
<td></td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>3.4 (2.5-4.0)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>11.8±2.5</td>
<td></td>
</tr>
<tr>
<td>Proteinuria (mg/dl)</td>
<td>4400 (1498-6628)</td>
<td></td>
</tr>
<tr>
<td>Hematuria (%)</td>
<td>53 (71.6)</td>
<td></td>
</tr>
<tr>
<td>Low C3, (%)</td>
<td>36/71 (50.7)</td>
<td></td>
</tr>
<tr>
<td>Low C4, (%)</td>
<td>7/67 (10.4)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Histologic features</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitial fibrosis</td>
<td>10.4 (1.5-30.3)</td>
</tr>
<tr>
<td>- Grade 0</td>
<td>31 (41.9)</td>
</tr>
<tr>
<td>- Grade 1</td>
<td>28 (37.8)</td>
</tr>
<tr>
<td>- Grade 2</td>
<td>13 (17.6)</td>
</tr>
<tr>
<td>- Grade 3</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Tubular atrophy (%)</td>
<td>21 (28.4)</td>
</tr>
<tr>
<td>- Grade 0</td>
<td>39 (52.7)</td>
</tr>
<tr>
<td>- Grade 1</td>
<td>10 (13.5)</td>
</tr>
<tr>
<td>- Grade 3</td>
<td>4 (5.4)</td>
</tr>
<tr>
<td>Arterio- and arteriolosclerosis (%)</td>
<td>28 (37.8)</td>
</tr>
<tr>
<td>Endocapillary proliferation (%)</td>
<td>35 (47.3)</td>
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<table>
<thead>
<tr>
<th>Treatment, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any immunosuppression</td>
</tr>
<tr>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Eculizumab</td>
</tr>
<tr>
<td>Azathioprine</td>
</tr>
<tr>
<td>Calcineurin inhibitors</td>
</tr>
<tr>
<td>Rituximab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study outcome</td>
</tr>
<tr>
<td>Dialysis or transplantation</td>
</tr>
<tr>
<td>Doubling of serum creatinine</td>
</tr>
<tr>
<td>Stage 5 chronic kidney disease</td>
</tr>
<tr>
<td>Death</td>
</tr>
</tbody>
</table>

Results: Baseline features, treatment characteristics and outcomes were detailed in Table 1. Median follow-up duration was 36 (12-60) months. Overall, 19 patients (25.7%) experienced the study outcome over a median of 24 (6-51) months. Three patients died due to infections (n = 2) and unknown causes (n = 1) including a patient who died shortly after becoming dialysis-dependent. Median TCS was 3 (1-5). Univariate analyses showed that IF, hemoglobin, serum creatinine and serum albumin levels were associated with the outcome, but only grade 3 IF predicted the outcome in the multivariate Cox regression (HR: 6.623, 95% CI: 1.269-34.564, p = 0.025). Since the median follow-up was 36 months, separate analyses for the outcome at 3 years were conducted. IF, TA, TCS, hemoglobin, serum creatinine and albumin were associated with the outcome in univariate analyses. In a multivariate Cox regression model encompassing IF, TA, hemoglobin, serum creatinine and albumin, only hemoglobin was identified as a predictor. A second model including TCS instead of IF and TA demonstrated that TCS (HR: 1.288, 1.021-1.626, p = 0.033) and hemoglobin (HR: 0.617, 0.407-0.935, p = 0.025) predicted the study outcome. Kaplan-Meier analysis showed that 3-year kidney survival was lower in patients with TCS ≥4 (72.4%) compared to TCS <4 (91.1%) (p = 0.036 with log-rank test).

REFERENCE


REAL WORLD DATA-DRIVEN IDENTIFICATION OF ANCA VASCULITIS RELAPSE

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Background and Aims: The relapsing-remitting, multi-system pattern of disease in ANCA vasculitis (AAV) results in incremental tissue injury. For those with renal involvement, there is a 9-fold increased risk of end-stage kidney disease after renal relapse. Relapse is defined by the Birmingham Vasculitis Activity Score (BVASv3) >0, particularly in the clinical trial setting. However, this metric may be missing or incorrectly scored in real world registry data, resulting in incomplete or inaccurate ascertainment of this key outcome. Our aim was the development, internal validation and evaluation of a pragmatic data-driven algorithm to automate the retrospective identification of AAV relapse in real-world data.

Method: The Rare Kidney Disease (RKD) Registry is a national longitudinal, multi-centre cohort study, including 663 patients with AAV, of whom those with ≥6 months follow up post diagnosis were eligible for inclusion. We followed five steps to develop and validate the algorithm: 1) independent expert adjudication of encounters using primary medical record information to assign the reference probability of relapse (ground truth), 2) selection of data elements and corresponding value sets using literature review, expert opinion and with a consideration of likely data availability, 3) development
of a computable phenotype definition, with an embedded logistic multi-level regression model using complete case analysis, 4) internal validation, 5) development of additional models (using the same method) to account for combinations of variable missingness (models described in Fig. 1). We also developed a Shiny web application to implement the final algorithm, which determines the appropriate model based on available variables, outputting an individualised probability of relapse, with a suggested binary interpretation.

Results: In the first step of the algorithm, encounters with diagnostic histopathology were labelled as relapse. For encounters without histopathological confirmation, we selected five objective data elements to build the model: change in ANCA level, suggestive blood/urine tests, suggestive imaging, immunosuppressive (IS) status at the time of the encounter and the change of this IS in response (‘IS response’) (Fig. 2). Development and validation datasets comprised 1209 and 377 separate encounters, respectively. An optimal cut-point of 0.48 was determined by maximising the F1-Score (0.85) for the complete 5-variable model. Sensitivity and specificity were 0.91 and 0.95 respectively. Performance metrics were stable across fifty random-split resamples. Calibration-in-the-large was satisfied. Where ‘IS response’ was missing, ‘suggestive bloods/urine’ (Data Element [DE]2) with at least either ‘ANCA level’ (DE1) or ‘suggestive imaging’ (DE3) was required to achieve an accuracy as good as gold standard BVAS (Fig. 1).

Conclusion: In settings where accurate BVAS may not be available, this algorithm accurately quantifies the individualised probability of AAV relapse using objective, readily accessible registry data. In addition to our web application, the model can be directly embedded in a registry database. This framework could serve as an exemplar for other relapsing-remitting diseases and for automating the identification of other key outcomes or cohorts in registry data.
THE NATURAL HISTORY OF IGA NEPHROPATHY IN THE GERMAN CHRONIC KIDNEY DISEASE (GCKD) COHORT

Eleni Stamellou1, Jennifer Nadal2, Claudia Seikrit3, Bruce Hendry3, Alex Mercer4, Markus Johannes Müller4, Matthias Schmidt5, Mario Schifo4, Kai-Uwe Eckardt6,7 and Jürgen Floege8

1RWTH Aachen University Hospital, Division of Nephrology and Rheumatology, Germany; 2Faculty of Medicine, University Hospital Bonn, Department of Medical Biometry, Informatics and Epidemiology, Germany; 3Traverce Therapeutics, Inc., San Diego, United States of America; 4JAMCO, Pharma Consulting, Sweden; 5Friedrich-Alexander University Erlangen-Nuremberg, Department of Nephrology and Hypertension, Erlangen, Germany and 6Charité-Universitätsmedizin Berlin, Department of Nephrology and Critical Care Medicine, Germany.

Background and Aims: Primary IgA nephropathy (IgAN) is the most common form of glomerulonephritis and a major cause of kidney failure. Here we describe the natural history of individuals with IgAN in the German Chronic Kidney Disease (GCKD) cohort.

Method: From 2010 to 2012, 421 patients with biopsy-proven IgAN have been enrolled into the GCKD study, a prospective observational cohort study (N = 5217). Inclusion criteria were an estimated glomerular filtration rate (eGFR) of 30-60 mL/min/1.73 m² or overt proteinuria in the presence of an eGFR < 60 mL/min/1.73 m². The adjudicated composite renal endpoint (Major Adverse Kidney Events; MAKE) was defined as eGFR decline 40%, eGFR < 15 mL/min or initiation of kidney replacement therapy. The associations between the incidence of MAKE and baseline risk factors were analyzed using the Cox proportional hazards regression model. Data relating to baseline demographics, laboratory, comorbidity, and mortality were used.

Results: The mean age at baseline of IgAN patients was 51.6 years (±13.6) and 67% were male. Duration of disease at baseline was 5.9 ± 8.1 years. Baseline median UACR was 0.4 g/g (0.1-0.8) and mean eGFR was 52.5 ± 22.4 mL/min/1.73m². Over a follow-up of 6.5 years, 53 (12.6%) initiated kidney replacement therapy, 64 (15.2%) experienced eGFR decline >40%, eGFR < 15 mL/min or initiation of kidney replacement therapy. The associations between the incidence of MAKE and baseline risk factors were analyzed using the Cox proportional hazards regression model. Data relating to baseline demographics, laboratory, comorbidity, and mortality were used.

Conclusions: The GCKD study reflects a large cohort with long follow up allowing for a thorough analysis of the natural history of IgAN. More than every fourth patient experienced a MAKE event within 6.5 years. Our findings support the use of albuminuria as a surrogate for poor kidney outcomes.

REFERENCES

THE NATURAL HISTORY OF IGA NEPHROPATHY IN THE GERMAN CHRONIC KIDNEY DISEASE (GCKD) COHORT

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REFERENCES
Methods: A single-center retrospective cross-sectional study was conducted to compare the time spent on the procedure and the number of glomeruli obtained in a group using the SIGN technique (n = 81) and a group using the standard ultrasound-guided renal biopsy technique with a needle guide (n = 143). Biopsies were performed by four board-certified nephrologists of the Japanese Society of Nephrology and four fellows. It was left to the operator to decide whether to use the standard technique or the SIGN technique. In the standard technique, an operator inserted a biopsy gun through a needle guide attached to the ultrasound probe and obtained a biopsy core from the lower pole of the kidney. In the SIGN technique, after local anesthesia, an operator inserted a 17-gauge guide needle (TSK Laboratory, Tochigi, Japan) through the needle guide without making a skin incision. The guide needle was placed in the fascia of the posterior abdominal wall. Then the operator inserted a biopsy gun through the guide needle into the lower pole of the kidney and obtained the biopsy core. The puncture time was calculated by subtracting the minute of the last puncture from the first. The number of glomeruli in the specimen for light and fluorescence microscopy was counted by kidney pathologists who did not have procedural information.

Results: The proportion of fellows using the SIGN method was significantly higher than that of specialists (56.9% and 27.7%, respectively, P = 0.001). The median age of subjects in the SIGN group (58 years old) was younger than that of subjects in the standard technique group (64 years old) (P = 0.009). There was no significant difference between the two groups in gender, BMI, clinical diagnosis, kidney depth, kidney volume, eGFR, or hemoglobin level. The median puncture time in the SIGN group (2 min, IQR: 1–3 min) was significantly shorter than that in the standard technique group (3 min, IQR: 2–4 min) (P < 0.001). The number of glomeruli obtained in the SIGN group (29 ± 15) was significantly larger than that in the standard technique group (24 ± 12) (P = 0.008). The prevalence of major complications in the SIGN group (1.2%) was similar to that in the standard technique group (2.1%) (P = 1.0). Logistic regression analysis with adjustment for age, gender, BMI, kidney depth, kidney volume, and the operator's experience showed that the use of the SIGN technique was independently associated with the puncture time ≤ 2 min (odds ratio: 5.84, 95% CI 3.0–11.4). In addition, multiple linear regression analysis with adjustment for age, gender, BMI, number of punctures, use of an 11 mm stroke biopsy gun, kidney depth, kidney volume, and operator's experience showed use of SIGN method was independently associated with a significantly larger number of glomeruli to be obtained (P = 0.015).

Conclusion: Use of the SIGN technique reduces the procedure time and enables adequate biopsy tissue to be obtained with complication rates comparable to those of the standard technique regardless of the operator's experience. Since the biopsy procedures in the current study were performed by multiple nephrologists, including fellows, the SIGN technique can be applied in a nephrology training program and can be used as the standard biopsy procedure.

#2813
INCREASED RISK OF CARDIOVASCULAR DISEASE PRECEDING DIAGNOSIS OF INCIDENT ANCA-ASSOCIATED VASCULITIS: A DANISH NATIONWIDE STUDY

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Background and Aims: ANCA-associated vasculitis (AAV) is associated with an increased risk of cardiovascular disease (CVD). The risk of CVD seems to be increased shortly after initial diagnosis as well as in the long-term setting. However, no studies have addressed the risk of CVD in the period preceding an AAV diagnosis. Since the diagnosis of AAV often is associated with a substantial diagnostic delay, we hypothesize that patients with AAV consistently are at an increased risk of developing CVD already before they even are diagnosed with AAV.

Method: Using a nested case-control framework, patients with AAV were identified through the Danish Nationwide Registries from 1996-2021 and matched 1:3 with age- and sex-matched controls without AAV. Each control was assigned the same index date (date of AAV-diagnosis) as their corresponding case. Conditional logistic regression was used to compute age, sex and comorbidity adjusted Hazard Ratios (HRs) for major adverse cardiovascular events (MACE), ischemic heart disease, heart failure, venous thromboembolism, atrial fibrillation, ischemic stroke, pericarditis, and ventricular arrhythmias/ICD-implantation/cardiac arrest (VA/ICD/CA) within 12 months, 6 months, 3 months, 2 months and 1 month before the index date.

Results: A total of 2371 patients with AAV (median age: 63 yrs, 53.7% male) were matched with 7113 controls. In patients with AAV, 10.33% had a cardiovascular outcome within 12 months preceding diagnosis as compared to 3.84% of controls (HR 3.05 [95% CI, 2.48–3.75]). The associated risk of cardiovascular outcomes was similarly increased in the temporal proximity of the diagnosis, with the highest HR at 1 month prior to index date (HR 10.73 [95% CI, 7.05–16.32], Fig. 1). In individual analysis, a significantly higher HR was observed for all outcomes (excluding VA/ICD/CA), Fig. 2.

Conclusion: AAV disease is associated with an increased risk of CVD in the months preceding diagnosis, which underlines the importance of early clinical vigilance toward CVD starting in the diagnostic phase of AAV.
Figure 1: Conditional logistic regression of the association between AAV and having any cardiovascular outcome in close proximity to AAV diagnosis. Any cardiovascular outcome was defined as having either ischemic heart disease, acute myocardial infarction/percutaneous coronary intervention/coronary-artery bypass graft surgery, coronary angiogram, heart failure, venous thromboembolism, atrial fibrillation, ischemic stroke, pericarditis, VA/ICD/CA, or any combination thereof. HRs were adjusted for age, sex, chronic kidney disease, hypertension, hyperlipidemia, peripheral artery disease, diabetes, chronic obstructive pulmonary disease, malignancies, chronic liver disease and a previous history of cardiovascular disease.

Figure 2: Logarithmic radar chart of cardiovascular outcomes expressed as HRs of the association between AAV, and cardiovascular outcomes compared to age- and sex-matched controls preceding AAV diagnosis. HRs are adjusted for age, sex, and comorbidities. HRs of pericarditis and venous thromboembolism are not available at 1 month preceding index date, due to no events in the control group. MI, myocardial infarction, PCI, Percutaneous coronary intervention; CAGB, Coronary artery bypass graft surgery, VA/ICD/CA, ventricular arrhythmia and/or implantable cardioverter-defibrillator and/or in-hospital cardiac arrest with subsequent recirculation.
#4706
THERAPEUTIC AND PROGNOSTIC IMPACT OF KIDNEY BIOPSY FINDINGS IN PATIENTS AGED 80 YEARS AND OLDER: A MULTICENTER RETROSPECTIVE COHORT STUDY (KB-OLD)
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Lille University, Lille University Hospital Center, Nephrology, France

Background and Aims: The great phenotypic heterogeneity in the presentation of kidney diseases makes the diagnostic strategy all the more complex in the elderly. While kidney biopsy should play a pivotal role, its non-negligible risk of bleeding complications (2-5% in the general population) justifies a certain reluctance to its application in the elderly. To date, however, there is little data on the benefit-risk ratio of kidney biopsy in the elderly. Most of these studies have focused on a relatively young population (60-70 years old) and on a limited number of patients. Concerning patients aged 80 years and older, very few studies have described the real therapeutic influence of kidney biopsy findings with regard to the rate of complications. Moreover, none of these studies have evaluated the long-term prognostic impact of therapeutic changes induced by the results of the kidney biopsy. The main objectives of this study are to describe the indications, diagnoses, complication rate, therapeutic influence and the prognostic impact of a change in therapeutic management after native kidney biopsies performed in patients aged 80 years and older.

Method: The KB-Old study (Kidney Biopsy for Old) is a retrospective multicenter cohort that consecutively included all patients aged 80 years and older who underwent percutaneous native kidney biopsy in 17 centers in the northern region of France, between 2010 and 2020. Clinical, biological and anatomopathological data as well as post-biopsy follow-up (therapeutic strategy, occurrence of complications) were collected from medical records. All pathology examinations were analyzed centrally by a team of experienced nephropathologists. Events of death or kidney failure were identified by specific registry cross-linking. To analyze the prognostic impact of therapeutic management following kidney biopsy (either initiation of a specific treatment or simple nephroprotection) on the risk of kidney failure and death, we performed Cox models weighted by propensity score (Inverse Probability of Treatment Weighting - IPTW-) in the population potentially eligible for treatment (exclusion of diseases without specific treatment). The areas under Kaplan Meier curves were calculated up to 6 years of follow-up (Restricted Mean Survival Time - RMST) and compared according to the initiation of a specific treatment after the kidney biopsy. This study was approved by Institutional Review Board (#AUG-20-707).

Results: Overall, the cohort included 453 patients (54% men, median age 83 years), half of whom underwent biopsy in the context of acute kidney injury (median serum creatinine level 3.0 mg/dl). The main diagnoses were nephroangiosclerosis (15%), renal involvement of hematological malignancies (13%), acute tubulointerstitial nephritis (12%) and vasculitis (10%). The complication rate was approximately 10%, with only 2.8% of serious complications requiring therapeutic intervention (mostly transfusion). The kidney biopsy identified a disease potentially accessible to a specific treatment in 73% of cases. After exclusion of patients with ineligible diseases, a specific treatment was initiated in about one out of two cases (163/332, 49%). After weighting on propensity score, the two treatment groups were globally balanced. A beneficial effect of treatment on dialysis-free survival was observed (HR = 0.51 [0.28-0.92], p = 0.02), without any major influence on mortality (Figure 1). Over a 6-year follow-up period, there was a gain in dialysis-free survival in the treated group estimated by the delta RMST at +10.46 months [3.39 - 17.54] compared with the untreated group (p = 0.004), with no difference in overall life expectancy.

Conclusion: To the best of our knowledge, this is the largest multicenter cohort of patients aged 80 years and over who have undergone kidney biopsy. It seems to confirm the interest and safety of this examination for specific indications, and a potentially important benefit on the prognosis when it leads to an adapted therapeutic management.

Figure 1: Dialysis-free survival and mortality by treatment group (weighted Kaplan Meier curves).
#3618

CLINICAL SIGNIFICANCE OF MILD ABNORMALITIES IN GLOMERULAR FILTRATION BARRIER (GBM) DIAGNOSED BY RENAL BIOPSY

Julee You and Ho Jun Chin

1Seoul National University Bundang Hospital, Seongnam-si, Rep. of South Korea and 2Seoul National University College of Medicine, Seoul, Rep. of South Korea

Background and Aims: The well-known GBM abnormalities without immunological reaction are Alport syndrome (ALPORT) and thin basement membrane disease (TMD). Two diseases occasionally share common genetic abnormalities, although, clinical outcomes are worse in ALPORT. Sometimes, there are also mild abnormalities of GBM unable to be classified into ALPORT or TMD without any immunological or hemodynamical abnormalities in the kidney. We compared clinical and pathologic findings among ALPORT, TMD, and GBM abnormalities not classified (GBM NOS) diagnosed by renal biopsy.

Method: Among 18,134 adult patients who underwent kidney biopsy from 1979 to 2018 in 17 hospitals in Korea (number of IRB: B1707/408-106), we selected patients with ALPORT, TMD, or GBM NOS diagnosed by renal biopsy. GBM NOS was defined as any abnormality of GBM structure of lamellation, thickness, and integrity by electron microscopic examination, which are not able to classify into specific pathologic diagnosis. We excluded ALPORT, TMD, and GBM NOS combined to the other pathologic diagnosis or showing electron dense deposit. We collected clinicopathologic findings at renal biopsy and the last visit to clinics and incidences of mortality and end stage renal disease during follow-up period.

Results: There were 179 (0.99%) TMDs, 33 (0.18%) ALPORTs, and 8 (0.04%) GBM NOSs among all patients. The clinicopathologic findings were presented in Table 1. Age and gender proportion at renal biopsy were not different among groups. Patients with ALPORT showed the lowest level of estimated glomerular filtration rate by MDRD equation (eGFR) ($p<0.001$) and the highest level of urine protein to creatinine ratio (UPCR) ($p<0.001$). Patients with GBM NOS had similar levels of eGFR and UPCR compared to patients with TMD at renal biopsy. Under microscopic examinations, segmental sclerosis in glomeruli was most prevalent in patients with ALPORT compared to patients with the other disease. Global sclerosis in glomeruli was prevalent in patients with ALPORT and GBM NOS. Other glomerular changes, such as cellular infiltration and matrix change in mesangium, and ischemic glomerular change, were not different among groups. Patients with GBM NOS showed more severe change of interstitial fibrosis and tubular atrophy compared to patients with TMD ($p<0.001$). During 97.9 ± 61.8 months of follow-up period, one (3.0%) patient was dead and 10 (30.3%) patients must have renal replacement therapy (RRT) among patients with ALPORT. The other patients with GBM NOS or TMD had survived and did not need RRT.

Conclusion: Clinical findings of GBM NOS were similar to TMD, although pathologic changes of glomerular global sclerosis and tubulo-interstitial changes are more severe in GBM NOS compared to TMD. GBM changes in GBM NOS might be related to tubulo-interstitial damages which needs to be defined with more studies.
# RISK FACTORS FOR VENOUS AND ARTERIAL THROMBOEMBOLIC COMPLICATIONS IN NEPHROTIC SYNDROME: A COHORT STUDY

Sarah Kelldal, Bawer Tofig, Anne-Mette Hvast, Erik Grove, Christian Fynbo Christiansen and Henrik Birn

Background and Aims: Venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) are serious complications of nephrotic syndrome (NS). Studies are needed to identify patients at high risk for VTE and ATE. We aimed to describe patient-related risk factors for VTE and ATE in a mixed population of nephrotic patients.

Method: This multicentre cohort study included adult NS patients with plasma albumin <30 g/l and urine albumin-creatinine ratio (uACR) >2,200 mg/g, who were hospitalized or followed at an outpatient clinic in the Central Denmark Region between 2014-2018. Using computerized data extraction from medical files, patients were identified and followed until dialysis, transplantation, or end of study. We recorded comorbidities, family history, renal parameters and, histological diagnosis at index time as well as, renal parameters and medication at the time of VTE/ATE event. Categorical and continues data were compared using a risk difference and mean difference respectively. The incidence of event is presented as incidence rate.

Results: Among 531 included patients, 22 patients had their first VTE and 46 their first ATE within the first observation year (median time to event VTE 0.8 vs. ATE 0.9 years). Incidence rates were 11 per 1000 person-years (95% CI: 7-17) for VTE and 24 (95% CI: 18-32) for ATE. Plasma-albumin levels (27 g/l) were identical in the VTE and ATE group at event time, but eGFR was lower (Table 1), and uACR was higher in the ATE group (median uACR; VTE 1055 mg/g vs. ATE 2752 mg/g). Hypercholesterolemia was more prevalent among patients with VTE, and they were more often on corticosteroids.
<table>
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<tr>
<th></th>
<th>Baseline (N = 531)</th>
<th>No event (n = 463)</th>
<th>Events (n = 68)</th>
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<td></td>
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<td>Venuous (n = 22)</td>
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<td>Males, n (%)</td>
<td>321 (60)</td>
<td>275 (59)</td>
<td>46 (68)</td>
<td>13 (59)</td>
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<td>Age, yr. median (IQR)</td>
<td>63 (50-73)</td>
<td>63 (48-73)</td>
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<td>67 (60-71)</td>
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<td>114 (21)</td>
<td>96 (21)</td>
<td>18 (26)</td>
<td>6 (27)</td>
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<td>&gt; 7/14 alcohol units/week, n (%)</td>
<td>49 (9)</td>
<td>36 (8)</td>
<td>13 (19)</td>
<td>4 (18)</td>
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<td>Comorbidities, n (%)</td>
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<tr>
<td>Diabetes</td>
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<td>Previous ATE</td>
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<td>CHADS2-VASC score ≥ 3, n (%)</td>
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<td>147 (32)</td>
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<td>Renal biopsy, n (%)</td>
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<td>Proliferative glomerulonephritis</td>
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<td>32 (89)</td>
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<td>147 (88)</td>
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<td>223 (42)</td>
<td>186 (83)</td>
<td>37 (17)</td>
<td>8 (3.6)</td>
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<td>eGFR (mL/min/1.73m²)</td>
<td>43 (40-46)</td>
<td>44 (41-47)</td>
<td>40 (32-47)</td>
<td>48 (32-64)</td>
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<td>Medication, n (%)</td>
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<td>Anticoagulant drugs</td>
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<td>106 (23)</td>
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<td>Corticosteroids</td>
<td>48 (9)</td>
<td>44 (10)</td>
<td>4 (6)</td>
<td>6 (27)</td>
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</table>

IQR Interquartile range

*Medication data were collected baseline and 21 days prior to VTE or ATE.
than patients with ATE. Diabetes, hypertension, and heart failure was more prevalent at baseline in patients with ATE resulting in an increased CHADS2-VASC score. Mortality was higher among patients with ATE (83%) than VTE patients (32%).

Conclusion: Patients with NS have a high risk of VTE and ATE. Corticosteroid use was more common among patients with VTE than ATE. ATE was associated with a higher uACR, higher CHADS2-VASC score, and increased mortality compared to patients with VTE.

#3480

PATIENT REPORTED OUTCOMES IN GLOMERULAR DISEASES: A NEW MODEL OF CARE BASED ON MEDICAL CARE, TELEHEALTH AND NURSE-COACHING: THE HUMAN-C PROJECT

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Background and Aims: Glomerular diseases (GD) affect young and working-age people. Questionnaires for assessing health-related quality of life in GD patients are scarce. The implementation of telehealth and nurse coaching support (Humanization Coaching Project: Human-C Project) in a multidisciplinary team may influence the patient-reported-outcomes (PROs), patient-reported experiences (PREMs) and could open new perspectives on these patients, which should be taken into account. We report the results of PROMs and PREMs after the introduction of the Human-C Project. The objective of the study was to describe PROMs and PREMs in a glomerular disease unit of a third-level hospital after the implementation of the Human-C Project.

Method: Telehealth was implemented in 2019, and nurse-coaching support in 2021. The survey was online and anonymous to improve the accuracy of self-reports. The questionnaire consists of 15 items (based on Promis-29 (3 questions), SF-36 (2 questions) scales, and 10 questions previously obtained through personal interviews during nurse-coaching support). The questionnaire was sent to 233 patients included in our telehealth program.

Results: 89 (38%) patients responded to the questionnaire. The mean age (SD) was 46 (14). The questionnaire was stratified into 6 domains and the percentage of responses preference were: employment status (100%), knowledge of the disease (94%), social function (96%), psychological health (86%), type and periodicity of the medical appointments (84%), and therapy preferences (80%). 87% of the patients are of working age, 16% consider that they know little or nothing about their disease, 20% know little or do not know its severity, 53% reported fatigue, 50% their sleep quality is regular or very poor, 40% are not satisfied with their work performance (including at home), 34% reported poor health status; 34% reduced their activity (at work and home) due to emotional problems, 19% do not ask all questions or do not come up with clear information during the appointment, 80% report taking the medication correctly, 80% know what each pill is for, 35% want to retire and or reduce the number of tablets even adding intravenous medication, 53% develop anxiety about the disease, 72% consider that telehealth helps to reconcile work schedule and illness and helps to clarify doubts and in remission period 67% prefer to have an appointment as long as 6-9 months if they can directly access their health team if necessary.

Conclusion: A relevant percentage of GD patients reported health-related quality-of-life problems. Telehealth and nurse coaching support are opening specific perspectives of care in GD patients, with important implications for the health system.

#5344

EPIDEMIOLOGY OF GLOMERULAR DISEASES IN THE PRE- AND POST-COVID-19 ERA IN CENTRAL QUEENSLAND, AUSTRALIA

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Background and Aims: Development of new onset and recurrent glomerular diseases (GD) following Covid-19 infection or vaccination are increasingly reported in the literature with various proposed pathogenic mechanisms. Australia reported its first case of Covid-19 in January 2020. Currently in Australia, there has been 11.3 million cases of Covid-19 infection and 98% of individuals aged ≥ 16 years received at least one dose of Covid-19 vaccination. However, there are no studies in Australia that evaluate the risk of GD after Covid-19 infection or vaccination. We compared kidney biopsy results pre- (01/01/2017-31/12/2019) and post- (01/01/2020-31/12/2022) Covid-19 era to assess for potential changes in the epidemiology of kidney biopsy-proven GD.

Method: In this single-centred retrospective study, all renal biopsies performed in Central Queensland (CQ) between 01/01/2017 and 31/12/2022 were reviewed. This pilot study is a subset of Queensland Kidney Biopsy Registry which has captured all renal biopsies of adults residing in CQ with a regional population of 220,912 with a land area of 497,714 km².

Results: Eighty-seven percent of the CQ population received at least one dose of Covid-19 vaccination and 53,234 cases of Covid-19 infection were confirmed by rapid antigen test (RAT) as of the end of January 2023. The total number of kidney biopsies performed pre- and post-Covid-19 era were 47 vs 58, respectively, and the majority were native kidney biopsies (94% vs 95%) in CQ whereby the number of nephrologists in the respective catchment areas and access availability to kidney biopsies remained similar. The mean age of patients was 55.3 years (standard deviation, SD 16.4) vs 55.6 years (SD 15.6) and the majority were males (70% vs 62%) and Caucasians (77% vs 76%). No case of recurrent GD was diagnosed in pre-Covid-19 era whereas 5 cases of recurrent GD (2 membranous nephropathy, 1 minimal change disease, 1 lupus nephritis class III-IV, and 1 ANCA associated vasculitides (AAV)) in post-Covid-19 era, p = 0.025. The commonest cause of GD in the pre-Covid-19 era was IgA nephropathy (IgAN) whereas diabetic nephropathy and AAV was the most common GD during the post-Covid-19 era. The incidence of IgAN decreased from 12 cases (18.1 cases/million person years) in pre-Covid-19 era to 3 cases (4.5 cases/million person years) in the post-Covid-19 era (incidence rate ratio, IRR of 0.25, 95% CI 0.05-0.93, p = 0.020). The incidence of diabetic nephropathy increased from 1 case (1.5 cases million person years) during the three years pre-Covid-19 era to 13 cases (19.6 cases/million person years) for three years post-Covid-19 era (IRR of 3.4, 95% CI 0.86-18.85, p = 0.052). In the post-Covid-19 era, the mean age of patients with diabetic nephropathy was 51.2 years (SD 11.9) and the majority were indigenous Australian (n = 8, 62%) with poor diabetic control. They had kidney biopsies for nephrotic range proteinuria with or without acute kidney injury and haematuria. The incidence of AAV increased from 3 cases (4.5 cases/million person years) during the three years pre-Covid-19 era to 10 cases (15.1 cases/million person years) for three years post-Covid-19 era (IRR of 3.4, 95% CI 0.86-18.85, p = 0.052). In the post-Covid-19 era, the mean age of patients with AAV was 68.4 years (SD 16.1) with Caucasian (n = 10, 100%). PR3-AAV (n = 5) and MPO-AAV (n = 5) are equally prevalent, and 3 patients (30%) had comorbid pulmonary complications. Three cases of AAV each occurred in the first and second years and 4 cases in the third year during the post-Covid-19 era. There was no increase in the incidence rate for other types of glomerular diseases.

Conclusion: Our findings suggest the frequency of incident and recurrent GD may vary with the emergence of Covid-19 and steps taken to minimise viral complications that include primary preventative measures via vaccination. Larger epidemiological studies are required to better elucidate the risk of Covid-19 infection and vaccination in relation to GD.

#2664

CHRONIC MYELOMONOCYTIC LEUKEMIA (CMML) PATIENTS WITH LYSOZYME NEPHRAPHY AND CMML: INFILTRATION DISPLAY MARKERS OF SEVERE DISEASE

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**Background and Aims:** Chronic myelomonocytic leukemia (CMML) is a hematologic disorder which is an overlap syndrome between myelodysplastic syndromes, and myeloproliferative neoplasms, and can be associated with autoimmune and inflammatory diseases. The objective of this study was to describe kidney involvement in CMML patients, their treatments, and outcomes.

**Method:** We conducted a French and American multicenter retrospective observational study in fifteen centers, identifying CMML patients with acute kidney injury (AKI), chronic kidney disease (CKD), and urine abnormalities.

**Results:** Sixteen patients (males, n = 14, median age 76.5 [71.9-83]) developed a kidney disease 6 months [1.6-25.6] after the diagnosis of CMML. Median urinary protein to creatinine ratio was 2 g/g [1.5-3.4], and median serum creatinine was 2.26 mg/dL [1.46-2.68]. Fourteen patients (87.5%) underwent a kidney biopsy. The two main renal diagnoses were either a lysozyme nephropathy (n = 9, 56%), or a renal infiltration by the CMML (n = 6, 37.5%). Histological findings showed lesions of acute tubular injury with focal tubular epithelial necrosis (n = 4), a vacuolization of the epithelial cells of the proximal tubules (n = 7), and an inflammatory infiltrate with mostly mononuclear myeloid cells (n = 9). Ten patients received a new treatment following the CMML-associated kidney injury. The effect of CMML treatment on kidney injury could be assessed in 10 patients, and renal function evolution was heterogeneous. After a median follow-up of 15 months [9.9-34.9], 4 patients had CKD stage 3, 4 CKD stage 4, 1 an end-stage kidney disease. Two patients evolved to an acute myeloid leukemia (AML), and 5 died. Compared with 116 CMML controls, patients who had a kidney involvement had a higher monocytes count (p<0.001), had more CMML-1 (p = 0.005), were more susceptible to develop an AML (p = 0.02), and were more eligible to receive a specific hematologic treatment, with hydroxyurea, or hypomethylating agents (p<0.001), but no survival difference was seen between the two groups (p = 0.6978).

**Conclusion:** In this largest published cohort of CMML patients with a kidney injury, the two most frequent renal complications were lysozyme-induced nephropathy, and renal infiltration by the CMML. The development of a kidney injury during CMML appears to worsen the patient prognosis.

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**#4789**

**ROUTINE CARDIAC BIOMARKERS FOR THE PREDICTION OF INCIDENT MAJOR ADVERSE CARDIAC EVENTS IN PATIENTS WITH GLOMERULONEPHRITIS: A REAL-WORLD ANALYSIS**

Elin Davies1, Garry McDowell1,2, Benjamin Buckley4, Philip Austin5, Gregory Lip1,6 and Anirudh Rao1,3

1Royal Liverpool University Hospital, Liverpool, United Kingdom, 2Liverpool John Moores University, Pharmacy and Biomolecular Sciences, Liverpool, United Kingdom, 3University of Liverpool, Liverpool Centre for Cardiovascular Science, Liverpool, United Kingdom, 4Liverpool John Moores University, School of Sport and Exercise Science, Liverpool, United Kingdom, 5TriNetX, London, United Kingdom and 6Liverpool Heart and Chest Hospital, Liverpool, United Kingdom

**Background and Aims:** Patients with glomerulonephritis (GN) frequently have both proteinuria and decreased kidney function, and together with immunosuppressive therapies used to treat it could lend these patients to a high risk for cardiovascular disease (CVD). We aimed to investigate the prognostic significance of routine cardiac biomarkers (troponin) in predicting incident Major Adverse Cardiovascular Events (MACE) within 5 years of diagnosis of GN.

**Method:** A retrospective cohort study was performed using electronic medical records from a global federated research network from the US (TriNetX). The TriNetX network was searched on 31st January 2023. Data censoring for MACE was invoked prior to the index event of GN. Cardiac biomarkers were the first reported result within 3 months of diagnosis of GN. Cohorts were grouped according to biomarker-specific thresholds and 1:1 propensity-score matched for age, gender, and co-morbidities (hypertension, diabetes mellitus and smoking status). Logistical regression produced odds ratios with 95%CI for 5-year incident MACE. MACE was defined, a priori, as a composite of ischaemic heart disease, angina pectoris, acute myocardial infarction, heart failure, AF, stroke, and all-cause mortality. The analysis was carried conducted by all-cause GN and individual primary GNs: IgA nephropathy (IgAN), membranous nephropathy (MN), focal segmental glomerulosclerosis (FSGS), and minimal change disease (MCD). All statistical analysis was performed on the TriNetX online platform.

**Results:** The results are shown below for all-cause GN. Results that reached statistical significance (p<0.05) are shown. The risk of MACE and its components was consistent across the individual GN sub-types IgAN (N = 1802), MN (N = 1674), FSGS (N = 1844) and MCD (N = 2014).

**Conclusion:** Routinely available cardiac biomarkers can predict incident MACE and outcomes in patients with glomerulonephritis. The results suggest the clinical need for CV mortality and morbidity risk profiling in patients with glomerular disease using a combination of clinical and laboratory variables.
Table 1: Three commonest diagnoses made on native kidney biopsy, by indication.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Diagnosis 1</th>
<th>Diagnosis 2</th>
<th>Diagnosis 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI query cause</td>
<td>ATIN (18.5%)</td>
<td>Microscopic polyangiitis (11.4%)</td>
<td>IgAN (8.0%)</td>
</tr>
<tr>
<td>CKD query cause</td>
<td>IgAN (20.7%)</td>
<td>ATIN (8.9%)</td>
<td>Diabetic nephropathy in type II diabetes (7.2%).</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>MGN (24.7%)</td>
<td>Minimal change nephropathy (20.5%)</td>
<td>Primary focal segmental glomerulosclerosis (13.7%).</td>
</tr>
</tbody>
</table>

Method: All 9 adult nephrology centres covering a population of over 5 million people report complete data on all kidney biopsies undertaken to the SRR. This includes indication, age, gender and diagnosis. The SRR collects requirement for KRT and death. Risk of KRT at 6 months, 1 year and 2 years from date of first native kidney biopsy in patients with IgAN, MGN or ATIN were recorded.

Results: 5095 native kidney biopsies undertaken in 4702 patients between 01/01/2014 and 31/12/2021 were included. This averages 117.1 biopsies per million population / year. 54.7% were male with mean age 57.2 (SD 17.2) years. 98.2% of kidney biopsies were deemed adequate for diagnosis. Data completeness is over 99%. The commonest indications for native kidney biopsy were acute kidney injury query cause (AKI - 30.0%), chronically reduced eGFR (CKD) (28.1%) and nephrotic syndrome (19.7%). Overall, the commonest diagnoses made were: IgAN nephropathy (IgAN 13.1%), tubulointerstitial nephritis (ATIN 8.5%) and membranous nephropathy (MGN 7.2%). Table 1 shows diagnoses made by biopsy indication.

Conclusion: In a complete national dataset, AKI is the commonest indication for native kidney biopsy and most commonly leads to a diagnosis of ATIN. IgAN remains the commonest primary glomerulopathy diagnosed on kidney biopsy, with MGN being the most likely diagnosis in patients biopsied for indication of nephrotic syndrome. Kidney and patient survival varies at 2 years depending on diagnosis. Table 2 shows that at 2 years the mortality rate (Fig. 1) is highest in patients with MGN (11.4%) and risk of KRT highest in patients with IgAN (10.2%).

Table 2: Overall outcomes for commonest diagnoses made on kidney biopsy: number starting KRT or dying within defined time period.

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Outcome at 6 months, biopsies from 2014-2021</th>
<th>Outcome at 1 year, biopsies from 2014-2020</th>
<th>Outcome at 2 years, biopsies from 2014-2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA nephropathy</td>
<td>Total: 632</td>
<td>Total: 570</td>
<td>Total: 541</td>
</tr>
<tr>
<td></td>
<td>KRT: 35 (5.5%)</td>
<td>KRT: 42 (7.4%)</td>
<td>KRT: 55 (10.2%)</td>
</tr>
<tr>
<td></td>
<td>Death: 29 (4.6%)</td>
<td>Death: 33 (5.8%)</td>
<td>Death: 45 (8.3%)</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
<td>Total: 370</td>
<td>Total: 327</td>
<td>Total: 298</td>
</tr>
<tr>
<td></td>
<td>KRT: 14 (3.8%)</td>
<td>KRT: 13 (4.0%)</td>
<td>KRT: 16 (5.4%)</td>
</tr>
<tr>
<td></td>
<td>Death: 16 (4.3%)</td>
<td>Death: 30 (9.2%)</td>
<td>Death: 34 (11.4%)</td>
</tr>
<tr>
<td>Tubulointerstitial nephritis</td>
<td>Total: 507</td>
<td>Total: 432</td>
<td>Total: 372</td>
</tr>
<tr>
<td></td>
<td>KRT: 14 (2.8%)</td>
<td>KRT: 20 (4.6%)</td>
<td>KRT: 24 (6.5%)</td>
</tr>
<tr>
<td></td>
<td>Death: 16 (3.2%)</td>
<td>Death: 18 (4.2%)</td>
<td>Death: 33 (8.9%)</td>
</tr>
</tbody>
</table>
IN LANCASHIRE, UK
ASSOCIATED VASCULITIS AMONGST INDO-ASIAN PATIENTS
INCIDENCE AND CLINICAL PRESENTATION OF ANCA

Primary MN includes forms of MN in which there is a humoral autoimmune response to a normal podocyte antigen in the absence of secondary features or etiologies of disease. Antigens implicated in primary MN include PLA2R, thrombospondin type-1 domain-containing 7A (THSD7A), neural epidermal growth factor-like 1 (NEIL1), semaphorin 3B (Sema3B), the serine protease high-temperature requirement A1 (HTRA1), protocadherin 7 (PCDH7), and others. PLA2R associated MN is most common MN among primary MN. Nowadays, a significant number of newer antigens implicating MN are being discovered. Research is ongoing for a better understanding of the role of these antigens in pathophysiology, and targeted therapeutic implications in future if possible. We aim to analyze the etiological spectrum associated with different antigens in patients with Membranous Nephropathy. We assessed the renal tissue staining of autoantigens PLA2R, THSD7A, and NEIL-1 in patients with biopsy-proven Membranous Nephropathy.

Method: This was a single center ambispective observational study. The study was performed up till September 2022 for prospective data, and retrospective data from January 2018 to March 2021 was retrieved from the medical records department of the institute. The study included patients with biopsy-proven Membranous Nephropathy (Primary and secondary). The primary outcome was to study the etiological spectrum of Membranous Nephropathy.

Results: A total of 90 patients were included in the study of membranous nephropathy over the period of 4 years. 72 cases had primary MN whereas 18 cases had secondary MN. The mean age was 42.01 ± 14.6 years. Among 18 cases of Secondary MN, the majority of the cases were of lupus nephritis 14 (78%), while other etiologies of secondary MN were malignancy related (11%), rheumatoid arthritis (5.5%) and HCV (5.5%). PLA2R renal tissue positivity was found in 8 (11.1%) cases of primary MN, whereas it was found in 4 (22.2%) cases of Secondary MN. The THSD7A was found in 4 (5.6%) cases of primary MN. One patient of MN was dual PLA2R and NEIL1 positive. Two cases of MN were dual PLA2R and THSD7A positive. Renal tissue staining for NEIL-1 was found in 8 (11.1%) cases of primary MN whereas it was found in 1 (5.6%) case of secondary MN. In terms of clinical presentation, proteinuria is the most common clinical finding present in nearly all the patients (80%). Most of the cases with nephrotic syndrome (60%) belonged to primary MN.

Conclusion: PLA2R is the most common etiology of Primary membranous nephropathy. None of the antigens was exclusive to primary membranous nephropathy. None of the antigens was exclusive to Primary membranous nephropathy. The antigens were also positive in the secondary forms of MN.

Background and Aims: ANCA associated vasculitis (AAV) is a rare autoimmune condition that is predominately seen in white Caucasian populations [1]. Across the UK, Europe and the USA, the prevalence of AAV is between 4.6 - 18.4 per 100,000. Studies have shown significant geographical differences in the presentation and phenotype of AAV. PR3 positivity and granulomatosis with polyangiitis (GPA) is more common in Northern European countries at higher latitudes. In contrast, MPO positivity is seen more frequently in Japanese, Chinese and Southern European populations [1]. Comparatively, few studies have looked at the incidence, phenotype and outcomes in ethnic minority patients in particular Indo-Asian populations.

Method: We completed a retrospective cohort study of patients with AAV from a central referral centre in Lancashire, UK between December 2010 and December 2022. Patients with a diagnosis of AAV according to the Chapel Hill consensus conference and who belonged to the following ethnic groups; ‘Indian, British Indian, Pakistani, British Pakistani, Asian or Asian British,’ were included. Using data from the 2021 census, available from the Office of National Statistics, denominator populations were obtained [2]. Patients ethnic group were determined by self-reported ethnicity records on hospital e-health records or via GP summary care records. Ethical approval was obtained (IRAS 257174).

Results: Using 2021 census data, the total population of Lancashire (Fig. 1), aged >18 years old was 1,149,626. Of this population, the majority identified as white (1,059,000) and the second most common ethnic group was Asian / Asian British (74,523). Black/African/Caribbean/Black British made up <1% of the population and mixed/multiple ethnic groups and other ethnic groups made up just over 1%. Eighteen Indo-Asian patients with newly diagnosed AAV were identified. The mean age was 46 ±16.7 yrs, which is younger than our cohort of white patients who had a mean age of 65.1 ± 14.6 yrs. There was an equal gender split, the majority were PR3 positive (n = 12, 67%) and 6 patients had MPO positive AAV. Nine patients had renal involvement, with only 2 having renal limited disease and 1 requiring dialysis at presentation. Over half of the patients (n = 11, 61%) had ENT involvement. The crude incidence of AAV in Indo-Asian patients in Lancashire was 20.1 per million person years (95% CI 10.7, 28.5). This is higher than that reported in other areas of the UK [3]. When compared to age and gender matched white patients, white patients had more renal involvement (89.5% Vs 50%, P = 0.01) and more renal limited disease (31.6% Vs 11.1% P = 0.13). Pulmonary involvement was similar between the ethnic groups whereas ENT involvement was more prevalent in Indo-Asian patients (61.1% Vs 26.3%, P = 0.03).

Conclusion: Our findings demonstrate that whilst the crude incidence of AAV is lower in Indo-Asian populations compared to white Caucasians, there is a significantly high incidence rate in the Lancashire area, which is greater than in other areas of the UK. Pearce et al. reported an incidence of 10.6 per million person years in Nottingham which was almost half that seen in our cohort [3]. Our Indo-Asian patients were on average younger and had less renal involvement compared to our cohort white patients. This contrasts some studies which report Indo-Asian populations to have more PR3 positivity and higher rates of renal involvement [1]. This may reflect an under diagnosis of extra renal disease and non-renal phenotypes in Indian subcontinent populations. There remains a gap in our understanding as to the genetic role in the pathogenesis and clinical phenotype of AAV disease. Further research is needed to determine if the differences seen between ethnic minorities are due to genetic or environmental factors.
Background and Aims: While immunoglobulin A nephropathy (IgAN) has been shown to be associated with clinical and economic burden, the humanistic burden associated with IgAN is less understood. HONUS is a multi-national, cross-sectional survey study to evaluate the humanistic burden associated with rare kidney diseases, including IgAN, from the patient and caregiver perspectives in the US and Europe.

Method: The study recruited adult patients (≥18 years old) with their care-partners and parents/care-partners of youth (8-17 years old) with IgAN or focal segmental glomerulosclerosis (FSGS). Participants completed an online survey with questions on demographic and clinical characteristics, health-related quality of life (HRQoL) (ie, 12-Item Short Form Survey [SF-12]), anxiety and depression (ie, Generalized Anxiety Disorder Assessment [GAD-7], Patient Health Questionnaire [PHQ-9]), most burdensome symptoms, fear and uncertainty for the future, and disease impact on work productivity (ie, Work Productivity and Activity Impairment [WPAI]). The current analysis is based on information from adults with IgAN and their care-partners in the US before September 2022. Descriptive analyses were conducted, with continuous variables summarized using means, medians, and standard deviations (SD), and categorical variables summarized using frequency counts and percentages.

Results: A total of 96 pairs of adults with IgAN and their care-partners in the US were included in the analysis. The mean age of adult patients was 37.5 and the majority were Caucasian (86.5%) and female (53.1%). Median time since diagnosis was 5.6 years. More than half of patients (59.4%) were in chronic kidney disease stage 3 or 4, while 5.2% were in end-stage renal disease and had received a kidney transplant. Hypertension (31.3%), anemia (25.0%), and depression (18.8%) were the most common comorbidities. In terms of HRQoL, patient’s mean (SD) SF-12 physical and mental component scores (PCS, MCS) were reported at 46.9 (7.4) and 41.1 (9.1), respectively, reflecting worse HRQoL (lower score) than previously published US general population scores (PCS and MCS of 50 [10]). Moderate and severe anxiety was reported by 28.1% and 1.0% of patients, respectively; moderate, moderately severe, and severe depression was reported by 51.0%, 2.1% and 1.0% of patients, respectively. The most burdensome symptoms reported by patients were constipation (82.3%), lower back pain (79.2%), and bone or joint pain (77.1%). Based on a 4-week recall period, 25.0% of adult patients reported being ‘very much bothered’ or ‘extremely bothered’ by bone or joint pain (22.9% for lower back pain, 10.4% for constipation). Most patients (96.9%) reported feeling fear and uncertainty for the future due to their disease, of which 52.1% reported the frequency of fear and uncertainty to be ‘often’. Among employed patients (72.9%), percent absenteeism was reported in 6.9%, presenteeism in 27.1%, overall work productivity loss in 31.4%, and activity impairment in 36.2% because of IgAN-related reasons. Most paired care-partners (87.5%) were partners of patients, with a mean age of 39.5 years. The mean SF-12 PCS and MCS of care-partners were 50.4 and 43.6, respectively. Moderate anxiety was reported in 13.5% of care-partners, with none reporting severe anxiety; moderate and moderately severe depression was reported in 35.4% and 5.2% of care-partners, respectively. Almost all care-partners (99.0%) reported feeling fear and uncertainty for the future due to the disease of their cared ones, of which 39.6% reported the frequency of this worry to be ‘often’. Among employed care-partners (93.8%), 9.8% reported absenteeism, 27.3% reported presenteeism, 33.2% reported overall work productivity loss, and 31.9% reported activity impairment due to IgAN-related reasons.

Conclusion: Patients with IgAN experience impaired HRQoL, depression, anxiety, and poor productivity, compared to previously reported US general population estimates. This also impacts the HRQoL, in terms of mental components, and productivity of care-partners. Both patients with IgAN and their care-partners also report widespread fear and uncertainty for the future.
#5402
ASSOCIATION BETWEEN URINARY N-ACETYL-β-D-GLUCOSAMINIDASE AND BISPHENOL AND ITS SUBSTITUTE EXPOSURE IN TAIWANESE ADULTS

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Background and Aims: Urinary N-acetyl-β-D-glucosaminidase (NAG) is a sensitive and reliable indicator of renal damage, like proximal tubular cell injury. Bisphenol A (BPA), a known endocrine disruptor, or its substitute has been reported as a risk factor that caused kidney damage in experimental studies. We aimed to investigate the correlation between urinary NAG and Bisphenol and its Substitute Exposure in Taiwanese Adults.

Method: We collected urine samples including 271 adults (145 female and 126 men) from Taiwan Environmental Survey for Toxictants 2013, and analyzed for three urinary BPA, BPS and BPF by using ultraperformance liquid chromatography–tandem mass spectrometry. The bisphenol and their substitutes in the human urine samples were converted into daily intake (DI) values. We measured by the indicators of renal function, included urine creatinine (crea, mg/dL), microalbumin (mg/dL), NAG (IU/L), etc. We used logistic regression analysis to elucidate their correlations and adjustment for significant covariate.

Results: We found the median levels were 7.96 for BPA, 7.89 for BPF, and 1.96 (μg/L) for BPS, respectively, and yielded a median estimate daily intakes were 3.01 (BPA), 2.99 (BPF), and 0.76 (BPS) (ng/kg/day) in the Taiwanese adults. We found that the ratio of urinary NAG and creatinine (NAG/crea) was a significantly increased trend with exposure doses of BPA, BPF and BPS whereas no similar trend for ACR. After adjustment for age, sex, BMI and other covariate, we found that DI of BPA increased the risk of NAG/crea by 5.8 times (OR Adj: 5.8, p < 0.01, 2nd tertile) and 9.6 times (OR Adj: 9.6, p < 0.01, 3rd tertile).

Conclusion: Our findings supported that the exposure of bisphenol and its substitute may increase the risk of renal tubular injury. Further large and longitudinal studies are warranted.

#3269
EPIDEMIOLOGY OF PRIMARY FSGS INCLUDING CLUSTER ANALYSIS OVER A 20-YEAR PERIOD

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Background and Aims: Focal segmental glomerulosclerosis (FSGS) is one of the leading causes of nephrotic syndrome (NS) in adults. This epidemiological study describes a renal centre’s 20 year ‘real world’ experience of patients with primary FSGS including cluster analysis.

Method: This retrospective analysis was conducted on patients diagnosed with primary FSGS at a tertiary renal centre with a catchment population of 1.55 million, over 2 decades. Data collection included baseline demographics, laboratory results, immunosuppression (IS) and outcomes: Complete & partial remission, relapse, progression to renal replacement therapy (RRT) and mortality. A two-step cluster analysis was used to reveal groupings to aid prognostication and treatment decisions. Pre-specified cluster variables were: Serum albumin (sAlb), urine protein: creatinine ratio (uPCR) & estimated glomerular filtration rate (eGFR).

Results: 87 patients were identified with primary FSGS after exclusion of secondary causes. Mean age was 49.3 years, 60.9% male, 86.2% white with median eGFR 46 ml/min, uPCR 284 mg/mmol and sAlb 33 g/l (Table 1). Rates of partial and complete remission were 23% & 49.4% respectively. Progression to RRT occurred in 27.4%, death in 27.4%. Comparing those receiving IS vs not: sAlb was lower 23 g/L vs 40 g/L (p < 0.001), uPCR was higher 795 mg/mmol vs 318 mg/mmol (p < 0.001). The IS group was more likely to achieve complete remission (62% vs 40%, p = 0.041), but relapsed more 48.6% vs 22% (p < 0.027). There were no statistically significant differences between mortality or RRT. The 2-step cluster analysis separated the cohort into 3 clusters, see Fig. 1: Cluster 1 (n = 26) with ‘nephrotic range proteinuria’ mean sAlb 30 g/L, uPCR 778 mg/mmol and eGFR 72 ml/min; Cluster 2 (n = 43) with ‘non-nephrotic range proteinuria’, mean sAlb 39 g/L, uPCR 284 mg/mmol and eGFR 46 ml/min; Cluster 3 (n = 18) ‘NS’ sAlb 20 g/L, uPCR 1117 mg/mmol and eGFR 25 ml/min. IS use was comparable in the NS (cluster 3) and nephrotic range proteinuria (cluster 1) cohorts, but lower in cluster 2 (non-nephrotic range proteinuria) 77.8% & 69.2% vs 11.6% p < 0.001. Rates of complete remission were greatest in clusters 1 & 3 vs cluster 2: 57.7% & 86.7% vs 37.2% though this did not achieve statistical significance (p 0.067).

Conclusion: Although there have been several recent US & Asian reviews of primary FSGS, this study provides a review of the epidemiology of FSGS over a 20-year period in a predominantly white cohort in the UK. In general, the patients who received IS had lower sAlb and achieved remission more frequently. Although the aetiology of primary FSGS is unknown, it is hypothesised that it is due to an undiscovered circulating permeability factor. After the exclusion of secondary causes, KDIGO suggests only making the diagnosis in the presence of NS. Despite this the average sAlb in most epidemiological studies of primary FSGS have been above 30g/L. This is likely because of the inclusion of undiagnosed genetic or adaptive FSGS, but it may also be true that NS phenotype alone is too insensitive to diagnose primary ‘antibody driven’ FSGS. Our cluster analysis highlighted 3 potential FSGS phenotypes: A nephrotic cluster that clearly require IS; a cohort with preserved sAlb and non-nephrotic range proteinuria who will benefit from supportive care; lastly a cluster with heavy proteinuria but a sAlb > 30g/L. This group may still have antibody driven disease and thus benefit from immunosuppression and potentially genetic testing. The study received grant support from CSL Vifor.
Table 1:

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 87)</th>
<th>No IS (n = 50)</th>
<th>IS (n = 37)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years (+/- SD)</td>
<td>49.3 (+/-17.9)</td>
<td>46.7 (+/-17.0)</td>
<td>52.7 (+/-18.7)</td>
<td>0.118</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>53 (60.9)</td>
<td>29 (58)</td>
<td>24 (46.9)</td>
<td>0.516</td>
</tr>
<tr>
<td>Caucasian ethnicity (%)</td>
<td>75 (86.2)</td>
<td>42 (84%)</td>
<td>33 (89.2)</td>
<td>0.488</td>
</tr>
<tr>
<td>eGFR, ml/min (IQR)</td>
<td>46 (27 – 76)</td>
<td>46 (28.5–70)</td>
<td>42.5 (25–71.3)</td>
<td>0.874</td>
</tr>
<tr>
<td>uPCR, mg/mmol (IQR)</td>
<td>573 (210–811)</td>
<td>318 (193–692)</td>
<td>795 (627–998)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, g/L (IQR)</td>
<td>33 (23–41)</td>
<td>40 (33–43)</td>
<td>23 (19.5–29.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relapse (%)</td>
<td>20 (23)</td>
<td>12 (24)</td>
<td>8 (21.6)</td>
<td>0.794 0.041</td>
</tr>
<tr>
<td>Remission (%)</td>
<td>29 (33.7)</td>
<td>11 (22)</td>
<td>18 (48.6)</td>
<td>0.027</td>
</tr>
<tr>
<td>Immunosuppression (%)</td>
<td>37 (42.5)</td>
<td>14 (28)</td>
<td>10 (27)</td>
<td>0.920</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>24 (27.6)</td>
<td>14 (28)</td>
<td>10 (27)</td>
<td>0.920</td>
</tr>
</tbody>
</table>

#6905
PREVALENCE OF ANTIPLA2R ANTIBODIES IN EGYPTIAN PATIENTS WITH NEPHROTIC SYNDROME
Magdy Elsharkawy, Reem Elsharabasy, Mohamed Megahed and Ahmed Emara

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Background and Aims: Primary membranous nephropathy (PMN), a common form of the nephrotic syndrome, is an antibody-mediated autoimmune glomerular disease. Autoimmunity is driven by circulating autoantibodies that bind to one or more antigens on the surface of glomerular podocytes. PLA2R antigen is the most common and prevalent one among these antigens. Anti-PLA2R antibodies are measured in serum and detected within biopsies of primary membranous nephropathy patients. Up to the moment, no clear data about the prevalence of AntiPLA2R antibodies associated PMN in Egyptian patients. The aim of this work was to study the prevalence of antiPLA2R antibodies in Egyptian patients with nephrotic syndrome underwent renal biopsy.

Method: In this cross-sectional study we recruited 70 adult patients presented with nephrotic range proteinuria to Ain-shams university hospital and a private nephrology center in Cairo during a period of 20 months (from March 2020 to October 2021). All patients first presentation for whom laboratory investigations including serum anti-PLA2R antibodies titer by indirect immunofluorescence and kidney biopsy were done. Anti-PLA2R antibodies were measured in serum, checked in biopsies and correlated with biopsy findings.

Results: Membranous nephropathy (primary and secondary) was found by biopsy finding in 25 of 70 patients (35.7%) presenting with nephrotic range proteinuria. 21 patients (84%) of the cases of membranous nephropathy had been diagnosed with primary membranous nephropathy and 4 (16%) had been diagnosed with secondary membranous nephropathy. Circulating anti-PLA2R antibodies were detected within serum in 9 (42.85%) of primary MN cases while detection of anti-PLA2R antibodies within the glomerular extracts of primary MN cases was much higher; 17 patients (80.95%). There was positive correlation between serum AntiPLA2R Antibodies titer and U PCR (r = 0.839, P = 0.005) (Fig. 1).

Conclusion: A we may conclude that, most patients with primary membranous nephropathy have anti-PLA2R antibodies. Detection of anti-PLA2R antibodies within the biopsy has higher sensitivity than serum (80.95% versus 42.85%). Specificity of PLA2R to primary membranous nephropathy is 100%. Patients with high anti-PLA2R titer had higher baseline proteinuria than patients with lower anti-PLA2R titer.

Figure 1: Correlation between serum AntiPLA2R Antibodies titer and U PCR. U PCR: urine protein/creatinine ratio

#5142
THE NATURAL HISTORY OF FSGS IN THE GERMAN CHRONIC KIDNEY DISEASE (GCKD) COHORT
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Background and Aims: FSGS is a heterogenic glomerular disease and a common cause of kidney failure in adults. Here we describe the natural history of individuals with FSGS in the German Chronic Kidney Disease (GCKD) cohort.
Method: From 2010 to 2012, 159 patients with biopsy-proven FSGS were included in the GCXD study, a prospective observational cohort study (N = 5217). Inclusion criteria were an estimated glomerular filtration rate (eGFR) of 30–60 ml/min/1.73 m² or overt proteinuria in the presence of an eGFR < 60 ml/min/1.73 m². Baseline date was defined as first study visit. Endpoint endpoints were the composite renal endpoint (MAKE); eGFR decline >40%, eGFR < 15 ml/min/1.73 m² or initiation of kidney replacement therapy. The associations between the incidence of MAKE and clinical parameters were analyzed using the proportional hazards regression model. Data relating to baseline demographics, laboratory, comorbidities, and mortality were used.

Results: The mean age at baseline of patients with FSGS was 52.1 ± 13.6 years. Median proteinuria at baseline was 0.7 g/g (Q1 0.1; Q3 1.8), while mean eGFR was 55.8 ± 23 ml/min/1.73 m². Mean duration of the disease before enrollment was 4.7 ± 6.8 years. The majority (101;63.5%) were male; 69 (43.4%) were diagnosed as primary FSGS using clinical and pathological criteria, 55 (34.6%) as secondary FSGS and for 35 (22%) the etiology was uncertain. At baseline, 37 (23.3%) were under immunosuppressive treatment. Over a follow-up of 6.5 years, 44 reached MAKE, in detail 19 (12%) initiated kidney replacement therapy, an additional 25 (15.8%) experienced a >40% eGFR decline. Albuminuria <0.7 g/g was associated with MAKE, with a HR 0.7/g/g. Higher eGFR at baseline (per 10 ml/min) protected from MAKE with a HR of 0.8 (95% CI: 0.68-0.95).

Conclusion: The GCXD cohort represents a large study population with lengthy and adjudicated follow-up data. Lower eGFR and higher albuminuria are significant risk factors for progressive kidney disease and ESKD in patients with FSGS.

#3476 CHARACTERISTICS AND SURVIVAL DATA OF PATIENTS WITH PRIMARY FOCAL SEGMENTAL SEGMENTAL GLOMERULOSCLEROSIS: TSN-GOLD MULTI-CENTER STUDY
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Background and Aims: We aimed to investigate the characteristics and survival data of biopsy-proven primary focal segmental glomerulosclerosis (FSGS) in adult patients across Turkey.

Method: Patients with primary FSGS were included by retrospectively scanning the database of the Turkish Society of Nephrology Glomerular Diseases Study Group (TSN-GOLD). Demographic and laboratory data of the patients at baseline, sixth month, first year, and third year were recorded. Patients with secondary FSGS, missing data were excluded.

Results: The study included 1668 patients with primary FSGS who met the criteria. 1386 patients were included. The mean age of the patients was 41.16±13.88 years, and 712 patients (51.4%) were male. The total follow-up period from the biopsy date was 37.63±40.45 (IQR:1-249) months. The mean blood pressure of the patients, respectively; 130.43±7.63±1.73 mmHg, serum creatinine 1.29±1.28 mg/dl, e-GFR: 86.10±42.70 ml/min/1.73 m², serum albumin: 3.41±0.92 g/dl and proteinuria amount was 4687±4658 g/day. Microscopic hematuria was detected in 40.2% of the patients. The rate of admission with nephrotic syndrome was 45.7%. In light microscopy, the mean glomeruli count was 17.36±10.58, with 3.32±4.08 global sclerosis and 0.08±0.06 glomeruli had segmental sclerosis. Mesangial proliferation was found in 53.1% of the patients and interstitial inflammation was found in 69.7% of the patients. Interestingly, the most common immunoglobulin staining was IgM (19.3%) in the immunofluorescent microscope. The rate of receiving immunosuppressive therapy was 36%. A positive correlation was found in terms of serum creatinine, albumin, and proteinuria in the 3-year follow-up (p<0.001). In the univariate analysis, the group with eGFR < 60 ml/min/1.73 m² was older, hypertensive, uremic, anemic, had more interstitial fibrosis/tubular atrophy and less interstitial inflammation and mesangial proliferation (p<0.001). In terms of quantitative proteinuria, Patients with proteinuria > 3.5 g/day were more hypertensive, hyperlipidemic, hypoalbuminemic and anemic (p<0.05).

Conclusion: Our study presented important data on the status of patients with national primary FSGS. Approximately one-third of patients receive immunosuppressive therapy. The most important factors determining the

Table 1: Baseline clinical and laboratory characteristics of patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>41,16±13,88</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>27,57±5,23</td>
</tr>
<tr>
<td>Hypertension, no, %</td>
<td>852 (962,6)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>130,43±17,63</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>81,47±10,85</td>
</tr>
<tr>
<td>Prebital edema, no, %</td>
<td>581 (641,9)</td>
</tr>
<tr>
<td>Complaint period before applying to the nephrologist, days</td>
<td>17,67±5,86</td>
</tr>
<tr>
<td>Serum creatinine, mg/dl</td>
<td>1,29±1,28</td>
</tr>
<tr>
<td>e-GFR, ml/dk/1.73 m²</td>
<td>86,10±42,70</td>
</tr>
<tr>
<td>Serum albumin, gr/dl</td>
<td>3,41±0,92</td>
</tr>
<tr>
<td>T-Cholesterol, mg/dl</td>
<td>256,49±100,16</td>
</tr>
<tr>
<td>LDL, mg/dl</td>
<td>163,55±82,49</td>
</tr>
<tr>
<td>Hemathocrit, %</td>
<td>39,20±5,74</td>
</tr>
<tr>
<td>Proteinuria, gram/day</td>
<td>4,687±4,659</td>
</tr>
<tr>
<td>Rate of receiving immunosuppressive therapy, %</td>
<td>500 (963,1)</td>
</tr>
</tbody>
</table>

Table 2: Disease remission and recurrence rates during 3-year follow-up.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial remission, no, %</td>
<td>233 (960,5) (No = 385)</td>
</tr>
<tr>
<td>Complete remission, no, %</td>
<td>152 (939,5) (No = 385)</td>
</tr>
<tr>
<td>Recurrers rate, no,%</td>
<td>107 (936,9)</td>
</tr>
<tr>
<td>No</td>
<td>183(963,1)</td>
</tr>
</tbody>
</table>
prognosis of primary FSGS are the initial nephrotic proteinuria and the degree of renal function.

#5121

IGM POSITIVE MINIMAL CHANGE DISEASE: CHARACTERIZING DISEASE SEVERITY AND OUTCOMES

Ana Cristina Santos Cunha1, Beatriz Gil Braga1, Sofia Sousa1, Sofia Ventura1, Sofia Correia1, Jorge Malheiro1, Andreia Campos1 and Josefina Santos1

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Background and Aims: Minimal change disease (MCD) is the main cause of nephrotic syndrome in pediatric age and it is responsible for 10-25% of the cases in adults. It is characterized by minimal glomerular abnormalities in light microscopy, usually without immunoglobulins or complement deposits in immunofluorescence (IF). There is a subgroup of patients that presents with IgM deposition in IF, which has been described as a more aggressive disease, with frequent relapses [1], dependence of steroids [2] and worse outcomes.

Method: This is a retrospective study that analyses the follow up of 50 adult MCD patients in the nephrology consult, with diagnosis in childhood or adulthood. They had renal biopsies performed between 2009 and 2022. We did not include inappropriate biopsy samples, biopsies without IF or positive for C1q. We compared the characteristics between IgM positive (IgM+) and IgM negative (IgM-) patients at diagnosis, as well as the number of relapses per year, age of presentation and association with steroid-dependence or steroid-resistance.

Results: There were 23 (46%) patients in the IgM+ group and 27 (54%) in the IgM- group, with a mean follow-up of 10.2± 7.8 years. The IgM- subgroup was older at biopsy time (52 (30-74) years vs IgM+ 15 (13-23) years; p = 0.001) and this is probably related with the age of disease presentation, which was younger in the IgM+ group (12 (5-16) years vs IgM- 52 (73-13) years; p = 0.001). The groups were similar in sex distribution (IgM+ male n = 15 (55.6%) vs IgM- male n = 10 (44.0%); p = 0.395). There were no differences in diabetes and dyslipidemia frequencies between the two groups (Diabetes: IgM+ n = 1 (4.3%), IgM- n = 3 (11.3%), p = 0.614; Dyslipidemia: IgM+ n = 7 (30.4%), IgM- n = 7 (25.9%), p = 0.723), but the IgM- group had more patients with hypertension (IgM+ n = 2 (8.7%), IgM- n = 9 (33%), p = 0.046). The estimated glomerular filtration rate based on creatinine (eGFRcr) at biopsy time was higher in the IgM+ group (124 (104-130) ml/min/1.73 m² vs IgM- with 96 (84-111) ml/min/1.73 m²; p = 0.003), but this happens probably due to the age as a confounding variable. In regard to the number of relapses per year, the IgM- group had significantly more relapses than the IgM+ group (IgM+ with 0.61 (0.27-1.00) relapses per year; IgM- with 0.17 (0.01-0.65) relapses per year; p = 0.011). The steroid-dependence (IgM+ n = 15 (65%); IgM- n = 11 (47%); p = 0.084) and the steroid-resistance (IgM+ n = 6 (26%); IgM- n = 3 (11%); p = 0.270) isolated outcomes were not significantly different in the two groups, but when we analyze the composed outcome of steroid-dependence plus steroid-resistance we have worse outcomes in the IgM+ subgroup (IgM+ n = 21 (91.3%); IgM- n = 14 (51.8%); p = 0.04; ORR 9.72; IC 95% 2.37-33.33). An IgM+ patient has 9.7 times the odd of being steroid-dependent or steroid-resistant of an IgM- patient. From our 50 patients, 3 evolved to stage 5 chronic kidney disease with dialysis dependency, being all of those patients IgM+. One of those patients had a recurrence of MCD after kidney transplant. There were 3 deaths with non-related to kidney disease causes, 1 in the IgM+ and 2 in the IgM- groups. Genetic test was performed in 5 of the IgM+ patients, with 4 positive results for mutations. Only 2 IgM+ patients did genetic test, all without mutation’s identification. 

Conclusion: This study supports the evidence that MCD patients with IgM+ biopsies have younger age MCD’s presentation, more relapses per year and more steroid dependence plus resistance. Dialysis was started in 3 IgM+ patients and this group seems to have higher frequency of genetic mutations. This suggests that genetic testing could be important for future prognosis prediction and treatment options in the IgM+ patients, but further studies with a bigger study population need to be done to establish this relation.

REFERENCES

ASSESSMENT OF THE INTERNATIONAL IGA NEPHROPATHY PREDICTION TOOL AFTER IGA TREATMENT: A CASE-SERIES STUDY

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Background and Aims: IgAN have a variable clinical course and a considerable risk of ESKD. The 2021 KDIGO guidelines recognize the International IgAN Prediction Tool (IIgAN-PT) as a quantifier of progression risk at the time of kidney biopsy. The possible application of the IIgAN-PT to re-evaluate the risk after treatment and during follow-up is debated. We analyzed the possible association between treatment response and changes of IIgAN-PT risk estimation.

Method: Retrospective study including patients with IgAN undergone kidney biopsy from Jan 2010 to Dec 2020. Inclusion criteria: treatment with glucocorticoids, age > 18, follow-up at 3-6-12-24 months, availability of risk estimation. Progression risk evaluated by IIgAN-PT at time 0 (biopsy) and after 6-12 months. Two risk groups were identified based on the IIgAN-PT at time 0: Low-Intermediate risk group (Low-risk, IIgAN-PT < 23%) and High-risk group (High-risk; IIgAN-PT risk ≥ 23%).

Results: A total of 22 patients were included (59% Low-risk; 31% High-risk). Patients at low-risk had significantly higher eGFR with respect to high-risk group (78 vs 40 ml/min/1.73 m² respectively) (p < 0.001). Age, MAP, and RASi use at biopsy did not differ significantly. Proteinuria was comparable among groups: 3.14 g/24 h in High-risk and 2.49 g/24 h in Low-risk (p = 0.17). In the Low-risk group the median proteinuria swiftly decays below 1.0 g/day already at three months, and below 0.5 g/day after six. Conversely, in the high-risk group, it remained above 1 g/day until 12 months (Fig. 1). Regarding risk progression assessment: 89% of patients at higher risk at baseline became at lower risk at 6 months (Fig 2; Table 1).

Conclusion: Treatment response was associated with a reduction in the IgAN progression risk as demonstrated by changing of IIgAN-PT already after 6 months. These data suggest a possible dynamic use of IIgAN-PT for IgAN progression risk re-evaluation even in the short follow-up period.

Figure 1: Proteinuria and eGFR variation during follow-up in different risk group identified according to IIgAN-PT.
Figure 2: Predicted 5-year risk of progression (IIgAN-PT) at biopsy, 6, and 12 months for each patient on supportive and immunosuppressive therapy and with a follow-up of at least 12 months. Values are presented according to increasing risk of progression at biopsy. Red line separates patients at lower-intermediate risk from those at higher risk. IIgAN-PT, International IgA Nephropathy Prediction Tool.

Table 1: Predicted 5-year risk of progression (IIgAN-PT) at biopsy, 6, and 12 months.

<table>
<thead>
<tr>
<th>Risk subgroups</th>
<th>Predicted 5-year risk, %</th>
<th>Baseline</th>
<th>6 months</th>
<th>p-value</th>
<th>12 months</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>21.29 (±16.21)</td>
<td>10.70 (±8.72)</td>
<td></td>
<td>9.36 (±8.03)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>17.83 (7.19–33.57)</td>
<td>8.31 (2.51–19.80)</td>
<td>&lt;0.001ª</td>
<td>6.99 (2.27–16.12)</td>
<td>&lt;0.001ª</td>
</tr>
<tr>
<td>Lower-intermediate risk</td>
<td></td>
<td>11 (55%)</td>
<td>19 (95%)</td>
<td>0.008 b</td>
<td>19 (95%)</td>
<td>0.008 b</td>
</tr>
<tr>
<td>Higher risk</td>
<td></td>
<td>9 (45%)</td>
<td>1 (5%)</td>
<td></td>
<td>1 (5%)</td>
<td></td>
</tr>
</tbody>
</table>

#5924

LATE DIAGNOSIS OF IGA NEPHROPATHY IN LOWER SAXONY (GERMANY) – CLINICAL AND HISTOPATHOLOGICAL DATA FROM 246 PATIENTS AT TIME OF INITIAL RENAL BIOPSY
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Background and Aims: IgA Nephropathy (IgAN) is the most frequent glomerulonephritis and contributes significantly to the burden of dialysis dependence. If not detected in the context of screening health examinations e.g. for the military service, decline in renal function is usually unnoticed due to the lack of specific symptoms. After decades of limited pharmacological options, the advent of new therapies provides opportunities for early intervention. Age and renal function as well as proteinuria at the time of renal biopsy varies depending on healthcare systems but might influence the use of novel interventions. Publications from outside Germany report that eGFR at the time of first renal biopsy in IgAN varies between 73.8 and 94.9ml/min/1.73 m². The age at the time of diagnosis is between 27 and 40 years. The aim of our study was to investigate renal function, degree of proteinuria as well as histological parameters at the time of first renal biopsy in patients with IgANephropathy.

Method: This retrospective study evaluated data from two different tertiary care hospitals in Germany that sent their renal biopsies to the Nephropathology Department at the Hannover Medical School from January 2012 – October 2022. Only initial biopsies from native kidneys were included. Histopathological parameters and clinical as well as laboratory parameters at the month of biopsy were obtained. eGFR was calculated according to the CKD-EPI formula.

Results: First time diagnosis of IgA nephropathy was made in 246 patients at a median age at of 45 (range 4–79) years, 76.8% were male. The median serum creatinine level was 1.44mg/dl, corresponding to a median eGFR of 43.0 (3.8–132) ml/min/1.73 m². Surprisingly 49.5% of all patients were at CKD K/DOQ GFR stage 3B or higher at the time of first biopsy (Figure 1). Median proteinuria was 1.84 (0.08 – 16.5) g/d in those patients where 24h urine collection was performed. 156 of 246 patients had microhematuria at the time of biopsy. Based on the Oxford classification >50% had hypercellularity. Endocapillary hypercellularity was present in 24%. Segmental glomerulosclerosis was almost evenly distributed (S0:116 | S1:112). Tubular atrophy and interstitial fibrosis were visible in most biopsies in 0-25% of cortical area (T0:153 | T1:59 | T2:16). In 27.2% the C-score was analyzed, showing cellular and/or fibrocellular crescent in 26.8% of those patients. Thrombosis and necrosis were rather uncommon in initial biopsies of IgA Nephropathy.

Conclusion: The study shows that an IgA Nephropathy shows severe renal impairment at the time of diagnosis i.e. first renal biopsy, suggesting that patients are referred rather late for this diagnostic procedure. These regional data have to be validated in larger cohorts. If confirmed, measures for earlier screening and referral should be implemented to allow timely intervention thus lowering need for renal replacement therapy.

Figure 1: GFR categories of the IgAN patients at the time of first biopsy.
IS DIABETES MELLITUS ASSOCIATED WITH WORSE KIDNEY OUTCOME IN PATIENTS WITH GLOMERULOPLANITIES?

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Background and Aims: Diabetes mellitus (DM) is the leading cause of end stage kidney disease and a major risk factor for cardio-vascular disease and death. While it is known that subjects with diabetic nephropathy (DN) have a worse kidney outcome compared to other non-diabetic glomerulopathies, it is not certain whether DM independently influences the kidney outcome in subjects diagnosed with glomerulopathies (GP) other than diabetic nephropathy.

Method: This retrospective study included 1200 adults [50 (95% CI 48 to 51) years, 56% males, eGFR 48.5 (95%CI 45.9 to 51.3) mL/min], with kidney biopsy (KB) proven GP between 1st Jan. 2008 and 31st Dec. 2017. Subjects were followed for a mean of 89 (95%CI 85.5 to 92.4) months until 31st May 2018. The primary endpoints were the initiation of chronic renal replacement therapy (RRT) or death. Subjects with inappropriate biopsy sample, insufficient data and RRT prior to KB were excluded. Demographic, clinical and laboratory data at the time of biopsy were retrieved from medical records. Kidney survival was evaluated by Kaplan-Meier method and a competitive risk to event analysis was used to estimate the risk of RRT, considering death as a competing event. Variables related to kidney outcome were evaluated by the subdistribution hazard function using Fine-Gray model. According to the presence or absence of DM and the types of GP, subjects were divided in three groups: GP without DM (n = 987 pts.), GP with DM (n = 65 pts.), and DN (n = 148 pts.).

Results: GP with DM subjects were older (60 (95% CI 56 to 64) years vs. 55.5 (95%CI 54 to 59) years in DN group vs. 47 (95%CI 45 to 48) years in GP without DM; p<0.001). Males were predominant in all groups, with higher frequency in DN group (66.9% vs. 54.9% - GP without DM vs. 61.5% - GP with DM; p = 0.01). DN group had higher Charlson comorbidity index [5 (95% CI 4 to 5) vs. 2 (95%CI 2 to 2) in GP without DM vs. 3 (95%CI 3 to 4) in GP with DM; p<0.001], lower eGFR (31.3 (95%CI 25.4 to 36.7) mL/min vs. 51.9 (95%CI 48.9 to 55.8) mL/min in GP without DM vs. 43.2 (95%CI 35.4 to 51.3) mL/min in GP with DM; p<0.001) and higher proteinuria (4.9 (95%CI 3.8 to 6) g/g in GP without DM vs. 2.6 (95%CI 2.35 to 2.9) g/g in GP without DM vs. 4.3 (95%CI 2.7 to 6.7) g/g in GP with DM; p<0.001]. During the follow-up period, 24.3% needed RRT, while 11.4% died. The highest RRT initiation and death frequency was in DN group (40.5% vs. 21.7% in GP without DM vs. 27.7% in GP with DM; p<0.001, and 18.2% vs. 10% in GP without DM vs. 19.9% in GP with DM; p = 0.004). In the univariate time-dependent analysis, subjects with DN had the worse kidney outcome (log rank p<0.001) (Fig. 1), however the kidney survival was similar between GP with DM and GP without DM subjects (log rank p = 0.1). In the competitive risk time to event analysis where death is considered the competing event, diabetic nephropathy subjects had worse kidney survival than GP with DM subjects [CIF 2.3 vs. 1.3, p<0.001], while GP with DM had similar survival with GP without DM (CIF 1.3; p = 0.2) (Fig. 2). After adjusting for the risk factors for CKD progression, DM was not associated with an increased risk of
Over all all-cause death was 1167 / 6575 (17.74%) cases. In non-
Results: using multiple imputation for missing data.
causal effect of ALLO or FEB versus control with weight for adjust covariate
concomitant drugs, marginal structural models (MSM) that examined the
analized using 3 years of longitudinal data versus control at each visit, including
associations for outcomes of allopurinol (ALLO) or febuxostat (FEB) were
and CVD events, defined by ICD coding using longitudinal data. Causal
was no difference of preventive effect between ALLO and FEB for all cause mortality
FEB 2117 events. MSM indicated that ALLO estimated HR 0.35 for all cause
cvd events for each treatment group non-treated 11229 events, ALLO 1377,
136 / 970 (14.20%) in FEB-treated group. CVD events 14723, and number of
Method: 6575 dialysis patients were divided into baseline 3 groups (ALLO
treatment categories. In CVD events, ALLO indicated preventive effect of HR
< 0.81 versus control (p = 0.001). There was no difference of preventive effect between ALLO and FEB for all cause mortality, but each drugs indicated preventive effect in each base line XOR treatment categories. In CVD events, ALLO indicated preventive effect of HR 0.81 versus control (p = 0.001). But FEB did not indicated preventive effect of HR 0.98 (95% CI: 0.91 - 1.04). ALLO was estimated preventive effect for CVD events against FEB in HR 0.83 (95% CI 0.75-0.92).

Conclusion: ALLO and FEB had a prevent effect for all-cause mortality, further FEB was not inferior to ALLO in all-cause mortality in the realm of XOR inhibition. Nevertheless, FEB could not indicate preventive effect for CVD events compared with ALLO and control, which is assumed of ABCG2 inhibitory effect. But was not increase risk for all cause mortality or CVD events compared with ALLO and control. This study provide a new suggestion that it is important for CKD patients to apply extrarenal excretion pathway ABCG2 of uremic toxin and uric acid to prevent CV events because of impaired renal function. In humans 70% of uremic toxin is excreted from urine, and 30% from gut. It is required further investigation and treatment strategies of uric acid lowering therapy should be considered about excretion of uremic substances outside of the kidneys.

**#6950**

**FEBUXIOSTAT AND ALLOPURINOL VERSUS NON-TREATMENT IN HEMODIALYSIS PATIENTS WITH OUTCOMES**

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**Background and Aims:** Uric acid is relatively low in hemodialysis because it is removed during dialysis. The therapeutic intervention for hyperuricemia is controversial. RCT of allopurinol and febuxostat has been performed in hyperuricemic patients to inhibit xanthine oxidoreductase (XOR) and reduce uric acid levels further improve outcomes. Nonetheless, we reported preventive effect of XOR inhibitors for dialysis patients on Sci Rep 2017, but the difference in the protective effect for CVD events and mortality between XOR inhibitors is insufficient in dialysis patients. Furthermore, febuxostat is also known to be a potent ATP-binding cassette transporter subfamily G member 2 (ABCG2) inhibitor that promotes the accumulation of uremic toxins by excretion from the gut in dialysis patients and hyperuricemic patients. We investigated the preventative effect of XOR inhibitors on outcomes under three year observation for 6575 hemodialysis patients.

**Method:** 6575 dialysis patients were divided into baseline 3 groups (ALLO group, FEB group, non-treatment group). Outcomes were all-cause mortality and CVD events, defined by ICD coding using longitudinal data. Causal associations for outcomes of allopurinol (ALLO) or febuxostat (FEB) were analyzed using 3 years of longitudinal data versus control at each visit, including concomitant drugs, marginal structural models (MSM) that examined the causal effect of ALLO or FEB versus control with weight for adjust covariate using multiple imputation for missing data.

**Results:** Over all all-cause death was 1167 / 6575 (17.74%) cases. In non-treated group 993 / 4827 (20.57%), ALLO-treated group 98/778 (12.60%), and 136 / 970 (14.20%) in FEB-treated group. CVD events 14723, and number of

Conclusion: In conclusion, AKI, glomerulonephritis (GN) and tubulointerstitial nephritis (TIN).

**#4100**

**ACUTE KIDNEY INJURY, GLOMERULONEPHRITIS AND TUBULOINTERSTITIAL NEPHRITIS FOLLOWING VACCINATION: VIGIBASE ANALYSIS**

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¹Kyung Hee University Hospital, Division of Nephrology, Department of Internal Medicine, Seoul, Rep. of South Korea, ²Kyung Hee University, Department of Biomedical Engineering, Yongin, Rep. of South Korea and ³Medical Science Research Institute, College of Medicine, Kyung Hee University, Center for Digital Health, Seoul, Rep. of South Korea

**Background and Aims:** Vaccination is the long-term established measure for disease prevention and worldwide outbreak of COVID-19 necessitates mass scale vaccination. However, there is a public concern on the risk of renal adverse reactions from several types of vaccination.

**Method:** We analyzed VigiBase (n = 120,715,116 reports), the World Health Organization pharmacovigilance database from Dec 1967 to Jul 2022 using disproportionate Bayesian reporting. Information component (IC) compares observed and expected values to find the associations of vaccines with acute kidney injury (AKI), glomerulonephritis (GN) and tubulointerstitial nephritis (TIN).

**Results:** We found 5,484 AKI (13.8% fatal), 2,846 GN (29.4% fatal) and 289 TIN reports (23.2% fatal) as vaccine-associated adverse reactions. Almost reports indicated single drug suspected cases (>99.5% reports). The cumulative number of reports on vaccine-associated AKI, GN and TIN gradually increased and Americas was most prevalent regions of reporting. Examining the different vaccines separately, reporting count of COVID-19 mRNA vaccines sharply increased and it solely was associated with significantly higher reporting of AKI (IC025 1.09) and TIN (IC025 0.48). Patients aged 12-17 years had the highest IC values for COVID-19 mRNA vaccine-associated AKI and TIN. Hepatitis B (IC025 3.22), influenza (IC025 2.64) and COVID-19 mRNA vaccine (IC025 2.89) were prominently over-reported among ten types of vaccines with significant signals of GN.

**Conclusion:** In conclusion, AKI, GN and TIN substantially occurred following vaccination and it was most noticeable in patients exposed to COVID-19 mRNA vaccines. Clinicians should consider the increased risk of renal adverse reactions after vaccination.

**Figure 1:** Preventive effect for All-Cause Mortality and CVD events in MSM models.
LONG-TERM OUTCOMES IN A COHORT OF PATIENTS WITH SYSTEMIC VASULTIDIES (SV) AND KIDNEY INVOLVEMENT

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1University General Hospital of Heraklion, Nephrology, Heraklion, Greece and 2National Kapodistrian University of Athens, Pathology, Athens, Greece

Background and Aims: Many randomized trials address the issue of SV therapy. Nevertheless, individualized treatment in patients with SV and renal involvement requires long term data and is often center specific. We present the experience of our center, a tertiary University hospital in Crete, Greece.

Method: Medical records were reviewed for clinical signs and symptoms. Statistical analysis was performed using SPSS 20 (IBM). Data were tested for normality, statistical significance was set at <0.05. Chi-Square test, Student’s T-Test, Multiple-Regression analysis were utilized for statistical analysis.

Results: We examined 58 patients (37 females) with a mean follow-up of 5 years (Range 1-31) and a mean age of 66 years (Range 12-102). Serology revealed 46 pANCa+ve (79%), 8 cANCa+ve (14%) and 4 p/c ANCA negative patients (7%). Nine patients lost renal function and 16 patients died during follow-up. All patients received immunosuppressive induction therapy (Cyclophosphamide N = 42, Rituximab N = 7, Steroid monotherapy N = 9). All patients with pulmonary hemorrhage underwent plasmapheresis. The severity of clinical manifestation was associated with need for plasmapheresis and rapid renal function deterioration. Plasmapheresis resulted in the remission of pulmonary hemorrhage in all patients. Renal death was associated with renal function decline in months 1 and 6 post diagnosis. Treatment with cyclophosphamide or rituximab did not affect outcome (death or renal death). Number of relapses (14 patients), surprisingly, was not associated with renal function deterioration. Death was not associated with renal function deterioration in months 1 and 6 post diagnosis. Loss of follow up was associated with increased mortality.

Conclusion: In this cohort either cyclophosphamide or Rituximab does not seem to affect prognosis. plasmapheresis efficiently contains pulmonary hemorrhage and, as expected, loss of follow-up is associated with poor outcomes.

B4 - PREVENTION, TREATMENT & CLINICAL TRIALS

THE TYPE II ANTI-CD20 MONOCLONAL ANTIBODY MIL62 OR CYCLOSPORINE IN CHINESE PRIMARY MEMBRANOUS NEPHROPATHY: PRELIMINARY RESULTS OF A PHASE IB/II TRIAL

Zhao Cui1, Yimiao Zhang1, Heng Li1, Hua Zhou1, Hongli Lin2, Guangquan Xing1, Wei Chen1, Wei Liang4, Ping Luo2, Xiaolan Chen2, Hui Xu1, Yan Zha1, Yue Wang1, Xin Chen1, Zhaohui Ni3, Junjun Zhang1, WanHong Lu1, Haitao Zhang1, Haibo Long1, Dong Sun1, Yu Cao1, Minghui Zhao1, Song Meng2 and Min Wei2

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Background and Aims: Anti-CDD20 monoclonal antibody has become one of the first-line therapies for the treatment of moderate and high-risk primary membranous nephropathy (pMN). A novel glycoengineered type II anti-CD20 antibody, MIL62 with a nearly completely afucosylated N-glycans in Fc region, has demonstrated superior activity compared with rituximab and obinutuzumab in vitro and in vivo, respectively. To evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of MIL62 in pMN, we conducted a multicenter, randomized, controlled, open-label, phase Ib/II study (NCT05398653).

Method: This study aims to investigated MIL62 or Cyclosporine for the treatment of Chinese pMN. Eligible patients with pMN diagnosed by kidney biopsy, proteinuria of at least 3.5 g per 24 hours received intravenous MIL62 (two infusions, 600 or 1000 mg each, administered 14 days apart; repeated at 6 months) or Cyclosporine (starting at a dose of 3.5 mg per kilogram of body weight per day for 12 months). Patients were followed up for up to 104 weeks. The primary outcome was one of complete or partial remission of proteinuria and stable eGFR at 76 weeks. Laboratory variables and safety were also assessed.

Results: From February 23th, 2022 to December 21th, 2022, 85 patients were randomly enrolled from 19 centers in China, and received at least one dose of MIL62 or Cyclosporine. At the data cut-off date (January 30th, 2023), 60 patients were followed up for at least 12 weeks, 24/40 (60%) patients in the MIL62 group and 7/20 (35%) patients in the Cyclosporine group achieved complete or partial remission; 26 patients were followed up for at least 24 weeks, 11/18 (61.1%) patients in the MIL62 group and 2/8 (25%) patients in the Cyclosporine group achieved partial remission. In the 56 patients who were positive for anti-PLA2R antibodies (≥14RU/mL) at baseline and followed up for at least 12 weeks, 29/38 (76.3%) patients in the MIL62 group achieved immunological remission (PLA2R Abs<14RU/mL), which was superior to the Cyclosporine group where 8/18 (44.4%) patients achieved immunological remission (P<0.05). The remission to MIL62 in our study was rapid because 61.1% of patients achieved complete or partial remission at 24 weeks compared with the 35% 6-month response rate reported in the Membranous Nephropathy Trial of Rituximab study [1]. Among the 85 safety-evaluable patients, treatment emergent adverse events (TEAEs) occurred in 23/30 (76.7%) patients in the MIL62 600 mg group, 26/30 (86.7%) patients in the MIL62 1000 mg group and 24/25 (96.0%) patients in the Cyclosporine group respectively; Grade 3 or above TEAEs were observed in 5 (16.7%), 1 (3.3%) and 2 (8.0%) patients in the MIL62 600 mg, MIL62 1000 mg and Cyclosporine group respectively; Grade 3 or above TEAEs were observed in 5 (16.7%), 0 (0.0%) and 2 (8.0%) patients in the MIL62 600 mg, MIL62 1000 mg and Cyclosporine group respectively. Only one patient in the MIL62 600 mg group experienced serious treatment-related thrombocytopenia and has recovered so far; Other SAEs are not related to treatment. B cell depletion occurred within 24 hours after MIL62 infusion and could last for 24 weeks.

Conclusion: The 12-week immunological remission rate in the MIL62 group was significantly higher than the Cyclosporine group. MIL62 had a manageable safety profile. This phase Ib/II preliminary data warrant further phase III clinical trials of MIL62 in pMN.

REFERENCE

#4337

**UPDATED INTERIM RESULTS OF A PHASE 1/2 STUDY OF BION-1301 IN PATIENTS WITH IGA NEPHROPATHY**

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**Background and Aims:** Immunoglobulin A nephropathy (IgAN) is the leading cause of primary glomerulonephritis worldwide with limited treatment options, especially for high-risk patients. Approximately 30-45% of IgAN patients progress to end-stage kidney disease over a period of 20-25 years and proteinuria is the strongest predictor of disease progression [1]. BION-1301 is a novel humanized monoclonal antibody that blocks a proliferation-inducing ligand (APRIL), a cytokine that is elevated in patients with IgAN. APRIL promotes the production of pathogenic galactose-deficient IgA1 (Gd-IgA1), leading to immune complex deposition and subsequent kidney injury. Blocking APRIL with BION-1301 is a potential disease-modifying approach to directly target the pathogenesis of IgAN. In a Phase 1/2 study (NCT03945318) in healthy volunteers and patients with IgAN, BION-1301 was well-tolerated with no serious adverse events (SAEs) and durably reduced free APRIL, IgA, Gd-IgA1, IgM and to a lesser extent, IgG [2].

**Method:** For the ongoing phase 1/2 open-label, multicohort trial, eligibility criteria include adults with biopsy-proven IgAN, eGFR > ≥0.5 g/g, and proteinuria > 0.5 g/24 hrs or UPCR > 0.5 g/l and on stable/optimized RASi (or intolerant). Cohort 1 received 450 mg of BION-1301 administered IV every 2 weeks, transitioning to SC at 600 mg every 2 weeks at least after 24 weeks. Cohort 2 received 600 mg of BION-1301 SC every 4 weeks.

**Results:** In both Cohorts 1 and 2, BION-1301 was generally well-tolerated, with no SAEs or terminations due to AEs as of the last reported interim analysis (November 2022) [2]. Durable reductions in serum levels of free APRIL and immunoglobulins were observed in both cohorts. No anti-drug antibodies have been observed in patients with IgAN to date. In Cohort 1, clinically meaningful reductions in proteinuria were seen as early as 12 weeks (30.4% geometric mean UPCR reduction, n = 7), and were sustained through 24 weeks (48.8% geometric mean UPCR reduction, n = 8) and 52 weeks (66.9% geometric mean UPCR reduction, n = 8). Reductions in proteinuria were consistent in Cohort 2 (53.8% geometric mean UPCR reduction, n = 9) at 24 weeks. Significant and durable reductions in serum Gd-IgA1 concentrations were observed and were consistent across both cohorts. Updated data will be reported at the time of presentation.

**Conclusion:** BION-1301 offers disease-modifying potential by directly targeting the initiating pathogenesis of IgAN. Interim biomarker and clinical activity responses support advancement of BION-1301 into later-stage development for patients with IgAN.

### REFERENCES


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#6649

**SIGNIFICANT CLINICAL IMPROVEMENT OF PAEDIATRIC AND ADULT PATIENTS WITH DISTAL RENAL TUBULAR ACIDOSIS AFTER 6 YEARS OF TREATMENT WITH SIBNAYAL®**

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**Background and Aims:** Distal renal tubular acidosis (dRTA) is a rare disease, inherited or acquired, characterized by hyperchloremic metabolic acidosis leading to negative effects on growth, bone and kidney, with growth retardation, rickets in children and osteomalacia in adults, nephrolithiasis and chronic kidney disease. No alkalizing treatment, necessary to control the metabolic acidosis and its consequences in growth, bone and kidney, has been shown, to date, to control the disease in the long term. The aim of this clinical study is to describe a cohort of adult and pediatric dRTA patients treated during 6 years by Sibnayal®, a new prolonged-release alkalizing formulation, in term of metabolic control, growth and long-term complications on bone mineralization and kidney function.

**Method:** Thirty patients with genetic dRTA taking Sibnayal® previously treated with alkalizing standard of care and enrolled in the short-term B21CS study, were followed up for six years on average in a multicenter open-label extension trial (B22CS) to evaluate long-term impact of treatment on standard deviation score (SDS) of height, SDS weight, body mass index (BMI), Z-score spine bone mineral density (BMD), phosphocalcic metabolism (up to 4 years). Glomerular filtration rate (GFR), nephrolithiasis, metabolic acidosis control, safety and compliance were also evaluated. Paired t-tests were done from baseline to end of study (EoS) when appropriate. The covariance ANCOVA test was performed to analyze spine BMD Z-score. Data are presented as mean ± standard error of mean.

**Results:** Clinical observations in this cohort, after an average of six years of treatment with Sibnayal®, confirmed the adequate control of metabolic acidosis (plasma bicarbonate from 22.0±6.0 mmol/L at baseline to 22.8±5.6 mmol/L at study end). The phosphocalcic metabolism analysis, from baseline to Month 48, demonstrated no significant change on Z-score for age of blood bone alkaline phosphatases, and a significant decrease of Z-score for age of blood phosphorus level (from -0.5±0.7 to -1.3±1.0, p = 0.03). From baseline to EoS, SDS of height and weight increased significantly (-0.6±1.0 to -0.3±0.9 p = 0.04 and 0.2±1.5 to 0.7±1.4 p = 0.03, respectively), without significant difference in BMI. The spine BMD Z-score, relevant skeletal area for both pediatric and adult patients, underwent a continuous and significant increase of the change from baseline values over 6 years of treatment (difference [95% CI] = 0.404 [0.170; 0.639]). At EoS, spine BMD Z-score was improved in pre- and post-pubertal patients (mean 0.76±0.54 and 0.56±0.22 respectively), while it was stabilized in pubertal patients (mean -0.01±0.39). There was no significant variation of GFR between baseline and EoS. Nephrolithiasis increased slightly according to the increased age of the patient, without surgical intervention for stones removal. Safety and adherence to treatment remained good throughout the study.

**Conclusion:** Our data show the positive effect of the long-term treatment with Sibnayal® on growth and spine BMD, nicely improved, in the dRTA patients who participated to this long-term follow-up clinical study. The kidney function is also stabilized in these patients during the follow-up. This is the first report describing the prevention effect on the long-term complications of the distal Renal Tubular Acidosis patients under 6 years of Sibnayal® treatment.
MATCHING-ADJUSTED INDIRECT COMPARISON OF SPARSENTAN VS DELAYED-RELEASE FORMULATION Budesonide FOR PROTEINURIA REDUCTION IN ADULTS WITH IGA NEPHROPATHY

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Background and Aims: Immunoglobulin A (IgA) nephropathy is a rare kidney disorder characterized by deposition of IgA in the glomeruli and associated with a reduction in renal function and increased risk of kidney failure [1,2]. In the absence of head-to-head trials, this study used matching-adjusted indirect comparison (MAIC) of randomized control trial data to compare 9-month efficacy outcomes between potential treatment options for IgA nephropathy, sparsentan and recently FDA and EMA approved delayed-release formulation budesonide [4,5].

Method: An unanchored MAIC was conducted using individual patient level data from the PROTECT trial for sparsentan and aggregate data from the NefIgArd trial for delayed-release formulation budesonide. Patients in the sparsentan arm of PROTECT were weighted to match the key baseline characteristics of patients in the budesonide delayed-release formulation arm of NefIgArd. After matching, the percentage reduction of urine protein-creatinine ratio (UPCR) at Month 9 relative to baseline were compared between sparsentan and delayed-release formulation budesonide. A two-tailed z-test was performed to estimate the p-value.

Results: Assessment of cross-trial heterogeneities suggested that PROTECT and NefIgArd trials were sufficiently similar in terms of patient population, key inclusion and exclusion criteria, and outcome definitions; however, due to differences in control arms (renin-angiotensin system blocker [RASB] optimization), an unanchored MAIC (comparing treatment arms directly) was selected. After matching, all matched baseline patient characteristics were well-balanced between corresponding treatment arms of the two trials. The comparative results showed that patients treated with sparsentan achieved a greater mean percentage reduction in UPCR at 9 months from baseline compared to budesonide-treated patients (p-value withheld pending FDA approval of sparsentan due to regulatory requirements).

Conclusion: The MAIC results showed that sparsentan was associated with a significantly larger percentage reduction in UPCR, a recognized surrogate of long-term kidney outcomes, from baseline to month 9 compared with delayed-release formulation budesonide.

REFERENCES
Background and Aims: Focal segmental glomerulosclerosis (FSGS) is a disease of podocytes. Complications include nephrotic syndrome and progressive kidney failure. FSGS is a condition with high unmet need and there is no approved treatment. The angiotensin II receptor type 1 (ATIR) and chemokine receptor 2 (CCR2) are G protein coupled receptors that form functional heteromers. Simultaneous antagonism of these receptors suggested synergistic renoprotective effects in preclinical and early phase clinical studies of proteinuric kidney disease. DMX-200 (repagerranium) is a C-C chemokine receptor type 2 (CCR2) inhibitor that, when administered concurrently with an angiotensin II receptor blocker (ARB), is designed to inhibit recruitment of monocytes implicated in the inflammatory chemokine environment of chronic disease. In a Phase 2a open-label study of 27 patients with proteinuric chronic kidney disease, 25% of patients achieved >50% reduction in uPCR with combined use of DMX-200 and irbesartan. A Phase 2a placebo-controlled cross-over study in 8 patients with primary FSGS receiving stable dose of irbesartan demonstrated evidence of promising efficacy with clinically relevant reduction in uPCR of 17% with DMX-200 compared with placebo. These encouraging data suggest that treatment with DMX-200 may result in relevant reduction in uPCR of 17% with DMX-200 compared with placebo.

Results:

- Eligible patients are adults (18-80 years) with biopsy-proven primary FSGS, genetic FSGS or FSGS of undetermined cause (FSGS-UC), and uPCR efficacy of DMX-200 in patients with FSGS receiving an ARB.
- The ACTION3 study design is a Phase 3 randomized, placebo-controlled efficacy and safety trial which evaluates the novel approach of combining an investigational CCR2 inhibitor, DMX-200, with angiotensin receptor blockade in patients with FSGS.
- The study is currently open in 11 countries at approximately 75 investigational sites and will be expanded to include more countries and sites subject to a successful first interim analysis.
- Results: ACTION3 is a trial in progress and is expected to be completed in 2026.
- Conclusion: ACTION3 is a Phase 3 randomized, placebo-controlled efficacy and safety trial which evaluates the novel approach of combining an investigational CCR2 inhibitor, DMX-200, with angiotensin receptor blockade in patients with FSGS.

Table 1:

<table>
<thead>
<tr>
<th>Varying covariate</th>
<th>eGFR</th>
<th>Percentile</th>
<th>Relative change in mean AUC0-24</th>
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<tr>
<td>eGFR</td>
<td>34.3</td>
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<td>1.38</td>
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<td>25th</td>
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#4341

ASSIST STUDY DESIGN: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER STUDY OF ATRASENTAN IN PATIENTS WITH IGA NEPHROPATHY (IGAN) ON SGLT2i

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Background and Aims: IgA nephropathy (IgAN) is the leading cause of primary glomerulonephritis. Approximately 30-45% of IgAN patients progress to ESKD over a period of 20-25 years and proteinuria is the strongest predictor of disease progression. Endothelin A (ET\(_{\alpha}\)) receptor activation drives proteinuria, kidney inflammation and fibrosis. Atrasentan, a potent and selective ET\(_{\alpha}\) antagonist, has potential to reduce proteinuria and preserve kidney function in IgAN. Interim results of a phase 2, open-label study in patients with IgAN (AFFINITY, NCT04573920) demonstrated that atrasentan was well tolerated and resulted in clinically meaningful and label study in patients with IgAN (AFFINITY, NCT04573920) demonstrated and CKD (SONAR), 6 week treatment with SGLT2i and atrasentan (n=230) resulted in substantial reduction in proteinuria in patients with IgAN who were also on stable background SGLT2i and RASi therapy.

Methods: The ASSIST trial is a randomized, double-blind, placebo-controlled, crossover clinical trial. Approximately 52 patients with biopsy-proven IgAN and eGFR ≥ 30 mL/min/1.73 m\(^2\) (CKD-epi) who are receiving maximally tolerated RASi for at least 12 weeks prior to screening will be enrolled. Patients on a stable dose of SGLT2i prior to screening (SGLT2i stable) must have total protein of >0.5 grams/day at screening. Patients who are not currently on SGLT2i or are not on a stable dose of SGLT2i must have total protein of >0.5 grams/day at screening and enter a run-in period during which they receive SGLT2i for 8 weeks (SGLT2i run-in), after which they must have a total protein of >0.5 grams/day confirmed at the Week-1 visit (Figure). Choice of SGLT2i will be at the discretion of the principal investigator and per local treatment standards. Thereafter, all eligible patients will be randomized 1:1 to sequence AB or sequence BA in which they receive SGLT2i for 8 weeks (SGLT2i run-in), after which they may have a total protein of >0.5 grams/day at screening and enter a run-in period during which they receive SGLT2i for 8 weeks (SGLT2i run-in), after which they may have a total protein of >0.5 grams/day confirmed at the Week-1 visit (Figure). Choice of SGLT2i will be at the discretion of the principal investigator and per local treatment standards. Thereafter, all eligible patients will have follow-up evaluations for safety approximately 4 weeks after the end of treatment. Fifty-two subjects will provide approximately 83% power using a two-sided pairwise test (α=0.05) to detect a treatment effect of at least 0.288 in natural log transformed UPCR (25% reduction) between atrasentan and placebo.

Results: Primary and secondary endpoints are change in proteinuria (UPCR from baseline to week 24), percentage of patients who achieve treatment success (at least 25% reduction in UPCR), and change in eGFR from baseline to week 24. Type, incidence, severity, seriousness, and relatedness of adverse events will be evaluated. Change in eGFR from baseline to week 24 in Treatment Period 2 will be evaluated as an exploratory endpoint.

Conclusion: Atrasentan is a potent and selective ETA antagonist. Interim results from the AFFINITY Phase 2 open-label study demonstrated that atrasentan resulted in reduced, significantly meaningful reductions in proteinuria in patients with IgAN. The phase 2 ASSIST study will examine the effects of atrasentan in combination with SGLT2i in patients with IgAN who are also receiving maximally tolerated RASI.

#5814

SGLT2 INHIBITORS IN IGA NEPHROPATHY: REAL-WORLD CLINICAL PRACTICE

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Background and Aims: Immunoglobulin A nephropathy (IgAn) is a common type glomerulonephritis that often progresses to advanced CKD despite the use of ACEi/ARBs and immunosuppression. DAPA CKD has demonstrated that dapagliflozin reduced the risk of CKD progression in patients with IgAn at high risk of progression (mean eGFR, 43.8 mL/min/1.73 m\(^2\), and median urinary albumin-to-creatinine ratio, 900 mg/g) for a median follow up of 2 years. EMPA KIDNEY demonstrated that empagliflozin was associated to a lower risk of progression of CKD than placebo in a pool of 853 patients with glomerular diseases also at higher risk of progression at 2 years of follow up. Based on both RCT, SGLT2i have been proposed as new therapeutic tools for management of IgAn. However, there is a lack of studies in real-world clinical practice. Thus, we aimed to evaluate the renal effect of SGLT2i at 12 months in a cohort of patients with biopsy proven IgAn.

Method: Multicenter retrospective observational study including all patients with biopsy proven IgAn who received SGLT2i in 2 hospitals in Spain. Results: 19 patients were included, followed up for 12 months. 73.7% were men with a mean age of 48.37±16.74 and a mean evolution of IgAN of 3.5 years before SGLT2i initiation. 21% presented type 2 DM. Oxford scores were: M0 68.42%, M1 26.31%; E0 78.95%, E1 5.79%; S0 68.42%, S1 26.31%; T0 84.21%, T1 5.26%, T2 5.26%. No patient presented with crescents, and 63-42% presented IF and TA. Before SGLT2i, 21% have received immunosuppression, and 2 were on steroids at the time of SGLT2i initiation (one budesonide). 94.7% were on ACEi/ARBs, 59.9% received dapagliflozin, 15.8% empagliflozin and 26.3% canagliflozin. At baseline, patients showed creatinine 1.10 (0.91-1.49) mg/dL, eGFR 69.84±28.46 ml/min/1.73 m\(^2\), and UACR 315.00 (210.75-590.75) mg/g. As showed in Table 1, there is a transient decline in eGFR at month 1 after SGLT2i but then, there was a tendency to an improvement in eGFR (from 69.84±28.46 at baseline to 87.83±31.33), and a tendency to a decrease in UACR from 315.00 (210.75-590.75) at baseline to 152.00 (86.75-423.75) at month 12. From month 3 after SGLT2i, a significant decrease in uric acid was observed, and, at month 6, better systolic and diastolic BP control was achieved. A tendency to higher Hb levels was also observed, as well as a decrease in weight at the end of follow up. Interestingly, SGLT2i withdrawal was only necessary in 1 patient who presented acute pyelonephritis and AKI.
Background and Aims: IgA nephropathy (IgAN) is the leading cause of primary glomerulonephritis and has limited treatment options, especially for high-risk patients. Approximately 30–45% of IgAN patients progress to end-stage kidney disease over a period of 20–25 years and proteinuria is the strongest predictor of disease progression [1]. BION-1301 is a novel, humanized monoclonal antibody that blocks a proliferation-inducing ligand (APRIL), a cytokine that is elevated in patients with IgAN. APRIL promotes the production of pathogenic galactose-deficient IgA1 (Gd-IgA1), resulting in immune complex formation and subsequent glomerular deposition, leading to inflammation and kidney injury. Blocking APRIL with BION-1301 is a potential disease-modifying approach to treating IgAN. Interim results from a Phase 1/2 trial of BION-1301 in patients with IgAN (NCT03945318) demonstrate rapid and durable reductions in proteinuria in Gd-IgA1 and sustained, clinically meaningful reductions in proteinuria with an acceptable safety profile [2].

Methods: CHK02-02 is a Phase 3, randomized, double-blind, placebo-controlled study to evaluate the effect of BION-1301 in adults with primary IgAN at risk of progressive kidney function loss. Approximately 272 patients will be enrolled across North America, South America, Europe and Asia-Pacific. Key eligibility criteria include biopsy-proven IgAN within the past 10 years (not due to secondary causes), eGFR ≥ 30 ml/min/1.73 m² (CKD-EPI) and total urine protein ≥ 1.0 g/day at screening. Patients must be stable on a maximally tolerated dose of angiotensin-converting enzyme inhibitor (ACEI)/angiotensin II receptor blocker (ARB) for at least 12 weeks prior to screening or intolerant to ACEI/ARB. Patients may also be on a stable dose of SGLT2i, mineralocorticoid receptor antagonists, and/or endothelin receptor antagonists for at least 12 weeks prior to screening.

The study will be comprised of a screening period (6 weeks), a double-blind treatment period (104 weeks), and a safety follow-up period (24 weeks). Patients will be randomized 1:1 to receive subcutaneous 600 mg BION-1301 Q2W or placebo for 104 weeks. Randomization will be stratified by region (Asia vs. Rest of World), baseline proteinuria (≥ 2 g/day vs. < 2 g/day) and eGFR (< 45 ml/min/1.73 m² vs. > 45 ml/min/1.73 m²). An additional – 20 patients with eGFR 20 to < 30 ml/min/1.73 m² will be enrolled into an exploratory cohort not included in the primary or secondary analyses.

Results: The primary endpoint is change in proteinuria (UPCR from a 24-hour urine collection) from baseline to week 36. The key secondary endpoint is change in eGFR from baseline to week 104. Additional secondary endpoints will evaluate the effect of BION-1301 vs. placebo on composite clinical outcomes including patients experiencing at least one of the following: 30% or 40% reduction in eGFR, eGFR < 15 ml/min/1.73 m², dialysis, kidney transplantation or all-cause mortality. Safety endpoints include type, incidence, severity, and relatedness of adverse events (AEs) and serious AEs. Exploratory endpoints include impact of BION-1301 on disease biomarkers and health-related quality of life as well as analysis of BION-1301 pharmacokinetics and immunogenicity.

Conclusion: BION-1301 provides a potentially disease-modifying approach for the treatment of IgAN by directly targeting the disease pathogenesis. Interim results of the Phase 1/2 open-label trial demonstrated proof-of-concept for BION-1301 to reduce pathogenic Gd-IgA1 and provide sustained, clinically meaningful reductions in proteinuria while supporting SC dosing at 600 mg
Q2W [2]. The Phase 3 trial will evaluate the effect of BION-1301 vs. placebo on proteinuria, eGFR and composite clinical endpoints and key safety measures in adult patients with IgAN at risk of progressive kidney function loss.

REFERENCES
2. Barratt, J Kooienga, L Agha, I et al. Updated Interim Results of a Phase 1/2 Study of BION-1301 in Patients with IgA Nephropathy. ASN Kidney Week 2022;FR-PO659.

#5639
TARGETING BAFF AND APRIL IN IGA-NEPHROPATHY
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Background and Aims: B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are critical factors in the differentiation and longevity maintenance of the B-cells pool thereby mediating humoral immunity. BAFF and APRIL are involved in initiating B-cells to become self-reactive and elevated levels of these cytokines are detected in the sera of patients with systemic autoimmune diseases. The aim of the study was to estimate role of APRIL and BAFF in IgA-nephropathy (IgAN) patients and to determine the appropriate IgAN treatment based on the assessment of BAFF and APRIL dynamics in IgAN patients’ sera after 6 months of different treatments.

Method: The 52 IgAN patients aged 32.0 (27.0; 36.0) y.o., male/female ratio as 34/18 despite using of renin-angiotensin-aldosterone system inhibitors (RAASIs) for 6 months with PU 1,8 (1,0; 1,9) g/day and estimated glomerular filtration rate (eGFR) 78 (61; 103) ml/min were divided into 3 treatment groups: 1 group (n = 20) – received glucocorticoids (GC) regimen Pozzi protocol, 2 group (n = 20) – received hydroxychloroquine (HCQ) twice a day, 3 group (n = 12) – received (RAASIs) in maximal tolerated dose. The control group included age- and sex-matched healthy donors (n = 10). The number of B-cells in peripheral blood was identified by flow cytometry method. The concentrations of total IgM, IgG, IgA, IgE, APRIL and BAFF were determined by ELISA method using commercial kits. Statistical analysis was done using Statistica 10.0.

Results: Despite the absence of statistically significant differences in the number of B-lymphocytes the increased levels of total IgM, IgA and IgE (p = 0.001) as well as APRIL (5336 (3574;5965) pg/ml vs 4543 (4518 ÷ 4755) pg/ml (p = 0.05) and BAFF 378 (191;541) vs 336 (257;424) pg/ml (p = 0.07) were established in sera of IgAN patients as compared to control group, respectively. The initial APRIL level was correlated with the degree of tubular atrophy with interstitial fibrosis (R = 0.40, p = 0.05) and serum IgG level (R = 0.35, p = 0.05) in IgAN patients. After 6 months of treatment proteinuria was significantly reduced in HCQ (p = 0.03) and GC (p = 0.02) groups while kidney function was stable in all patients. The dynamic of immunological parameters is presented in the Table 1. It was established that HCQ treatment in IgAN patients decreased the production of IgM (p = 0.01) and IgG (p = 0.02) as well as serum concentration of the APRIL factor (p = 0.05) which correlated with the tendency to eGFR increase (R = –0.46, p = 0.06) as well as with clinical effect of therapy improvement of (R = –0.45, p = 0.04). There were no statistical changes in the level of the BAFF factor in patients with HCQ. After GC treatment a decrease in the synthesis of serum IgA (p = 0.01) as well as trend to decline of B-cells number (p = 0.07) were determined, while in patients treated with RAASIs a significant increase in IgE production (p = 0.05) and tendency in elevation in BAFF levels (p = 0.06) were observed.

Conclusion: Immunological changes may be the determining factors in the choice of treatment in IgAN patients.
blood pressure and serum K+ that received only standard treatment. Protein excretion in 24 h urine, eGFR, received 25 mg of eplerenone daily besides ACEi or ARBs, and a control group with ACEi or ARBs. Patients were divided in the active treatment arm, who

Method:
In this prospective open-label study, we evaluated the effects of treatment in patients with kidney disease due to glomerulonephritis.

deterioration. Nevertheless, there is scanty evidence on the effect of eplerenone in patients with kidney disease due to glomerulonephritis. Type 1 receptor blockers (ARB) can delay kidney disease progression, but plasma aldosterone levels may increase to a significant extent even after the initiation of such treatment. Thus, administration of mineralocorticoid receptor antagonists such as spironolactone, on top of treatment with ACEi or ARBs, can further reduce proteinuria and systolic blood pressure in patients with chronic glomerulonephritis.

Table 1: Immunological parameters in peripheral blood of IgAN patients before and 6 months after therapy, Me (25; 75)%. #4590

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<tr>
<th>Immunological parameters</th>
<th>HCQ (n = 20) after 1</th>
<th>HCQ (n = 20) after 2</th>
<th>GC (n = 20) after 3</th>
<th>GC (n = 20) after 4</th>
<th>RAASIs (n = 12) after 5</th>
<th>RAASIs (n = 12) after 6</th>
<th>p</th>
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</thead>
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<tr>
<td>CD19+ B-cells, %</td>
<td>10.2 (7.7; 13.9)</td>
<td>10.8 (7.2; 12.5)</td>
<td>10.4 (6.7; 14.1)</td>
<td>8.3 (7.0; 11.2)</td>
<td>8.8 (5.8; 9.7)</td>
<td>7.7 (5.9; 9.7)</td>
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<tr>
<td>IgM, g/l</td>
<td>1.99 (1.42; 2.99)</td>
<td>1.71 (1.08; 2.04)</td>
<td>1.93 (1.35; 2.61)</td>
<td>2.05 (1.67; 2.42)</td>
<td>1.74 (0.97; 2.45)</td>
<td>1.25 (1.20; 1.97)</td>
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<td>IgG, g/l</td>
<td>14.15 (12.38; 15.90)</td>
<td>10.72 (9.62; 12.30)</td>
<td>11.80 (9.80; 13.13)</td>
<td>12.21 (11.59; 17.63)</td>
<td>12.79 (11.47; 18.38)</td>
<td>13.09 (11.78; 20.51)</td>
<td>ps 1-2 = 0.02</td>
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<td>IgA, g/l</td>
<td>2.59 (1.98; 3.99)</td>
<td>3.45 (2.91; 4.28)</td>
<td>3.86 (3.61; 4.70)</td>
<td>2.60 (1.69; 3.33)</td>
<td>3.82 (2.28; 4.48)</td>
<td>3.25 (2.93; 3.89)</td>
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<tr>
<td>IgE, IU/ml</td>
<td>21.55 (7.45; 9.09)</td>
<td>11.29 (6.24; 132.53)</td>
<td>19.89 (6.82; 71.96)</td>
<td>23.69 (11.31; 92.31)</td>
<td>25.09 (13.97; 44.37)</td>
<td>52.78 (30.62; 61.30)</td>
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<td>APRIL, pg/ml</td>
<td>5639 (5567; 5946)</td>
<td>5305 (4747; 5693)</td>
<td>3906 (2944; 5409)</td>
<td>4760 (4638; 4920)</td>
<td>4937 (3534; 6784)</td>
<td>5081 (4641; 5463)</td>
<td>ps 4-6 = 0.05</td>
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<td>BAFF, pg/ml</td>
<td>498 (341; 864)</td>
<td>398 (249; 1493)</td>
<td>319 (178; 500)</td>
<td>390 (307; 822)</td>
<td>367 (121; 489)</td>
<td>626 (256; 1740)</td>
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#4463

A PROSPECTIVE STUDY OF EPLERENONE IN THE TREATMENT OF PATIENTS WITH GLOMERULONEPHRITIS

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Background and Aims: Clinical evidence suggests that high aldosterone plasma levels contributes to progressive kidney disease. Although administration of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin type 1 receptor blockers (ARB) can delay kidney disease progression, plasma aldosterone levels may increase to a significant extent even after the initiation of such treatment. Thus, administration of mineralocorticoid receptor antagonists such as spironolactone, on top of treatment with ACEi or ARBs has been shown to reduce albuminuria and slow down kidney function deterioration. Nevertheless, there is scanty evidence on the effect of eplerenone in patients with kidney disease due to glomerulonephritis.

Method: In this prospective open-label study, we evaluated the effects of eplerenone in patients with biopsy proven glomerulonephritis already treated with ACEi or ARBs. Patients were divided in the active treatment arm, who received 25 mg of eplerenone daily besides ACEi or ARBs, and a control group that received only standard treatment. Protein excretion in 24 h urine, eGFR, blood pressure and serum K+ levels were measured at 3, 6 and 12 months after study initiation.

Results: Out of 83 patients who were screened, 62 patients were included in the final analysis. Twenty-six received eplerenone and 36 were treated with ACEi (25) or ARBs (9) alone (controls). After 1 year of treatment with eplerenone, proteinuria decreased from 1597 to 1145 mg/24 h while it did not alter in controls. Eplerenone reduced proteinuria especially in those with baseline proteinuria of >1000 mg/24 h. Kidney function remained stable (from eGFR: 82.51±22.6 to 84.68±31.7 ml/min/1.73 m², p = 0.8) and showed a non significant deterioration in controls (from eGFR: 68.39±26.2 to 66.63±29.8 ml/min/1.73 m², p = 0.08). Systolic blood pressure was significantly reduced in the active treatment arm (from 128±17.3 to 126.3±10.93 mmHg, p = 0.03), whereas eplerenone did not increase serum K+ levels or had any other significant adverse effect.

Conclusion: Administration of eplerenone at a dose of 25 mg/day, on top of treatment with ACEi or ARBs, can further reduce proteinuria and systolic blood pressure in patients with chronic glomerulonephritis.

#4463

JAPANESE AND WHITES SHARE SIMILAR IPTACOPAN PHARMACOKINETICS AND PHARMACODYNAMICS

Robert Schmouder1, Guido Jung2, Prasanna Nidamarthy3 and Kenneth Kulmatycki4

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Background and Aims: Iptacopan (LNP023) is a first-in-class, oral, proximal complement inhibitor that specifically binds to Factor B and inhibits the alternative complement pathway (AP). Current Phase III studies of iptacopan focus on diseases associated with AP activation, such as paroxysmal nocturnal hemoglobinuria, C3 glomerulonephritis, IgA nephropathy, and atypical hemolytic uremic syndrome. These studies are enrolling patients across geographical regions and ethnicities, including those from Japan. The aim of this study was to evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of iptacopan in Japanese patients.

Method: CLNP023 × 1102 was a randomized, subject-blinded, placebo-controlled, single-dose Phase I study conducted in Japan in healthy Japanese male subjects to assess safety, tolerability, PK, and AP blood biomarkers (Wieslab, Bb) in three dose cohorts, 25, 100, and 400 mg (8 active/2 placebo per cohort). Subjects were dosed on day 1 and observed for 96 hours post-dose. PK and PD data from this study was compared to White data from the similarly designed, previous CLNP023 × 2101 first-in-human study.

Results: Iptacopan was well tolerated in both Japanese and White subjects. White subjects were on average 15.7 years older and 19.5 kg heavier than Japanese subjects. Iptacopan mean (±SD) Cmax and AUCinf as well as mean (±SD) % change from baseline at 12 hours post-dose for Wieslab and Bb by dose are shown in the table below. All three dose groups manifested a general trend of increased systemic exposure and increased AP biomarker inhibition with increasing dose in both Japanese and White subjects.

Conclusion: Japanese and White healthy subjects had similar PK and PD results at all dose levels. The slightly higher Cmax and AUCinf in Japanese subjects may be explained in part by the lower average weight of these subjects. This study provides reassurance that there are no clinically meaningful differences in the human pharmacology of iptacopan between these ethnic groups.
#5217

PROTOCOL AND PRELIMINARY RESULTS OF DAPAGLIFLOZIN IN INACTIVE LUPUS NEPHRITIS CROSS-OVER RANDOMIZED TRIAL

Gisele Vajgel1, Carlos Miranda Filho2, Camila Oliveira1, Denise Maria Costa1, Maria Alina Cavalcante1, Brazilian Silva Junior3, Camilla Lima3, Paula Sandrin-Garcia3 and Lucila Valente4

1Hospital das Clínicas, EBSERH/Universidade Federal de Pernambuco, Division of Nephrology, Recife, Brazil, 2Universidade Federal de Pernambuco, Centro de Ciências Médicas, Recife, Brazil and 3Universidade Federal de Pernambuco, Instituto LIKA, Recife, Brazil

Background and Aims: Sodium-glucose co-transporter 2 (SGLT2) inhibitors slow the progression of chronic kidney disease (CKD) with and without type 2 diabetes. Lupus nephritis (LN) patients under immunosuppression were excluded from the most important trials with SGLT2 inhibitors. Thus, efficacy and tolerance of these drugs are unknown in such patients. The present trial will assess the effect of Dapagliflozin in patients with inactive Lupus Nephritis with residual proteinuria.

Method: For this cross-over randomized trial, we will include adult patients with LN class III, IV (+/- V) without active nephritis but with proteinuria ≥ 20mg/24h or UPC > 200mg/g and eGFR ≥ 20ml/min, in the maintenance treatment. RAAS inhibition should be stable for at least four weeks before the randomization. We will exclude patients with other etiologies of CKD, those with active LN lesions on the recent biopsy (AI>2), use of induction therapy in the last 12 months (Cyclophosphamide, Mycophenolate Mofetil > 2 g/day and Calcineurin inhibitors) and prednisone dose ≥ 20 mg/day. Due to safety issues, we will exclude patients with recurrent urinary infections (> 3 times/year). They will be randomized to receive Dapagliflozin 10mg on top of standard of care therapy or not. After 24 weeks the groups will be switched and those without Dapagliflozin will receive it for the next 24 weeks. Primary endpoint will be reduction of proteinuria compared to baseline at 6 and 12 months. Secondary endpoints will include sustained reduction of eGFR > 30%; changes in weight and blood pressure compared to baseline; and number of infections on Dapagliflozin treatment versus exclusive standard of care therapy. The sample size was calculated for 28 patients enrolled providing 80% power to detect a 25% relative risk reduction in proteinuria (α level of 0.05).

Results: From 85 screened class III, IV (+/- V) LN patients under maintenance therapy, we excluded 65 due to active nephritis, low proteinuria or low eGFR. Until now we included 17 patients that were randomized 1:1 to start the treatment with Dapagliflozin on top of standard care or remain with the usual therapy for 24 weeks. Patients' baseline characteristics are described in Table 1. All patients randomized were using Mycophenolate Mofetil ≤ 2 g/day and RAAS inhibition and 14 of them were receiving Hydroxychloroquine.

Conclusion: We expect that the present trial will determine whether the SGLT2 inhibitor Dapagliflozin, added to LN maintenance therapy, could safely reduce the residual proteinuria of inactive LN patients.

Table 1: Patients’ baseline characteristics.

<table>
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<tr>
<th>Patient</th>
<th>Initial Group</th>
<th>Sex</th>
<th>Age (years)</th>
<th>NL class</th>
<th>Activity index (AI)</th>
<th>Chronicity index (CI)</th>
<th>Time from Biopsy</th>
<th>Systolic Pressure</th>
<th>Diastolic Pressure</th>
<th>BMI</th>
<th>SCI (mg/dL)</th>
<th>eGFR (ml/min)</th>
<th>Proteinuria 24h (mg)</th>
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Iptacopan (LNP023) is a first-in-class, oral, proximal complement inhibitor that specifically binds to Factor B and inhibits the alternative complement pathway (AP). Current Phase III studies of iptacopan focus on diseases associated with AP activation, such as paroxysmal nocturnal hemoglobinuria, C3 glomerulonephritis, IgA nephropathy, and atypical hemolytic uremic syndrome. Early modeling efforts suggested that an iptacopan concentration of ~1000 ng/mL would provide near-maximal AP inhibition. The aim of this study was to evaluate the PK of oral iptacopan in healthy subjects to determine the dose that results in a steady-state concentration over the entire 12-h dosing interval.

**Background and Aims:** Iptacopan (LNP023) is a first-in-class, oral, proximal complement inhibitor that specifically binds to Factor B and inhibits the alternative complement pathway (AP). Current Phase III studies of iptacopan focus on diseases associated with AP activation, such as paroxysmal nocturnal hemoglobinuria, C3 glomerulonephritis, IgA nephropathy, and atypical hemolytic uremic syndrome. Early modeling efforts suggested that an iptacopan concentration of ~1000 ng/mL would provide near-maximal AP inhibition. The aim of this study was to evaluate the PK of oral iptacopan in healthy subjects to determine the dose that results in a steady-state concentration over the entire 12-h dosing interval.

**Method:** In this blinded, controlled, randomized study, a total of 32 healthy subjects were enrolled into 5 cohorts receiving twice-daily dosing for 14 days: placebo (n = 8) or iptacopan 25, 50, 100, or 200 mg (n = 6 per group). Plasma iptacopan concentration was intensively measured for 72 hours post day 14 dose using a validated LC-MS/MS assay (LLOQ = 1 ng/mL).

**Results:** Iptacopan treatment was safe and well tolerated at all dose levels. Iptacopan steady-state concentration-time curves are shown below (Figure 1). The mean half-life was moderately long at 18 to 25 hours. The inter-subject variability (CV%) of iptacopan Cmax and AUCinf was low at approximately 12% to 27%, and both parameters were under-dose proportional with increasing dose. At all time points from 0 to 12 hours, mean iptacopan concentration for the 200-mg dose cohort was >1000 ng/mL.

**Conclusion:** Iptacopan was rapidly absorbed, had low inter-subject variability, and a moderately long half-life. Only the 200-mg b.i.d dose produced mean iptacopan concentrations of >1000 ng/mL over the dosing interval, and thus is expected to result in near-complete, continuous AP inhibition. These results support the rationale for use of iptacopan 200 mg twice daily as the therapeutic dose in ongoing clinical trials and provide evidence of durable AP inhibition in patients administered oral iptacopan therapy.

**Conclusion:** Combined oral diuretics with furosemide, amiloride and hydrochlorothiazide is more effective and safer than intravenous furosemide for the treatment of refractory nephrotic edema. These results make amiloride a promising diuretic and further trials with larger sample sizes and longer follow-up are needed in this regard.

**Method:** We conducted a prospective randomized trial in 22 patients with diuretic resistant nephrotic edema. Based on a computer-generated randomization we assigned patients to receive either intravenous furosemide (40 mg bolus and continuous administration of 5 mg/h) or oral furosemide (40 mg/day) and hydrochlorothiazide/amiloride (50/5 mg/day). Clinical and laboratory measurements were performed daily, for five days (body weight, urinary output, blood pressure and hydration status by bioimpedance twice, creatinine, urea, albumin, hematocrit, Na, K, Ca, Mg, bicarbonate, pH). The primary outcome was weight and hydration status change from baseline to day 5. Secondary outcomes were safety outcomes (low blood pressure, severe dyselectrolytemia, acute kidney injury or aggravated hypervolemia).

**Results:** The patients were equally distributed between the two groups. Mean age was 47.77 ± 15.97 (34.5% females and 45.5% males). Half of the patients had membranous nephropathy (45.5%), followed by minimal change disease (22.7%) and lupus nephritis (9.1%). 86.4% of patients had their first episode of nephrotic edema. The mean weight decrease was of significantly larger magnitude in the combined oral diuretics group compared with the intravenous furosemide group (-7.97 ± 2.83 [SD] vs -4.5 ± 2.6 [SD] kg; p = 0.018). Although the increase in 24-hour urine sodium excretion was higher in combined oral diuretics as compared to intravenous furosemide group, this increment was not statistically significant different (26.79 ± 33.48 [SD] vs 16.04 ± 42.81 mmol/24 h [SD]; p = 0.5). Mean values for changes in systolic and diastolic BP, 24-hour urine volume, hydration status measured by bioimpedance were not significantly different between the two groups. A total of 5 patients could not be followed through, 4 in the intravenous furosemide (two patients experienced low blood, one patient had no response to iv furosemide and one patient suffered from insomnia due to iv pump) and one patient in the oral combination of diuretics group had severe hyperkalemia (>6.5 mmol/l).

**Conclusion:** Combined oral diuretics with furosemide, amiloride and hydrochlorothiazide is more effective and safer than intravenous furosemide for the treatment of refractory nephrotic edema. These results make amiloride a promising diuretic and further trials with larger sample sizes and longer follow-up are needed in this regard.
Conclusion: 3 months after treatment with prednisone 1mg/kg was initiated, reducing proteinuria to 6g/day, and stabilized at that level, so proteinuria dropped from 9g to 6g/24H, and stabilized at that level. Immunofluorescence was negative. EVOLOCUMAB was stopped and promoted. No increase in cell number was observed by light microscopy and showed minimal changes in disease. There was a mild focal mesangial proliferative glomerulonephritis. AST and ALT, transaminase, and hepatitis B and C serology were performed.

Results: The occurrence of reversible glomerular lesions reported here should be considered as a potential adverse effect when administrating a prolonged treatment of EVOLOCUMAB. We suggest performing urine test at least once a week, to detect early proteinuria in patients receiving this medication.

#5680
FIRST REPORT OF AN EVOLOCUMAB INDUCED NEPHROTIC SYNDROME
Kayisi Saleh1,2,3, Hanaa Badawaki1, Mahmoud Baz4 and Ibrahim Farah4
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Background and Aims: Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9 inhibitors) reduce LDL-C and short-term risk of cardiovascular events by acting on the proprotein convertase subtilisin/kexin type 9 (PCSK9), an enzyme produced in the liver. This article highlights the case of a 69-year-old man who developed nephrotic syndrome (NS) secondary to EVOLOCUMAB injection. To our knowledge, this is the first time that minimal change disease is described as associated with EVOLOCUMAB.

Method: Case Report describing a 69-year-old male with coronary artery disease who started EVOLOCUMAB injection every two weeks. Six weeks later, after the third dose of EVOLOCUMAB, he developed edema, and high blood pressure 180/90 mmHg. Laboratory tests showed a creatinine of 88 μmol/l and a GFR of 77 ml/min/m² associated with severe proteinuria of 9g/24H, normal level of anti-PLA2R, negative ANA (<1/80) and ANCA (<1/80), and negative hepatitis B and C serology.

Results: Kidney biopsy was obtained to investigate this nephrotic syndrome and showed minimal change disease. There was a mild focal mesangial prominence not exceeding three or four cells per segment by light microscopy (LM). Immunofluorescence was negative. EVOLOCUMAB was stopped and proteinuria dropped from 9g to 6g/24H, and stabilized at that level, so treatment with prednisone 1mg/kg was initiated, reducing proteinuria to 3g/24H one month later with clinical improvement.

Conclusion: The occurrence of reversible glomerular lesions reported here should be considered as a potential adverse effect when administrating a prolonged treatment of EVOLOCUMAB. We suggest performing urine test at least once a week, to detect early proteinuria in patients receiving this medication.

#4209
A COMPARATIVE RETROSPECTIVE STUDY OF PATIENTS WITH ADPKD: FIRST RESULTS RELATING TO THE USE OF TOLVAPTAN
Theodora Oikonomaki, Alexandros Nikolaos Liatsos, Angeliki Paikopoulou, Dimitris Avgikos, Vasiliki Choutlidou and Christallenia Christodoulidou
Evangelismos General Hospital, Nephrology, Athens, Greece

Background and Aims: Autosomal Dominant Polycystic Disease (APKD) is the fourth leading cause of End Stage Renal Failure (ESRD). Since 2015, the administration of Tolvaptan has been approved in patients with APKD at high risk of progression to ESRD (Mayo classification criteria, classes 1C-D).

Method: In this study we compare the characteristics of APKD patients who received Tolvaptan (45/15 mg) in relation to those who did not receive but followed the periodic check-up. There are 33 people with an average age of 44.17 ± 13.6 years. Tolvaptan was administered to 9 (27.3%) patients who met the Mayo classification criteria for its administration. The mean follow-up time for all the patients was 11.41 ± 4.7 months and for those taking tolvaptan it was 10.6 ± 3.9 months. Values of urea, creatinine, plasma sodium, specific gravity and urine osmolarity were determined at the start of follow-up and compared with those at the last visit.

Results: A significant reduction was observed in the values of urea, osmolality and specific gravity of urine after one year of tolvaptan use compared to the group that did not receive the treatment and thus no titration of the drug dose was needed. In the same group, marginally higher values of the plasma sodium were observed, but within normal limits. The indicators of renal function in both groups did not show any change.

Conclusion: At one year of follow-up, APKD patients who received Tolvaptan did not exhibit worsening of the kidney function. We observed changes in the values of urea, urine specific gravity and urine osmolality associated with our instructions to drink more water, showing good compliance with the treatment.

#5801
EXTENDED LOW DOSE RITUXIMAB REGIMEN FOR THE TREATMENT OF ADULT PATIENTS WITH STEROID-DEPENDENT AND FREQUENTLY RELAPSING MINIMAL CHANGE DISEASE
Irene Mínguez Toral, Javier Villacorta Pérez, Maria García Vallejo, Jorge Sánchez Iglesias, Guillermo Fernández, Marcos Piris, Fernando Caballero Cebrían, Esther Casillas, Vanessa Lopes and Milagros Fernandez Lucas
Hospital Universitario Ramón y Cajal, Nephrology, Madrid, Spain

Background and Aims: Patients with frequently relapsing and steroid-dependent minimal change disease (MCD) imply a therapeutic challenge for nephrologists. The use of steroid sparing agents such as cyclosporine, rituximab and mycophenolate, allows minimization of steroids exposure among these patients. In children and adults, Rituximab has demonstrated safety and efficacy in some studies although there is no established treatment regimen. This study aims to demonstrate that a low dose extended regimen of rituximab is an effective alternative for preventing relapses among these patients.

Method: This is a single-centre retrospective descriptive study of a case series of adult MCD patients from Ramón y Cajal Hospital in Madrid, Spain. Since 2019, patients with steroids-dependent or frequently relapsing MCD were treated with a low dose extended protocol of Rituximab as follows: 500 mg of rituximab once remission is achieved with steroid therapy, and four additional doses at month +6, +18 and +30 during the follow-up. Relapse free survival was analyzed after rituximab therapy.

Results: Eight patients with a median age of 42 years (22–70 years) who received at least one dose of intravenous rituximab were included. Four of the patients (50%) had previously received additional immunosuppressive regimens (including cyclophosphamide, chlorambucil cyclosporine, mycophenolate or ACTH). Two of them (25%) had frequent relapses and the remaining six (75%) had steroid-dependent behaviour. After a median of 2 years (IQR, 1-3.3) of follow-up, 6 out of 8 (75%) patients stayed under remission.

Table 1: Values of urea, creatinine, plasma sodium, specific gravity and urine osmolality at the start of follow-up and at the last visit, of the two groups of the study.

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<tr>
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<th>Initial</th>
<th>Final</th>
<th>Initial (Tolvaptan)</th>
<th>Final (Tolvaptan)</th>
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<td>46.9 (30.6)</td>
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<td>1.26 (0.9)</td>
<td>1.45 (1.1)</td>
<td>0.98 (0.43)</td>
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<td>137.9 (2.1)</td>
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<td>444.7 (186.8)</td>
<td>444.7 (186.8)</td>
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REFERENCES
experiencing the remaining two one relapse at one month and at one year, respectively, after the first rituximab dose. Comparing relapses during the two years-period before and after rituximab use, the median relapse rate per patient dropped from 2.8 (IQR, 2-4) to 0.5 (IQR, 0-1; P = 0.001) (Fig. 1). No patient experienced rituximab related side effects nor infections during the study period.

Conclusion: In MCD patients, the administration of rituximab in an extended low-dose regimen as corticosteroid-sparing therapy appears to be safe and effective in most of the patients for preventing relapses. This regimen allows minimization exposure to rituximab as well as disease remission during a longer period of time.

#4052
IMMUNOSUPPRESSIVE TREATMENT RESULTS IN PATIENTS WITH PRIMARY IGA NEPHROPATHY IN TURKIYE: A NATIONWIDE STUDY

Aysegul Oruc1, Abdullah Sunnu2, Aydin Turkmen3, Taner Basturk4, Egemen Cebeci5, Kenan Turgutalp6, Hakki Çetinkaya7, Muge Uzerk Kibar8, Nurhan Seyahi9, Erhan Tatari2, Metin Ergül11, Ülver Dericl12, Deniz Ayli13, Musa Panar13, Betul Bakari5, Rumeyza Kazancioglu16, Abdullahic Yildiz17, Zulfikar Yilmaz18, Kultigin Turkmen19, Onur Tunca20, Mehmet Koc21, Sim Kutlau22, Hasan Mızıkozagioglu23, Alper Azak24, Burcu Boztepe25, Sedat Ustündag26, Seda Safak Ozturk1, Abdullahic Unsal1, Serhat Karadag1, Gulizar Manga Sahin1, Ezgi Coskun Yenigun15, Necmi Eren1 and Mustafa Gullulu1

1 Bursa Uludag University Faculty of Medicine, Nephrology, Bursa, Turkey, 2 Medipol University, Nephrology, Istanbul, Turkey, 3 Istanbul University, Faculty of Medicine, Istanbul, Turkey, 4 University of Health Sciences, Etfal Hamidiye Training and Research Hospital, Nephrology, Istanbul, Turkey, 5 Istanbul Provincial Directorate of Health Istanbul Haseki Training and Research Hospital, Nephrology, Istanbul, Turkey, 6 Mersin University Medical School, Training and Educational Hospital, Mersin, Turkey, 7 University of Health Sciences, Sultan 2. Abdülhamid Han Training and Research Hospital, Nephrology, Istanbul, Turkey, 8 Health Ministry of Turkey Republic Ankara Bilkent City Hospital, Nephrology, Ankara, Turkey, 9 Istanbul University, Cerrahpasa Faculty of Medicine, Nephrology, Turkey, 10 Izmir Provincial Directorate of Health Bozyaka Education and Research Hospital, Nephrology, Izmir, Turkey, 11 Kocaeli University, Faculty of Medicine, Nephrology, Kocaeli, Turkey, 12 Gazi University, Faculty of Medicine, Nephrology, Ankara, Turkey, 13 Ministry Of Health Dışkapı Yıldırım Beşazet Training And Research Hospital, Nephrology, Ankara, Turkey, 14 Sakarya University, Faculty of Medicine, Nephrology, Sakarya, Turkey, 15 Ankara Provincial Health Directorate Ankara Training and Research Hospital, Nephrology, Ankara, Turkey, 16 Bezmialem Yakif University, Faculty of Medicine, Nephrology, Istanbul, Turkey, 17 Istanbul Provincial Health Directorate Istanbul Bakırköy Dr.Sadi Konuk Education And Research Hospital, Nephrology, Istanbul, Turkey, 18 Dicle University Faculty of medicine, Nephrology, Diyarbakir, Turkey, 19 Necmettin Erbakan University Meram Faculty Of Medicine Hospital, Nephrology, Konya, Turkey, 20 Afyonkarahisar University of Health Sciences, Faculty of Medicine, Nephrology, Afyonkarahisar, Turkey, 21 Marmara University, Faculty of Medicine, Nephrology, Istanbul, Turkey, 22 Ankara University, Faculty of Medicine, Nephrology, Ankara, Turkey, 23 Baskent University Faculty of Medicine, Dr. Turgut Noyan Adana Application and Research Hospital, Nephrology, Adana, Turkey, 24 Balikesir Provincial Health Directorate Ataürk City Hospital, Nephrology, Balikesir, Turkey, 25 Istanbul Provincial Health Directorate Haydarpaşa Numune Training And Research Hospital, Nephrology, Istanbul, Turkey and 26 Trakya University, Faculty of Medicine, Edirne, Turkey

Background and Aims: IgA nephropathy (IgAN) is the most common cause of primary glomerulonephritis in Turkey, as well as all over the world. Along with the frequent occurrence, deleterious renal outcome odds make treatment approaches important. Additionally, for high-risk individuals immunosuppressive treatment (IST) is recommended. However, studies to date revealed conflicting results regarding IST. Therefore, we aimed to investigate IST results among IgAN patients which is the leading primary glomerulonephritis in Turkey.

Method: The data of 1656 IgAN patients in the Primary Glomerular Diseases Study of the Turkish Society of Nephrology Glomerular Diseases Study Group (TSN-GOLD) were analyzed. A total of 506 primary IgAN patients (63.4% male, mean age 38.9±12.5 years) were included and divided into two groups according to treatment protocols as isolated corticosteroid (69.6%) and combined IST (30.4%) groups. The median follow-up duration was 24 (3-218) months.

Results: Remission (66.6% partial remission, 33.4% complete remission) was achieved in 70.6% of patients. Systolic and diastolic blood pressures, urea, creatinine, and proteinuria levels were lower, and eGFR levels were higher in responsive patients (Table 1). There was no difference between the treatment groups in terms of remission rates (p = 0.147) and remission types' rates (p = 0.279). Remission rates were different between treatment subgroups. However, there was no difference between the treatment subgroups according to the remission types (p = 0.132) (Table 2). Complete remission was lower in the S1 and T1 categories (p = 0.003 and 0.039, respectively). The serious infection was higher in the combined IST group (17.1% vs 2.9%). The outcome data of 229 individuals was evaluated, 40 of 229 (17.5%) developed ESRD and 8 were dead. In the multivariate analysis, eGFR (OR 1.007, 95%CI 1.001-1.013, p = 0.020), proteinuria (OR 1.000, p = 0.009), MEST-C T2 (OR 1.912, 95%CI 1.216-3.065, p = 0.005), MEST-C T2 (OR 0.226, 95%CI 0.102-0.501, p = 0.001) were found to be significant regarding remission.

Conclusion: IST provides remission in high-risk IgAN patients but was associated with serious adverse events. The fact that the remission rates were similar between the treatment groups and that the complete remission rate was low in chronic changes supports the necessity of determining the treatment choice according to patient characteristics.

Figure 1: Box plot of the number of nephrotic syndrome relapses during the two years-period before and after rituximab administration in the study group.
The proportion of unaffected glomeruli was independent predictor of kidney outcome in patients with ANCA-associated GN.

#4834
THE PROPORTION OF UNAFFECTED GLOMERULI IS A ROBUST PROGNOSTIC FACTOR OF KIDNEY OUTCOME IN PATIENTS WITH ANCA-ASSOCIATED GLOMERULONEPHRITIS

Seung Min Song, Hyun Suk Lee, Minhyung Kim, Min Young Jang, Jeunseok Jeon, Hye Ryoun Jang, Gee-Young Kwon, Woosung Huh, Yoon-Goo Kim and Jung Eun Lee

Samsung Medical Center, Division of Nephrology, Department of Medicine, Seoul, Korea, Rep. of South Korea

Background and Aims: Anti-neutrophil cytoplasmic antibody (ANCA) associated glomerulonephritis (GN), the most common form of secondary GN in elderly (>60 years), requires immunosuppressive treatment that may increase risk of opportunistic infections. This study evaluated the prognostic value of clinical factors and histopathologic findings affecting kidney outcome in ANCA-associated GN patients.

Method: From 2000 to 2018, we identified 106 adults (≥ 18 years old) who were pathologically confirmed as ANCA-associated GN. The number of normal, crescent, and sclerotic glomeruli was recorded for each biopsy by slide review. The primary outcome was incident end stage kidney disease (ESKD).

Results: The age was 67 (57-73) years, the estimated glomerular filtration rate (eGFR) was 19 (11-36) mL/min/1.73 m², and % of normal glomeruli in kidney specimen was 25 (11-47) %. Overall kidney survival was 85% and 76% at 1 and 5 years, respectively. Among clinical variables, lower eGFR (<15.7 mL/min/1.73 m²) was independently associated with increased risk of incident ESKD. Multivariate Cox proportional hazard model including both clinical and histological variables demonstrated that % of normal glomeruli (aHR, 0.960; 95% confidence interval [CI], 0.935-0.986; p < 0.001) was independently associated with increased risk of incident ESKD, independently of eGFR and other pathological findings. When the % of normal glomeruli was divided by quartiles, the risk of incident ESKD in the lowest quartile was significantly increased compared to the highest quartile (<11%; HR, 5.986; 95% CI, 2.114-16.950 vs. > 46%; p < 0.001).

Conclusion: The proportion of unaffected glomeruli was independent predictor of kidney outcome in patients with ANCA-associated GN.

#5835
A LOW DOSE GLUCOCORTICOID, LOW DOSE CYCLOPHOSPHAMIDE, RITUXIMAB TREATMENT PROTOCOL AS INDUCTION THERAPY IN ANCA ASSOCIATED VASCULITIS PATIENTS

Georgios Spanos, Styliani Paschou, Marianna Bakou, Alexandros Atalla, Christos Bantis, Stylianos Fragidis, Livia Karmen Armetzoiou and Gerasimos Bamichas

General Hospital of Thessaloniki “G. Papanikolaou”, Nephrology Department, Thessaloniki, Greece

Background and Aims: There has been a considerable improvement in the survival of patients with ANCA associated vasculitis (AAV) since the introduction of immunosuppressive therapy. Nowadays early deaths are attributable to infection while cardiovascular disease, infection and malignancy are the most common causes in long term mortality in these patients. High-dose glucocorticoids and cyclophosphamide have numerous dose-dependent adverse effects and are associated with those events. The aim of this study is to investigate the efficacy and safety a low dose glucocorticoids, low dose cyclophosphamide, rituximab treatment protocol in AAV patients.

Method: This is a single-centre cohort study of patients on a combination of reduced-dose oral glucocorticoids, rituximab and low-dose pulsed intravenous cyclophosphamide followed by a maintenance regimen of rituximab and tapered steroid for the treatment of AAV (table). Data shown as median (IQR).

Results: Nine patients (3 women) aged 62.4 (55/67.8) years, with serum creatinine (sCr) 2.15 (1.8/2.5) mg/dL, eGFR CKD-EPI 28 (20/39) ml/min/1.73 m², albuminuria 0.98 (0.57/1.45) g/24 h and BVAS 14 at baseline were treated with the mentioned protocol. Seven patients had MPO and 2 had double MPO/PR3 positivity. Two were already on dialysis and 4 had pulmonary involvement. The median follow-up was 19 (12.5/39) months. One patient required the addition of plasma exchange and extended treatment due to aggressive disease and one was lost to follow-up after four months. The rest of the 7 patients were dialysis free with a sCr 2.15 (1.8/2.5) mg/dL, eGFR 28 (20/39) ml/min/1.73 m² at the end of follow-up. Patient and renal survival were 88% and 100% respectively. 85.7% of patients achieved ANCA-negative status and all remained B cell
Table 1: Treatment protocol.

<table>
<thead>
<tr>
<th></th>
<th>Per os Methylprednisolone</th>
<th>IV Cyclophosphamide</th>
<th>IV Rituximab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induction Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAY 0</td>
<td>0.8 mg/kg ΣB - max 48 mg</td>
<td>10 mg/kg ΣB (max 750 mg)</td>
<td>1 gr</td>
</tr>
<tr>
<td>DAY 7</td>
<td>36mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAY 14</td>
<td>24 mg</td>
<td>10 mg/kg ΣB (max 750 mg)</td>
<td>1 gr</td>
</tr>
<tr>
<td>WEEK 3</td>
<td>24 mg</td>
<td></td>
<td></td>
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<tr>
<td>WEEK 4</td>
<td>16 mg</td>
<td>500 mg</td>
<td></td>
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<tr>
<td>WEEK 6</td>
<td>12 mg</td>
<td>500 mg</td>
<td></td>
</tr>
<tr>
<td>WEEK 8</td>
<td>8 mg</td>
<td>500 mg</td>
<td></td>
</tr>
<tr>
<td>WEEK 10</td>
<td>4 mg</td>
<td>500 mg</td>
<td></td>
</tr>
<tr>
<td>WEEK 20</td>
<td>4mg every other day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WEEK 24</td>
<td>stop</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MAINTENANCE THERAPY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MONTH 4-6</td>
<td></td>
<td>1 gr</td>
<td></td>
</tr>
<tr>
<td>EVERY 6 MONTHS TILL 18</td>
<td></td>
<td>1 gr</td>
<td></td>
</tr>
</tbody>
</table>

deplete at 6 and 18 months. There were no major relapses, while two patients had infection related hospitalization. No unexpected side effects were observed during follow-up.

**Conclusion:** These findings confirm the literature that a combined regimen provides early disease control with low relapse rates, without significant adverse effects from immunosuppression. A regimen like this may provide the basis for further refinement of remission induction protocols in AAV, potentially allowing early withdrawal of corticosteroids.

###3253

**STUDY OF THE EFFECT OF TWO BARIATRIC SURGERY TYPES ON RENAL FUNCTION AND MCP-1 LEVELS**

Alaa Sabry and Ahmed Bahy
Mansoura, Mansoura, Egypt

**Background and Aims:** Bariatric surgery has been the most effective and permanent treatment for severe obesity and has resulted in significant improvement or reduction of comorbidities due to obesity. To evaluate and compare the outcome of two types of bariatric surgery (LMGB and LSG) on renal functions and urinary MPC-1 level in morbidly obese patients after three months of surgery.

**Method:** Forty morbidly obese patients underwent bariatric surgery between October 2018 and July 2019. Two types of bariatric surgery were done; laparoscopic mini gastric bypass (LMGB) and laparoscopic sleeve gastrectomy (LSG). Group A include 26 patients underwent LSG and Group B include 14 patients.

**Results:** There were no statistically significant difference in the postoperative mean weight, BMI, neck circumference, WC, Hip circumference, WHR, SBP and DBP in the cases between the 2 types of surgeries (LSG and LMGB) also, there were no statistically significant difference in the mean post urinary MCP1 (73.53±21.25 & 75.43±26.17, P>0.5), post microalbuminuria (8.83±6.26 & 8.6, P>0.05), post urinary creatinine (109.21±43.22 & 99.19±48.65, P>0.05), post MCP1/Cr ratio (0.78±0.36 & 0.75±0.37, P>0.05), post CRP (5.73±3.04 & 5.77±3.17, P>0.05), post serum creatinine (0.74±0.05 & 0.75±0.07, P>0.05), eGFR (100.32±9.54 & 104.39±9.54, P>0.05), s.cholesterol, s.HDL and s.TGs in the cases who had either LSG operation (group A) or LMGB operation (group B).

**Conclusion:** There were no statistically significant difference as regard renal function, urinary MCP-1 level and weight loss between LSG and LMGB.

Table 1: Analysis of study postoperative parameters according to the type of operation.

<table>
<thead>
<tr>
<th></th>
<th>LSG operation (n = 26)</th>
<th>LMGB operation (n = 14)</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post Urinary MCP1 (pg/ml)</td>
<td>73.53±21.25</td>
<td>75.43±26.17</td>
<td>z = -0.269</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.788</td>
</tr>
<tr>
<td>Post Albuminuria (mg/l)</td>
<td>8.83 ± 6.26</td>
<td>10.02 ± 8.62</td>
<td>z = -0.255</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.798</td>
</tr>
<tr>
<td>Post Urinary creatinine (mg/dl)</td>
<td>109.21±43.22</td>
<td>99.19±48.65</td>
<td>z = -0.582</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.561</td>
</tr>
<tr>
<td>Post MCP1/Cr ratio</td>
<td>0.78±0.36</td>
<td>1.01±0.70</td>
<td>z = -0.752</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.452</td>
</tr>
<tr>
<td>Post CRP (mg/l)</td>
<td>5.73±3.04</td>
<td>5.77±3.17</td>
<td>z = -0.036</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.971</td>
</tr>
<tr>
<td>Post Serum albumin (gm/dl)</td>
<td>4.38±0.26</td>
<td>3.99±0.34</td>
<td>t = 4.045</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>Post Serum creatinine (mg/dl)</td>
<td>0.74±0.05</td>
<td>0.75±0.07</td>
<td>t = -0.468</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.648</td>
</tr>
<tr>
<td>Post eGFR (ml/min/m²)</td>
<td>100.32± 9.54</td>
<td>104.39± 9.54</td>
<td>t = -1.287</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.206</td>
</tr>
</tbody>
</table>

P: probability.
Continuous data expressed as mean±SD
*t = Independent samples t-test; z: Mann Whitney U test
*Statistically significant (p < 0.05)
THE EFFECT OF GLOMERULAR C3 DEPOSITION ON RENAL OUTCOME IN PATIENTS WITH MEMBRANOUS NEPHROPATHY: DATA OF THE TSN-GOLD STUDY

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1 Bezmialem Vakif University School of Medicine, Nephrology, Istanbul, Turkey, 2 Istanbul Haseki Training and Research Hospital, University of Health Sciences, Nephrology, Istanbul, Turkey, 3 Istanbul University Istanbul School of Medicine, Nephrology, Istanbul, Turkey, 4 Kocaeli University, School of Medicine, Nephrology, Kocaeli, Turkey, 5 Bursa Uludag University, Faculty of Medicine, Nephrology, Bursa, Turkey, 6 Mersin University Medical School, Education and Training Hospital, Nephrology, Mersin, Turkey, 7 Sultan II. Abdulhamid Han Training and Research Hospital, University of Health Sciences, Nephrology, Istanbul, Turkey, 8 Istanbul University-Cerrahpasa Cerrahpasa School of Medicine, Nephrology, Istanbul, Turkey, 9 Ankara University, School of Medicine, Nephrology, Ankara, Turkey, 10 Trakya University School of Medicine, Nephrology, Edrine, Turkey, 11 Pamukkale University, School of Medicine, Nephrology, Denizli, Turkey, 12 University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Nephrology, Ankara, Turkey, 13 University of Health Sciences, Bozyaka Education and Research Hospital, Nephrology, Izmir, Turkey, 14 Sakarya University, School of Medicine, Nephrology, Sakarya, Turkey, 15 University of Health Sciences, Hamidiye Etfal Training and Research Hospital, Nephrology, Istanbul, Turkey, 16 Ankara City Hospital, Nephrology, Ankara, Turkey, 17 Dicle University, School of Medicine, Nephrology, Diyarbakir, Turkey, 18 Afyonkarahisar Health Sciences University School of Medicine, Nephrology, Afyonkarahisar, Turkey, 19 University of Health Sciences, Bakirkoy Doktor Sadi Konuk Training and Research Hospital, Nephrology, Istanbul, Turkey, 20 University of Health Sciences, Kartal Training and Research Hospital, Nephrology, Istanbul, Turkey, 21 University of Health Sciences, Ankara Training and Research Hospital, Nephrology, Ankara, Turkey, 22 Marmara University School of Medicine, Nephrology, Istanbul, Turkey, 23 Yildirim Beyazit University, School of Medicine, Nephrology, Ankara, Turkey, 24 Necmettin Erbakan University, Meram School of Medicine, Nephrology, Konya, Turkey, 25 Necmettin Erbakan University, Meram School of Medicine, Nephrology, Konya, Turkey, 26 Baaskent University, School of Medicine, Nephrology, Adana, Turkey and 27 Sutcu Imam University, School of Medicine, Nephrology, Kahramanmaras, Turkey

Background and Aims: We aimed to evaluate the effect of glomerular C3 deposits on clinical and laboratory findings and outcome in patients with idiopathic membranous nephropathy (MN) included in the Primary Glomerular Diseases Study of Turkish Society of Nephrology Glomerular Diseases Study Group (TSN-GOLD).

Method: The data of 1595 patients with MN in the database has been evaluated. 114 patients were excluded due to lack of data about C3 staining, 54 patients due to secondary MN and 523 due to lack of data about the follow-up. Patients with glomerular C3 deposits were compared with those with no C3 staining.

Results: Glomerular C3 deposits were detected in kidney biopsy specimens of 601 patients of the 888 patients analysed. The demographic data, clinical and laboratory findings at the time of diagnosis of C3 (+) and C3 (-) groups are presented in Table 1. They were similar except serum albumin level that was lower in C3 (+) group. Subepithelial deposits and interstitial fibrosis was more prominent, IgG, Kappa and Lambda staining more intense, positivity for C1q and IgA was more frequent in C3 (+) group (Table 2).

The study groups were similar regarding remission rates after the first immunosuppressive treatment (p = 0.582). 155 patients (25.8%) had partial, 152 (25.3%) had complete remission while no remission was detected in 92 patients (15.3%) in C3 (+) group. 69 patients (24.0%) had partial and 81 patients (28.2%) had complete remission; 40 patients (13.9%) had no remission in C3 (-) group. The relapse rates were 17.6% and 19.9% in C3 (+) and C3 (-) groups (p = 0.360). The percentage of patients who died or needed renal replacement therapy (RRT) were higher C3 (+) group (p = 0.013) (Figure 1).

Conclusion: Need for RRT and mortality is higher in patients with C3 deposition showing the importance of C3 deposition in the prognosis of MN. More prominent interstitial fibrosis may be related with the worse outcome.

Figure 1: The outcome in the study groups.
Table 1: Demographic, clinical and laboratory data at the time of diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>C3 (+) group (n = 601)</th>
<th>C3 (-) group (n = 287)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Female) [n (%)]</td>
<td>242 (40.3)</td>
<td>111 (%38.7)</td>
<td>0.651</td>
</tr>
<tr>
<td>Age (year)</td>
<td>48.04±13.92</td>
<td>46.81±14.82</td>
<td>0.227</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic urine abnormalities</td>
<td>48 (8.1)</td>
<td>19 (6.8)</td>
<td>0.944</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>504 (85.3)</td>
<td>239 (86.0)</td>
<td></td>
</tr>
<tr>
<td>Nephritic syndrome</td>
<td>14 (2.4)</td>
<td>6 (2.2)</td>
<td></td>
</tr>
<tr>
<td>Mixed nephrotic syndrome</td>
<td>15 (2.5)</td>
<td>8 (2.9)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10 (1.7)</td>
<td>6 (2.2)</td>
<td></td>
</tr>
<tr>
<td>Clinical findings</td>
<td></td>
<td></td>
<td>0.467</td>
</tr>
<tr>
<td>Systolic blood pressure [mmHg]</td>
<td>130.38±20.24</td>
<td>129.77±16.73</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure[mmHg]</td>
<td>80.78±1.73</td>
<td>80.39±4.94</td>
<td></td>
</tr>
<tr>
<td>Laboratory results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscopic hematuria</td>
<td>205 (35.4)</td>
<td>106 (37.3)</td>
<td>0.581</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>37.45±27.48</td>
<td>36.18±26.67</td>
<td>0.517</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.94±0.85</td>
<td>0.94±0.81</td>
<td>0.880</td>
</tr>
<tr>
<td>Estimated GFR (ml/min)</td>
<td>100.11±36.02</td>
<td>100.85±34.15</td>
<td>0.771</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>2.64±0.76</td>
<td>2.79±0.91</td>
<td>0.020</td>
</tr>
<tr>
<td>Proteinuria (mg/day)</td>
<td>6460 (50-32600)</td>
<td>6895 (138-33078)</td>
<td>0.362</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.1±21.80</td>
<td>13.65±1.95</td>
<td>0.075</td>
</tr>
</tbody>
</table>

Table 2: Pathological findings.

<table>
<thead>
<tr>
<th></th>
<th>C3 (+) group (n = 601)</th>
<th>C3 (-) group (n = 287)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesangial proliferation [n (%)]</td>
<td>196 (32.6)</td>
<td>101 (35.7)</td>
<td>0.606</td>
</tr>
<tr>
<td>Basal membrane thickening [n (%)]</td>
<td>562 (93.5)</td>
<td>261 (90.9)</td>
<td>0.105</td>
</tr>
<tr>
<td>Subendothelial deposits [n (%)]</td>
<td>18 (3.0)</td>
<td>12 (4.2)</td>
<td>0.328</td>
</tr>
<tr>
<td>Subepithelial deposits [n (%)]</td>
<td>247 (41.1)</td>
<td>70 (24.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Endocapillary proliferation [n (%)]</td>
<td>37 (6.2)</td>
<td>17 (5.9)</td>
<td>0.826</td>
</tr>
<tr>
<td>Exudative changes [n (%)]</td>
<td>33 (5.5)</td>
<td>23 (8.0)</td>
<td>0.197</td>
</tr>
<tr>
<td>Interstitial inflammation [n (%)]</td>
<td>321 (53.4)</td>
<td>159 (55.4)</td>
<td>0.758</td>
</tr>
<tr>
<td>Interstitial fibrosis [n (%)]</td>
<td>272 (45.3)</td>
<td>92 (32.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Vascular changes [n (%)]</td>
<td>234 (38.9)</td>
<td>95 (33.1)</td>
<td>0.082</td>
</tr>
<tr>
<td>Tubular atrophy [n (%)]</td>
<td>288 (47.9)</td>
<td>107 (37.3)</td>
<td>0.483</td>
</tr>
<tr>
<td>IgG [n (%)]</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(+)</td>
<td>39 (6.5)</td>
<td>32 (11.1)</td>
<td></td>
</tr>
<tr>
<td>(+++)</td>
<td>111 (18.5)</td>
<td>82 (28.6)</td>
<td></td>
</tr>
<tr>
<td>(++++)</td>
<td>438 (72.9)</td>
<td>138 (48.1)</td>
<td></td>
</tr>
<tr>
<td>IgM [n (%)]</td>
<td></td>
<td></td>
<td>0.078</td>
</tr>
<tr>
<td>(+)</td>
<td>110 (18.3)</td>
<td>39 (13.6)</td>
<td></td>
</tr>
<tr>
<td>(+++)</td>
<td>24 (4.0)</td>
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</tr>
<tr>
<td>(++++)</td>
<td>9 (1.5)</td>
<td>3 (1.0)</td>
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</tr>
<tr>
<td>IgA [n (%)]</td>
<td></td>
<td></td>
<td>0.042</td>
</tr>
<tr>
<td>(+)</td>
<td>70 (11.6)</td>
<td>17 (5.9)</td>
<td></td>
</tr>
<tr>
<td>(+++)</td>
<td>17 (2.8)</td>
<td>5 (1.7)</td>
<td></td>
</tr>
<tr>
<td>(++++)</td>
<td>8 (1.3)</td>
<td>5 (1.7)</td>
<td></td>
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<tr>
<td>C1q [n (%)]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(+)</td>
<td>47 (7.8)</td>
<td>7 (2.4)</td>
<td></td>
</tr>
<tr>
<td>(+++)</td>
<td>9 (1.5)</td>
<td>2 (0.7)</td>
<td></td>
</tr>
<tr>
<td>(++++)</td>
<td>7 (1.2)</td>
<td>0 (0.0)</td>
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<tr>
<td>Kappa [n (%)]</td>
<td></td>
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<td>&lt;0.001</td>
</tr>
<tr>
<td>(+)</td>
<td>71 (11.8)</td>
<td>39 (13.6)</td>
<td></td>
</tr>
<tr>
<td>(+++)</td>
<td>147 (24.5)</td>
<td>60 (20.9)</td>
<td></td>
</tr>
<tr>
<td>(++++)</td>
<td>147 (24.5)</td>
<td>35 (12.2)</td>
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</tr>
<tr>
<td>Lambda [n (%)]</td>
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<td>&lt;0.001</td>
</tr>
<tr>
<td>(+)</td>
<td>80 (13.5)</td>
<td>49 (17.1)</td>
<td></td>
</tr>
<tr>
<td>(+++)</td>
<td>153 (25.5)</td>
<td>47 (16.4)</td>
<td></td>
</tr>
<tr>
<td>(++++)</td>
<td>133 (22.1)</td>
<td>38 (13.2)</td>
<td></td>
</tr>
<tr>
<td>Number of sclerotic glomeruli</td>
<td>1 (0-35)</td>
<td>0 (0-16)</td>
<td>0.015</td>
</tr>
<tr>
<td>Number of segmental sclerotic glomeruli</td>
<td>0 (0-18)</td>
<td>0 (0-6)</td>
<td>0.093</td>
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<tr>
<td>Number of crescentic glomeruli</td>
<td>0 (0-6)</td>
<td>0 (0-5)</td>
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ANTICOAGULANT-RELATED NEPHROPATHY – AN UNDERDIAGNOSED COMPLICATION

Tefik Islami1, Marilena Gregorini2, Gioacchino D’Ambrosio2, Paolo Del Vino1, Eleonora Francesca Pattonieri1, Miriam Fusli3, Pietro Canu4, Carlo Maurizio Montecucco5 and Teresa Rampino6

1University of Pavia, Dipartimento di scienze clinico-chirurgiche, diagnostiche e pediatriche, Pavia, Italy, 2University of Pavia / IRCCS Fondazione Policlinico “San Matteo”, Department of Internal Medicine and therapeutics, Pavia, Italy, 3University of Pavia, Department of Internal Medicine and therapeutics, Pavia, Italy, 4IRCCS Fondazione Policlinico “San Matteo”, Nephrology, Dialysis and Transplant Unit, Pavia, Italy, 5University of Pavia, Scuola di Specializzazione in Nefrologia, Pavia, Italy, 6University of Pavia, Scuola di Specializzazione in Medicina Interna, Pavia, Italy, 7University of Pavia / IRCCS Fondazione Policlinico “San Matteo”, Reumatology, Pavia, Italy and 8University of Pavia / IRCCS Fondazione Policlinico “San Matteo”, Nephrology, Dialysis and Transplant Unit, Pavia, Italy

Background and Aims: Anticoagulant-related nephropathy (ARN) is an underdiagnosed complication of anticoagulant therapy (AT).

Method: We report 3 cases of ARN.

Patient 1: 31 year-old male (M), kidney transplanted for reflux nephropathy, with normal renal function (Rfx) and urinalysis (U), on therapy with tacrolimus (FK), everolimus and mycophenolate. He started edoxaban (E) (60 mg od) for deep vein thrombosis (DVT). After 10 days he developed hematuria and Acute Kidney Injury (AKI). Ruled out urological and infectious causes, we performed kidney biopsy (KB) which showed extensive tubular necrosis (TN), erythrocyte casts (cRBC) and glomerular hemorrhage (EG). Perl’s stain (PS) showed iron deposits in tubular cells released by erythrocytes lysis (Fig. 1). Although E posology was adequate the concomitant intake of FK by reducing CYP3A4 metabolism of E resulted in over anticoagulation (OAC), demonstrated by the dosage of the factor Xa (FXa) at peak. Upon withdrawal of AT, Rfx and U normalized.

Patient 2: 73-year-old M with hypertension and mild chronic kidney disease (CKD) on antiplatelet therapy (ASA 100 mg od) for biological valve prosthesis and AT with Enoxaparin sodium (Es) (4000UI od) for DVT prophylaxis. He was admitted to the hospital for fever and hypotensive episodes. Microbiological, neoplastic and immune investigations were negative. A progressive worsening of Rfx associated with macro-hematuria was observed, requiring renal replacement therapy (RRT). KB showed a post-infectious glomerulonephritis, but in the hypothesis that tubular damage was enhanced by antiplatelet/AT, PS was performed and resulted positive. OAC was confirmed by the dosage of the factor Xa (FXa) at peak. After withdrawal of therapy, progressive improvement of the Rfx and hematuria were observed, such as to allow the suspension of the RRT.

Patient 3: 54 year-old M with kidney and lung involvement of ANCA-associated vasculitis. After rituximab induction therapy he showed marked improvement on lung and renal function and antibody titer (c-ANCA PR3 positive). He experienced an unusual worsening of Rfx and hematuria after starting a AT (Es 6000 UI BID) to treat a DVT. A KB was performed in the suspicion of ARN. The histology revealed an extensive TN, numerous cRBC with extracapillary glomerulonephritis and PS positive. IF was negative. OAC was confirmed and adjustment of anticoagulation dose for glomerular filtration rate resulted in improvement of Rfx.

Results: ARN is a not uncommon occurrence in cases of OAC and glomerular fragility (Table 1).

Conclusion: ARN should be suspected in predisposed patients in whom glomerular hyperfiltration or preexisting GN during OAC facilitate EG. Attention should be given to drug interactions that can induce an unrecognized OAC. The cases described underline the need for careful monitoring of U, Rfx and FXa activity to promptly treat this complication, avoiding permanent damage.

Figure 1: Histology and pathophysiologic hypothesis.
#5827
MYCOPHENOLATE MOFETIL AS IMMUNOSUPPRESSIVE THERAPY IN IGA NEPHROPATHY

Henry Barrington-White1, Abigail Pomeranc2, Conor Murphy2 and Farid Ghalli2,3

1University Hospitals Sussex, Sussex Kidney Unit, Brighton, United Kingdom, 2University Hospitals Sussex, Sussex Kidney Unit, Brighton, United Kingdom and 3Brighton and Sussex Medical School, Brighton, United Kingdom

**Background and Aims:** IgaNephropathy is the commonest cause of primary Glomerulonephritis in developed countries. It is characterised by Iga-deposits on the mesangium. Classical presentation with asymptomatic non-visible haematuria or episodic visible haematuria 24-48 hours after an upper respiratory tract infection, raised BP and Proteinuria. End-stage renal disease (ESRD) can occur in up to 20-50% of patients. Treatment with ACEI/ARB has strong evidence in managing Iga. If there is evidence of progression, steroids and immunosuppression are recommended. Mycophenolate Mofetil's effectiveness in IgaNephropathy is controversial. KIGO guidelines authors suggest not to use it. In this work, we reviewed immunosuppression with mycophenolate Mofetil (MMF) retrospectively in IgaNephropathy patients managed at Sussex Kidney unit – Brighton -UK.

**Method:** We retrospectively reviewed 25 patients who had a diagnosis of IgaNephropathy and were treated with mycophenolate mofetil as immunosuppression for Iga nephropathy under the care of the Sussex Renal Unit at University Hospitals Sussex. Patients reviewed, had been diagnosed between 2011-2020. Data collected from our department's electronic system, including laboratory results, histopathology reports, clinic letters and medications. Data were collected until January 2023 for patients who had renal survival. For patients who started on renal replacement therapy (RRT), data were collected until the start of RRT. The work aimed at looking at MMF efficacy in IgANephropathy.

**Results:** We reviewed 25 patients, 13 male and 12 female. Twenty-four patients (96%) were of white Caucasian ethnicity while one patient (4%) was Asian. The mean age was 42.4± 16 years. All the patients were diagnosed with both clinical pictures and renal biopsies. Oxford classification score showed M1 (21) patients, E (5 patients), S (19 patients), T (1 = 10 patients, 2 = 4 patients), and C (1 = 15 patients, 2 = 4 patients). On presentation, 5 patients presented with a sore throat, 8 with skin rash and 7 with macroscopic haematuria. Seventeen patients (60%) presented with AKI. Eleven patients (44%) had nephrotic range proteinuria on presentation. The average duration of the disease was 6.1 years at the time of assessment. MMF was used in the 25 patients, five of them had prednisolone and cyclophosphamide for 3 months followed by MMF maintenance. Twenty patients were treated with MMF alone or in combination with steroids (17 patients) from the start. The average duration of treatment was 2 years, and the average dose was 1 gm twice daily. Five patients (20%) progressed to ESRD and three of them had renal transplantation while twenty patients (80%) maintained renal survival. For the 80% who maintained renal survival the mean eGFR at diagnosis was 54.5± 34.1 and at the time of assessment was 56.1±26.6. Of the 17 patients presented with AKI five patients (29%) recovered to normal renal function, five patients had ESRD (29.4%) and four had improvements of eGFR while three patients showed a decrease of eGFR (Mean 45.6± 1.1 ml/min) to eGFR (Mean 32± 8.2 ml/min). In total, 70.6% of AKI patients recovered either to normal or to CKD level and 80% of the total patients had renal survival without RRT during the time of review. Twenty patients (80%) achieved more than 50% reduction of proteinuria, with five patients (20%) having proteinuria less than 0.3 g/24 hours and 9 (36%) patients less than 0.5 g/24 hours. Comparison between the proteinuria at diagnosis and at the time of assessment was significant (P<0.001).

**Conclusion:** Mycophenolate mofetil was effective in maintaining renal survival and improving proteinuria in Iga nephropathy patients who were indicated for immunosuppression based on histopathology and risk of progression. It was well tolerated by patients. A randomised controlled trial is needed to compare the MMF effect in comparison with currently available therapies.

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**Table 1: ARN is a not uncommon occurrence in cases of OAC and glomerular fragility.**

<table>
<thead>
<tr>
<th>Pts</th>
<th>Why AT?</th>
<th>Which AT?</th>
<th>FXa at peak vs n.v</th>
<th>Glomerular damage susceptibility</th>
<th>Recovery after dose adjustment or suspension of AT</th>
</tr>
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<tbody>
<tr>
<td>#1</td>
<td>DVT</td>
<td>Edoxaban (60 mg mid)</td>
<td>↑</td>
<td>Glomerular hyper-filtration in reduced nephronic mass</td>
<td>Yes</td>
</tr>
<tr>
<td>#2</td>
<td>Post-TAVI + DVT prophylaxis</td>
<td>Enoxaparin sodium (4000UI mid) + ASA (100 mg/die)</td>
<td>↑</td>
<td>Post.infectious GN</td>
<td>Yes</td>
</tr>
<tr>
<td>#3</td>
<td>DVT</td>
<td>Enoxaparin sodium (6000UI bid)</td>
<td>↑</td>
<td>ANCA associated vasculitis</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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**CHRONIC KIDNEY DISEASE**

C1 - BASIC SCIENCES & EXPERIMENTAL

#5461
KIDNEY TUBULE POLYPLOIDIZATION DURING PHYSIOLOGIC AGEING IN MICE

Elena Lazzeri1, Giulia Antonelli1, Carolina Conte1, Maria Lucia Angelotti1, Benedetta Mazzinghi2, Giulia Carangio1, Letizia De Chiara1 and Paola Romagnani1,2

1University of Florence, Department of Biomedical, Experimental and Clinical Sciences "Mario Serio", Florence, Italy and 2Meyer Children's University Hospital, Nephrology Unit and Dialysis Unit, Florence, Italy

**Background and Aims:** The aged population is constantly increasing, and kidney-aging is a risk factor for both acute kidney injury (AKI) and chronic kidney disease (CKD). Accordingly, CKD is a major global health problem with an increasing prevalence in older population. Therefore, there is an urgent need to understand the age-related mechanisms underlying CKD development and progression. Renal function parameters were assessed at 2, 5, 11 and 20 months before sacrifice. Kidneys were analyzed for senescence and interstitial fibrosis at 2, 5, 11 and 20 months of age. Results: Genetic and single-cell transcriptomic approaches in mice were used to investigate TC polyploidization during physiologic ageing in mice. We retrospectively reviewed 25 patients who had a diagnosis of IgaNephropathy and were treated with mycophenolate mofetil as immunosuppression for Iga nephropathy under the care of the Sussex Renal Unit at University Hospitals Sussex. Patients reviewed, had been diagnosed between 2011-2020. Data collected from our department's electronic system, including laboratory results, histopathology reports, clinic letters and medications. Data were collected until January 2023 for patients who had renal survival. For patients who started on renal replacement therapy (RRT), data were collected until the start of RRT. The work aimed at looking at MMF efficacy in IgaNephropathy.

**Method:** We retrospectively reviewed 25 patients who had a diagnosis of IgaNephropathy and were treated with mycophenolate mofetil as immunosuppression for Iga nephropathy under the care of the Sussex Renal Unit at University Hospitals Sussex. Patients reviewed, had been diagnosed between 2011-2020. Data collected from our department's electronic system, including laboratory results, histopathology reports, clinic letters and medications. Data were collected until January 2023 for patients who had renal survival. For patients who started on renal replacement therapy (RRT), data were collected until the start of RRT. The work aimed at looking at MMF efficacy in IgaNephropathy.

**Results:** We reviewed 25 patients, 13 male and 12 female. Twenty-four patients (96%) were of white Caucasian ethnicity while one patient (4%) was Asian. The mean age was 42.4± 16 years. All the patients were diagnosed with both clinical pictures and renal biopsies. Oxford classification score showed M1 (21) patients, E (5 patients), S (19 patients), T (1 = 10 patients, 2 = 4 patients), and C (1 = 15 patients, 2 = 4 patients). On presentation, 5 patients presented with a sore throat, 8 with skin rash and 7 with macroscopic haematuria. Seventeen patients (60%) presented with AKI. Eleven patients (44%) had nephrotic range proteinuria on presentation. The average duration of the disease was 6.1 years at the time of assessment. MMF was used in the 25 patients, five of them had prednisolone and cyclophosphamide for 3 months followed by MMF maintenance. Twenty patients were treated with MMF alone or in combination with steroids (17 patients) from the start. The average duration of treatment was 2 years, and the average dose was 1 gm twice daily. Five patients (20%) progressed to ESRD and three of them had renal transplantation while twenty patients (80%) maintained renal survival. For the 80% who maintained renal survival the mean eGFR at diagnosis was 54.5± 34.1 and at the time of assessment was 56.1±26.6. Of the 17 patients presented with AKI five patients (29%) recovered to normal renal function, five patients had ESRD (29.4%) and four had improvements of eGFR while three patients showed a decrease of eGFR (Mean 45.6± 1.1 ml/min) to eGFR (Mean 32± 8.2 ml/min). In total, 70.6% of AKI patients recovered either to normal or to CKD level and 80% of the total patients had renal survival without RRT during the time of review. Twenty patients (80%) achieved more than 50% reduction of proteinuria, with five patients (20%) having proteinuria less than 0.3 g/24 hours and 9 (36%) patients less than 0.5 g/24 hours. Comparison between the proteinuria at diagnosis and at the time of assessment was significant (P<0.001).

**Conclusion:** Mycophenolate mofetil was effective in maintaining renal survival and improving proteinuria in Iga nephropathy patients who were indicated for immunosuppression based on histopathology and risk of progression. It was well tolerated by patients. A randomised controlled trial is needed to compare the MMF effect in comparison with currently available therapies.
and an age-related decline of renal function starting from 5 months of age. Collectively, these results suggest TC polyploidization is a potential trigger for CKD development and progression during physiologic kidney ageing in mice.

**Conclusion:** This study demonstrates the increase of TC polyploidization, which is associated with a progressive fibrosis, senescence and CKD development during physiologic kidney ageing in mice.

### #6643
**MOLECULAR PATHWAYS ASSOCIATED WITH VASCULAR CALCIFICATIONS IN CHILDREN WITH CHRONIC KIDNEY DISEASE**

**Julie Bernardor**, **Maria Bartosova**, **Conghui Zhang**, **Iva Marinovic**, **Rebecca Herzog**, **Klaus Kratchovill**, **Delphine Farlay**, **Armand Jaminon**, **Leon Schurgers** and **Claus Peter Schmitt**

1. Nice, France, 2. Center for Pediatric and Adolescent Medicine, University of Heidelberg, Division of Pediatric Nephrology, Heidelberg, Germany, 3. Medical University of Vienna, Department of Pediatrics and Adolescent Medicine, Vienna, Austria, 4. INSEME 1033, Lyon, France and 5. Cardiovascular Research Institute Maastricht, Maastricht, Netherlands

**Background and Aims:** Patients with advanced stages of chronic disease (CKD) suffer from 30-times higher risk of cardiovascular disease (CVD) as compared to the general population, vascular calcifications are prevalent. Underlying molecular mechanisms are only partly understood. Children are devoid of lifestyle and aging related CVD risk factors and therefore allow for a highly sensitive and specific analyses of CKD induced pathomechanisms.

**Method:** Arteriolar tissues of 55 children with normal renal function and 29 children with CKD5 (median age 9.2 years) underwent digital histomorphometry, calcium deposits were assessed by Von Kossa staining and 18F-sodium fluoride positron emission tomography (18F-NaF PET). Gene set enrichment analysis (GSEA) and Ingenuity pathway analysis were performed on multi-omics data sets obtained from micro-dissected ontal arterioles from children with normal renal function and with CKD5 (n = 7/group; age 7.3 ± 3.6/8 ± 3 years). Based on literature review, we established a vascular calcification (VC) pathway library comprising 442 biological processes/molecular functions and extracted linked genes from Gene Ontology database. Key identified mechanisms were validated in independent patient cohorts (n = 32) and controls (n = 20) by quantitative immunostaining.

**Results:** Significant arteriolar lumen obliteration was present in CKD5 children (p < 0.0001 and p = 0.02). Von Kossa staining was negative, but 18F-NaF PET revealed microcalcifications in children with CKD5. Subendothelial arteriolar inflammatory cells (CD68+ macrophages) were present in CKD5 cohort (p < 0.0001 compared to non-CKD controls) and correlated with serum inorganic phosphorus (R2 = 0.18; p = 0.04). GSEA identified top enriched pathways including telomere extension by telomerase and chromatin histone methylation. IPA cross-omics showed suppression of actin cytoskeleton, tight junction signaling, and focal adhesion. VC pathway analysis identified 30/442 pathways related to actin cytoskeleton, Wnt signaling, extracellular matrix (ECM) organization, complement activation, apoptosis, endoplasmic reticulum stress and ossification regulation. Fibronectin-1 (FN1) was identified as Hugene, involved in ECM regulation. In independent age-matched cohorts, complement factor C3d was higher in CKD5, vascular endothelial growth factor and endothelial cell number/μm endoluminal circumference were reduced. Arteriolar osteoglycin, a protein inducing ectopic bone formation, was increased and correlated with serum PTH (R2 = 0.61; p = 0.01). FN1 was less abundant in arterioles from CKD5 children and negatively correlated with serum creatinine levels (R2 = 0.62; p = 0.02).

**Conclusion:** Vascular disease and microcalcifications are present in young children with CKD5. We provide the first comprehensive analysis of the underlying molecular mechanisms associated with the vascular calcifications and identified specific molecular pathomechanisms, of which several represent potential therapeutic targets.

### #6741
**TRANSCRIPTION FACTOR ATF3 EXACERBATES RENAL FIBROSIS THROUGH RECRUITING HISTONE ACETYLASES**

**Lina Yang**, **Tilong Chen**, **Ping Fu**, **Liang MA** and **Haoping Yu**

1. West China Medical School, West China Hospital, Sichuan University, Kidney Research Institute, Cheng Du Shi, P.R. China and 2. West China Medical School, West China Hospital, Sichuan University, Biomedical Big Data Center, Cheng Du Shi, P.R. China

**Background and Aims:** Chronic kidney disease (CKD) threatens public health around the world. Renal fibrosis is a final common pathology in renal diseases of different etiologies. However, no efficient, broadly applicable anti-fibrotic therapies exist. Histone acetylation is an epigenetic modification involved in the regulation of multiple disease-specific gene expressions, balanced by histone acetyltransferases and histone deacetylases (HDAC) enzymes. Transcription factors (TF) could recruit histone-modifying enzymes and alter gene expression. But now, much remains unknown about the role of histone acetylation and whether there exists the regulator of it in fibrosis of CKD. Here, we for the first time explored a novel aspect of ATF3 promoting kidney fibrosis via recruiting the histone acetylases to fibrosis-related genes in CKD.

**Method:** We constructed a CKD mouse model by using adenine and oxolate. Serum were taken for the measurement of BUN and creatinine. Kidneys were harvested and processed for histological, sequencing, qRT-PCR, and western blotting analysis. RNA-seq and ChIP-seq (antibody: H3K27ac) of mouse kidneys were conducted for profiling the differential gene expression and H3K27ac. GO and KEGG analysis was performed for annotation of the function. Motif analysis was applied for searching the regulator of H3K27ac. Biopsies samples of patients with common CKD were used for immunohistochemical analysis. ATF3 KO mice were also conducted for defining the function of ATF3 in CKD. To profile the ATF3 binding site on chromatin, Chip-seq of ATF3 in mice kidneys of normal control and CKD were also performed. Besides, the data contained ATF3 interact protein in databases (Chip-atlas and BioGrid) and the results of protein interaction prediction were integrated for finding the protein-protein interaction of ATF3. Pip3 samples of patients with common CKD were used for immunohistochemical analysis. ATF3 KO mice were also conducted for defining the function of ATF3 in CKD. To profile the ATF3 binding site on chromatin, Chip-seq of ATF3 in mice kidneys of normal control and CKD were also performed. Besides, the data contained ATF3 interact protein in databases (Chip-atlas and BioGrid) and the results of protein interaction prediction were integrated for finding the protein-protein interaction of ATF3. Pip3 samples of patients with common CKD were used for immunohistochemical analysis. ATF3 KO mice were also conducted for defining the function of ATF3 in CKD. To profile the ATF3 binding site on chromatin, Chip-seq of ATF3 in mice kidneys of normal control and CKD were also performed. Besides, the data contained ATF3 interact protein in databases (Chip-atlas and BioGrid) and the results of protein interaction prediction were integrated for finding the protein-protein interaction of ATF3. Pip3 samples of patients with common CKD were used for immunohistochemical analysis. ATF3 KO mice were also conducted for defining the function of ATF3 in CKD. To profile the ATF3 binding site on chromatin, Chip-seq of ATF3 in mice kidneys of normal control and CKD were also performed. Besides, the data contained ATF3 interact protein in databases (Chip-atlas and BioGrid) and the results of protein interaction prediction were integrated for finding the protein-protein interaction of ATF3. Pip3 samples of patients with common CKD were used for immunohistochemical analysis. ATF3 KO mice were also conducted for defining the function of ATM5 regulated gene expression.

**Results:** Firstly, compared with the normal control, histone modification H3K27ac repertoire was changed in chronic kidney disease. H3K27ac/47 peaks specific to CKD, and L4996 H3K27ac peaks specific to healthy mice kidneys were found. The binding intensity of these regions has altered dramatically in the kidney of CKD. Pearson correlation analysis and function annotation showed that CKD-specific changes of H3K27ac were associated with fibrosis gene expression. Motif analysis showed that ATF3 in the top 10 TFs that may interact with H3K27ac. Among those TFs, ATF3 elicited the highest expression. Besides, ATF3 could co-localize with H3K27ac along the mouse genome globally. By immunohistochemical staining analysis, we observed the upregulation of ATF3 in the kidneys of patients with biopsy-proven CKD. We found that knocking out the ATF3 could significantly reduce kidney damage in CKD mice. In parallel with improved morphological injuries, the level of kidney fibrosis gene expression was also significantly reduced in AT3+/− mice. Furthermore, the H3K27ac on the mice chromatin altered along with the knockout of ATF3, and several fibrosis-related gene expressions which elevated in CKD were decreased by deficiency of ATF3. On the region of gene cd2, H3K27ac disappeared with the knockout of ATF3 in CKD. We found that ATF3 could interact with histone acetyltransferases (CBP, KAT7, P300) to promote the H3K27ac. Further evidenced by Chip-qPCR of fibrosis gene cd2, we found that ATF3 could recruit the histone acetyltransferases on the fibrosis gene to promote the H3K27ac to provoke the gene expression in the cell model.

**Conclusion:** We profiled the landscape of H3K27ac in CKD, explored the epigenetic regulator of H3K27ac, and revealed that ATF3 promotes renal fibrosis in CKD. Notably, we for the first time explored a novel mechanism of ATF3 about recruiting histone acetyltransferases to regulate the H3K27ac on fibrosis gene. Our data highlighted that ATF3 might represent a potential therapeutic target against fibrotic kidney diseases.
POLYPLOID TUBULAR CELLS INITIATE A TGF-BETA CONTROLLED LOOP THAT SUSTAINS POLYPLOIDIZATION AND TUBULOINTERSTITIAL CROSSTALK DURING AKI-CKD TRANSITION

Letizia De Chiara1, Elena Lazzeri1 and Paola Romagnani2

1Università degli Studi di Firenze, Department of Experimental and Clinical Biomedical Sciences, Firenze, Italy and 2University Hospital Meyer, Nephrology Unit and Dialysis Unit, Firenze, Italy

Background and Aims: Acute Kidney Injury (AKI) is characterized by a sudden kidney failure accompanied by a transient decrease of kidney functionality. It is regarded as an important risk factor for chronic kidney disease (CKD) development, but the link is still elusive. Renal fibrosis, especially tubulointerstitial fibrosis, is the final manifestation of CKD and is characterized by an excessive synthesis and deposition of extracellular matrix associated with inflammatory infiltration, tubular epithelial (TC) cell damage and fibroblast activation. Although no targeted therapy yet exists to slow the progression of tubulointerstitial fibrosis, recent findings contributed to clarify the cellular and molecular mechanisms underlying its development and progression, posing TC at the center of this process. Accordingly, we have recently demonstrated that fibrosis and senescence are trade-offs of TC polyploidy occurring immediately after AKI to support fast kidney function recovery, but promoting consequent CKD. However, the mechanisms turning TC polyploidy to senescence and fibrosis still need to be elucidated. In this study, we propose that TC polyploidy is the primary driver of CKD progression after AKI.

Methods: Polyploid TC are characterized by an increased DNA content in the absence of cell division. To discriminate polyploid cells from actively proliferating cells, we employed a series of in vitro and in vivo transgenic models based on the Fluorescence Ubiquitin Cell Cycle Indicator (Fucci) technology. AKI was triggered by unilateral ischemia reperfusion injury (IRI) or glycerol-induced rhabdomyolysis. This technology allows to follow the cell cycle phasing of living cells. Cell sorting and cytfluorimetric techniques were employed to isolate and characterize a subpopulation of polyploid TC that progressively accumulate DNA damage after AKI. These results were further corroborated by single cell RNA-sequencing (scRNA-seq) analyses in vitro and in vivo.

Results: In this study, we found that immediately after AKI, expression of cell cycle markers mostly identifies a population of DNA damaged polyploid TC. Employing transgenic mouse models and single cell RNA-sequencing we showed that after AKI, polyploid TC accumulate DNA damage and survive eventually resting in the G1 phase of cell cycle, while diploid cells do not survive DNA damage. This suggests that after AKI, polyploidization is a means to survive injury. Sorting of DNA-damaged polyploid TC showed that they express p21 and acquire a pro-fibrotic phenotype culminating in TGF-β signaling expressed by the cell. Cell cycle phases of living cells were identified by the Fluorescence Ubiquitin Cell Cycle Indicator (Fucci) technology. AKI was triggered by unilateral ischemia reperfusion injury (IRI) or glycerol-induced rhabdomyolysis. This technology allows to follow the cell cycle phasing of living cells. Cell sorting and cytfluorimetric techniques were employed to isolate and characterize a subpopulation of polyploid TC that progressively accumulate DNA damage after AKI. These results were further corroborated by single cell RNA-sequencing (scRNA-seq) analyses in vitro and in vivo.

Conclusion: In this study, we found that immediately after AKI, expression of cell cycle markers mostly identifies a population of DNA damaged polyploid TC. Employing transgenic mouse models and single cell RNA-sequencing we showed that after AKI, polyploid TC accumulate DNA damage and survive eventually resting in the G1 phase of cell cycle, while diploid cells do not survive DNA damage. This suggests that after AKI, polyploidization is a means to survive injury. Sorting of DNA-damaged polyploid TC showed that they express p21 and acquire a pro-fibrotic phenotype culminating in TGF-beta signaling expressed by the cell. Cell cycle phases of living cells were identified by the Fluorescence Ubiquitin Cell Cycle Indicator (Fucci) technology. AKI was triggered by unilateral ischemia reperfusion injury (IRI) or glycerol-induced rhabdomyolysis. This technology allows to follow the cell cycle phasing of living cells. Cell sorting and cytfluorimetric techniques were employed to isolate and characterize a subpopulation of polyploid TC that progressively accumulate DNA damage after AKI. These results were further corroborated by single cell RNA-sequencing (scRNA-seq) analyses in vitro and in vivo.

Method: In strict accordance to the admission criteria, collect peripheral venous blood and kidney samples of healthy donors and newly diagnosed IgAN patients, prepare single cell solution, verify cell viability by flow cytometry, and perform single-cell RNA-seq using a BD Rhapsody platform. Meanwhile, the clinical data of healthy donors and IgAN patients were collected and analysed. Finally, the correlation and association of differential expressed genes (DEGs) and cell clusters-identified by single-cell RNA-seq with the clinical data of IgAN were investigated.

Results: First, we established immune cells and kidney cells landscape of IgAN. The differentially expressed genes (DEGs) between the control group and IgAN were mainly concentrated in the NK cell-mediated cytotoxicity and cell killing pathways. Interestingly, we found significant decreases in NK cell numbers and cytotoxicity, and NK cell numbers and marker genes were negatively correlated with clinical parameters, including urinary protein creatinine ratio (UPCR) and serum galactose-deficient IgA1 and IgA. In contrast, B cell DEGs were enriched in different viral infection pathways, and one specific B cell subgroup showed inhibition of NFκB signaling, which was positively correlated with clinical parameters. In addition, a subpopulation of monocytes expressing interferon-inducing genes was positively associated with clinical severity of IgAN. In case of the kidney tissue, compared with the control group, mesangial cells of IgAN patients up-regulated extracellular matrix, transcription factors, kidney development and genes related to the regulation of Wnt signaling pathway. The expression of structural protein ITGAA8 on mesangial cells was significantly decreased, indicating the mesangial cells were damaged in early IgAN. Pseudo-time analysis indicated that extracellular matrix-related genes were involved in mesangial cell lesion. We also found that the mesangial cells expressed IgA1 and IgA, and the level of angiogenesis and VEGF-related genes. Moreover, podocytes of IgAN patients expressed genes of cytoskeletal recombination and FGFR activation.

Conclusion: We successfully established the single-cell landscapes of peripheral blood immune cells and kidney cells in early IgAN patients, which revealed changes in the number and status of immune cells and kidney cells closely related to clinical manifestations and phenotypic transformation. Our study offers new insights for the diagnosis and treatment of IgAN.

#STING IS INVOLVED IN THE CELLULAR SENESCENCE PROCESS ASSOCIATED WITH RENAL AGING

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Background and Aims: Cellular senescence is an adaptive process in response to damage or stress. It consists of a cell-cycle arrest (CCA) alternatively to the programmed cell death process, which is necessary for the regeneration of damaged tissues. However, permanent senescence promotes an immunosuppressive and inflammatory response associated to chronic diseases, fibrosis and aging. One of the mechanisms which triggers cellular senescence is the DNA damage response (DDR) activation, that leads to the emergence of a cellular senescence-associated secretory phenotype (SASP), inflammation and fibrosis. Sting is a detection protein of pathogenic DNA derived from cellular damage and genotoxic and environmental stresses, starting an innate immune response and inflammation. A deregulated DDR response and thus the process of senescence itself, are also able to activate Sting. Nevertheless, the role of Sting in senescence associated to renal aging is an unknown fact. The aim of this study is to evaluate the role of STING in aging-associated pathological changes in the kidney.

Method: Studies were carried out in C57BL/6 mice (wild type mice) and in mice with a phenotype deficient in the Sting gene (Ihog/Sting), of different ages: 3 (young) and 18 (aged) months. Renal function parameters, histology and aging. One of the mechanisms which triggers cellular senescence is the DNA damage response (DDR) activation, that leads to the emergence of a cellular senescence-associated secretory phenotype (SASP), inflammation and fibrosis. Sting is a detection protein of pathogenic DNA derived from cellular damage and genotoxic and environmental stresses, starting an innate immune response and inflammation. A deregulated DDR response and thus the process of senescence itself, are also able to activate Sting. Nevertheless, the role of Sting in senescence associated to renal aging is an unknown fact. The aim of this study is to evaluate the role of STING in aging-associated pathological changes in the kidney.

Method: Studies were carried out in C57BL/6 mice (wild type mice) and in mice with a phenotype deficient in the Sting gene (Ihog/Sting), of different ages: 3 (young) and 18 (aged) months. Renal function parameters, histology and gene expression were measured.

Results: Single-cell RNA-seq analysis of immune and kidney cells of young (3 months) and aged (18 months) mice revealed changes in the number and status of immune cells and kidney cells closely related to clinical manifestations and phenotypic transformation. Our study offers new insights for the diagnosis and treatment of IgAN.
basal levels in aged KO-Sting mice. However, Klotho gene expression levels are downregulated in all 18-month-old mice, wild type and KO mice.

**Conclusion:** In conclusion, these findings suggest that the absence of STING prevents age-related renal cellular senescence in a Klotho independent manner in a murine experimental model.

#3766
THE ROLE OF REGORAFENIB IN THE TREATMENT OF PERITONEAL FIBROSIS
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**Background and Aims:** Peritoneal fibrosis is an unmet issue for patients with peritoneal dialysis. Previously we proved imatinib, one kind of tyrosine kinase inhibitor, attenuated peritoneal fibrosis by blocking Platelet-derived growth factor receptor (PDGFR) β signaling, and blockade of chemokine (C-C motif) ligand (CCL) 17 signaling also attenuated peritoneal fibrosis by inhibiting inflammatory macrophages in mice models. Regorafenib is also tyrosine kinase inhibitor and anti-cancer agent. In this study, we aimed to clarify the effect of regorafenib in the treatment of peritoneal fibrosis.

**Method:** Mouse model of peritoneal fibrosis was induced by intraperitoneal hypochlorite injection. Mice were then treated by daily oral gavage of different doses of regorafenib or vehicle PBS for 7 days. Primary antibodies against the following protein were used for immunolabeling: α-smooth muscle actin (SMA) for detecting myofibroblasts and cluster of differentiation molecule (CD11b) for macrophages detection. Peritoneal fibrosis was quantified in Masson trichrome-stained paraffin section. Modified peritoneal equilibrium test (PET) and ultrafiltration amount were measure to monitor peritoneal function.

**Results:** The thickness of injured peritoneum, the number of α-SMA+ myofibroblasts and CD11b+ macrophages were decreased in regorafenib groups in a dose-dependent manner (P < 0.005; 0.005; 0.05, respectively). Peritoneal function tests displayed more ultrafiltration and higher D/D0 dialysate glucose in regorafenib groups (P < 0.005 and < 0.5).

**Conclusion:** Regorafenib attenuated peritoneal fibrosis by decreasing myofibroblasts and macrophages. And regorafenib also maintained peritoneal function. Regorafenib is a potential medication in the treatment of peritoneal fibrosis.

#4151
POLYCYSTINS ARE REQUIRED FOR RENAL TUBULOINTERSTITIAL FIBROSIS
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**Background and Aims:** Renal fibrosis is the common pathway of various chronic kidney diseases progressing to end stage renal failure. Polycystin-1 (encoded by PKD1 gene) and polycystin-2 (encoded by PKD2 gene) form a transmembrane complex and function as a stress sensor, which is located in the primary cilia. Polycystins are involved in the disease condition of different organs. Mutation of PKD genes causes autosomal dominant polycystic kidney disease and deletion of polycystin attenuates heart injury induced cardiac fibrosis. The role of polycystins in renal tubulointerstitial fibrosis is currently unclear.

**Method:** Unilateral ureteral obstruction (UUO), unilateral ischemia-reperfusion injury (UIRI), aristolochic acid or folic acid induced mouse models of renal fibrosis were established for this study.

**Results:** Here we showed that polycystin-2 is up-regulated in these three mouse models of renal fibrosis and tightly correlated with the expression of collagen-1 in a time dependent manner. Treatment with triptolide inhibited the expression of polycystin-2 and pro-fibrotic markers in UUO and UIRI models. Moreover, triptolide or PKD2 siRNA inhibited the expression of polycystin-2 and pro-fibrotic markers in vitro. Using Pkd2 conditional knockout mice, we showed that genetic deletion of Pkd2 reduced the expression of pro-fibrotic markers in UUO kidneys. Polycystin-1 was also up-regulated in renal fibrotic models and conditional deletion of Pkd1 reduced the expression of pro-fibrotic markers in UUO or folic acid induced fibrotic kidneys. Furthermore, the expression of the methyltransferase EZH2 is positively correlated with the expression of polycystins in fibrotic kidneys. Conditional knockout of EZH2 attenuated the anti-fibrotic responses induced by Pkd1 deletion in UUO kidneys.

**Conclusion:** In conclusion, polycystins are up-regulated in fibrotic kidneys and promote renal tubulointerstitial fibrosis through up-regulation of EZH2, suggesting that primary cilia are required for renal tubulointerstitial fibrosis.

#4504
QUANTITATIVE CHANGES IN INTRACARDIAC FLOW PARAMETERS DURING HEMODIALYTIC SESSIONS
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**Background and Aims:** Hemodialysis sessions exert an acute impact on cardiac geometry and mechanics. The recent development of quantitative measurement of intracardiac fluid-dynamics and analysis of vortexes offers a new opportunity to better understand the fine changes in intracardiac hemodynamic associated with hemodialysis sessions. Vortexes rise in cardiac chambers from blood flow and they are defined as circular fluid structures with rotational movement around a central virtual axis, capable of storing kinetic energy during rotation. They must be distinguished from turbulences, in which various vortexes of different sizes coexist chaotically, resulting in a rapid dissipation of kinetic energy. Our aim was to assess the impact of a hemodialysis session on new parameters originated from intracardiac flow dynamics.

**Method:** We included 26 consecutive patients on chronic hemodialysis in clinically stable phase. They underwent echocardiography including intracardiac fluid-dynamic analysis by Color Vector Flow Mapping (Hyperdoppler) before and after a single dialysis session (Fig. 1-A). Patients with hemodynamically relevant valvular disease were excluded. A complete fluid-dynamics evaluation included the measurement of multiple parameters such as vortex area (VA); vortex length (VL); vortex depth (VD); Bland Altman Plot has been used to assess intra and inter-observer variability. Changes in fluid dynamics after dialysis sessions were tested using the Wilcoxon matched-pairs test.

**Results:** The Mean Vortex Area (VA) (p = 0.034) (Fig. 1-B), Vortex Depth (VD) (p = 0.024) (Fig. 1-C) and Vortex Length (L) (p = 0.037) (Fig. 1-D) were significantly reduced after the dialysis session. A similar trend towards the reduction of Direct Flow (DF) parameter after the session was found, which was significantly larger for patients with larger baseline left ventricular (V) end-diastolic diameter (r = 0.446; p = 0.037) (Fig. 1-E). On the other hand, mean Vortex Intensity (VI) was significantly increased after dialysis (p = 0.046) (Fig. 1-F). Among energy parameters, the intradialytic change in Kinetic Energy Dissipation (KEF) (r = 0.4; p = 0.058) and Shear Stress Fluctuation (SSF) (r = 0.435; p = 0.038) (Fig. 1-G) were most closely correlated with intradialytic weight change. Fluid dynamic parameters had similar trends of intradialytic change, with stronger correlations among geometric parameters. Delta changes in VA were closely related to changes in VI (p = 0.001) or LV (p < 0.001). VI was also correlated with VL (p < 0.001) and with Kinetic Energy Dissipation (KEF) (p = 0.030), which was also correlated with VL (p = 0.044). KEF was correlated with KED (p = 0.001) and SSF (r = 0.022). Finally, changes in SSF were correlated with those in Flow Force Parameter (p = 0.033) and Flow Force Angle (p = 0.034), that were very closely correlated each other (p < 0.001).

**Conclusion:** This is the first study assessing the impact of hemodialytic sessions on intracardiac flow dynamics. Measurement of hyperdoppler indices on hemodialysis chair was feasible and reliable in the whole population. Our results uncovered quantitative changes of echocardiographic parameters of vortex geometry and energy during hemodialysis.
EPAC1- MEDIATED CAMP SIGNALLING PROMOTES CELLULAR ENERGY ADAPTATIONS IN PODOCYTES TO PROTECT FROM GLOMERULONEPHRITIS

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Background and Aims: Many efforts are made to identify new therapeutic targets to slow down, prevent or even reverse Chronic Kidney Disease (CKD) progression. One of the therapeutic approaches is activating the renoprotective CAMP pathway, especially by stimulation of its downstream effector, the protein kinase A (PKA). PKA was considered as the unique cAMP effector, however, the exchange factor directly activated by cAMP 1 (EPAC1) has been recently identified as a novel, PKA-independent, mediator of cAMP signalling. EPAC1 is a guanine exchange factor that promotes the exchange of GDP for GTP regulating important cellular functions. Epac1 activation exerts a renoprotective effect during acute kidney injury, via maintenance of epithelial adhesion and protection from oxidative stress. However, the role of EPAC1 in CKD remains poorly understood. Here we aim to determine the role of EPAC1 in CKD progression.

Method: Nephrotoxic serum glomerulonephritis (NTS-GN) is induced in genetically modified mice with total and conditional EPAC1 deletion. Then isolated glomeruli from mice with conditional EPAC1 deletion in podocytes are analysed by RNA-sequencing. The main metabolic energy pathways are studied in podocytes in vitro experiments in podocytes, including XOI and anakinra.

Results: Following the induction of NTS-GN, mice with genetic deletion of EPAC1 show aggravated renal disease, characterized by increased proteinuria, glomerular damage, tissue inflammation and fibrosis compared to wild-type mice. Conversely, pharmacological activation of EPAC1, with the agonist 8-pCPT-2-OMe-cAMP, delays NTS-GN progression. Since in human and wild type mouse kidney tissues we observe EPAC1 expression in podocytes, mice with conditional deletion of EPAC1 in podocytes (Nphs2Cre;epac1) are generated. Similar to the whole-body knockout, mice with EPAC1 deletion in podocytes show increased renal damage and worsened disease progression compared to control mice. RNA-sequencing analysis of glomeruli isolated from these mice show that gene expression of proteins linked to the pathway of glycolysis are abolished in early stage of NTS-GN (day 4). These data suggest that EPAC1-mediated activation of glycolysis in podocytes is essential to limit GN progression. This is substantiated by the in vitro experiments in podocytes, in which EPAC1 activation under oxidative stress promotes glycolysis with cellular energy production independently from mitochondrial respiration. The EPAC1-mediated glycolysis protected podocytes by increasing cell viability, decreasing LDH release and activating the AKT pathway.

Conclusion: Our results suggest a protective role of podocytes-derived EPAC1 against the development of GN through cellular energetic adaptations based on metabolic switch to glycolysis. Activating the cAMP-EPAC1 signalling axis could represent a therapeutic option to delay the development of CKD. Further investigations are needed to define its relevance in human CKD.

FEBUXOSTAT IN COMBINATION WITH ANAKINRA OR PH NEUTRALIZATION IMPROVE THE OUTCOMES IN HYPERURICEMIA-RELATED URIC ACID CRYSTALLURIA IN MICE

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Background and Aims: Currently, it is unknown whether CKD patients with hyperuricemia (HU)-related uric acid (UA) crystalluria, also known as chronic UA nephropathy, would benefit from targeting HU, UA crystallization, and/or inflammation to slow down the progressive decline of kidney function. Although large multi-center RCTs with xanthine oxidase inhibitors (XOIs) such as allopurinol and two Mendelian randomization studies have disproven a causal link between HU and CKD progression, one cannot rule out that XOIs may still represent a viable therapeutic approach for patients with HU-related UA crystalluria in order to prevent CKD progression. This issue requires clarification. To address this, we used our well-established CKD mouse model of HU with UA crystalluria and tested numerous therapeutic approaches including XOIs and anakinra.

Method: Alb-creERT2;Glut9lox/lox (male and female) mice were injected with tamoxifen and placed on an acidogenic diet with the purine inosine to induce HU and crystalluria-related CKD. After chronic UA nephropathy was established on day 14, mice were treated either 1) with the XOIs allopurinol or febuxostat, 2) with sodium bicarbonate supplementation to neutralize urinary pH to prevent UA crystallization, or 3) with anakinra to inhibit IL-1β-driven inflammation, or 4) a combination of the aforementioned therapies for 2 weeks. Saline was used as control. On day 0, 14, and 28, GFR (as primary endpoint) as well as serum UA levels and urinary UA crystals (as secondary endpoints) were determined. At the end of the study, we quantified kidney injury, immune cell infiltration, inflammation, and interstitial fibrosis using histological analysis, ELISA, RT-qPCR, and flow cytometry.

Results: Therapy with XOIs but not with sodium bicarbonate and anakinra reduced serum UA levels in mice with HU and UA crystalluria. Treating mice with febuxostat improved kidney function (increase in GFR) by preventing
Kidney injury, UA crystalluria, UA crystal granuloma formation, and interstitial fibrosis compared with the control group, while allopurinol worsened the outcomes of chronic UA nephropathy. On the other hand, sodium bicarbonate supplementation had no effects on serum UA levels, kidney inflammation, immune cell infiltration and interstitial fibrosis but improved kidney function due to less urinary UA crystal deposition (neutralization of urine pH) and granuloma formation as compared with saline-treated mice. As expected, anakinra did not slow down the progression of chronic UA nephropathy as noticed by similar GFR decline compared with the control group. Although, anakinra reduced the number of infiltrating immune cells and the mRNA expression of inflammatory mediators in the kidney as well as the serum IL-1/β concentrations, we observed more interstitial fibrosis. In combination, allopurinol with anakinra did not improve the outcomes of chronic UA nephropathy despite the inhibitory effect of anakinra on the inflammatory response. Use of allopurinol triggered tubulointerstitial nephritis and vasoconstriction. Interestingly, both combination therapies febuxostat with anakinra and febuxostat with sodium bicarbonate were protective by improving kidney function and preventing UA crystal deposition, kidney injury, inflammation, interstitial fibrosis and UA crystal granuloma formation compared with the single therapies.

Conclusion: Our interventional study is the first pre-clinical study, which reveals that the XOIs allopurinol and febuxostat have differential effects on the outcomes of HU-related UA crystalluria. While allopurinol contributes to the progression of CKD by causing tubulointerstitial nephritis in mice, febuxostat rather seems to be renoprotective similar to urinary pH neutralization with sodium bicarbonate. We identified both combination therapies febuxostat with anakinra and sodium bicarbonate as most beneficial in order to prevent CKD progression in mice. Thus, febuxostat in combination with IL-1β inhibition or prevention of urinary UA crystallization may represent therapeutic approaches for patients with chronic UA nephropathy.

#3680
CALPAIN INHIBITION PREVENTS FIBROSIS IN PROGRESSIVE CHRONIC KIDNEY DISEASE
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Background and Aims: Kidney fibrosis is one of the main pathological processes of chronic kidney disease (CKD), although the pathogenesis of renal scar formation is not fully understood. Calpains (CAPN) are intracellular cysteine proteases that play a key role in multiple biological processes linked to tissue damage and repair mechanisms, such as fibrosis and epithelial-mesenchymal transition. However, CAPN contribution in CKD genesis and progression remains to be fully elucidated. The aim of this study was to investigate the possible role of CAPN in the development of CKD and renal fibrosis in an experimental model of CKD induced by adenine and in human kidney proximal tubular cells (HK-2).

Method: C57BL/6 mice were treated with an adenine-supplemented diet (0.2% adenine) or control diet for eight weeks. At the end of treatment, kidney function was assessed (serum creatinine, proteinuria), animals were euthanised, and the kidneys removed. A transverse section of the kidney was prepared for histology. Whole kidney cortical tissue was analysed using two-dimensional correlated spectroscopy (2D-COSY), a form of proton nuclear magnetic resonance (NMR) spectroscopy. Biochemical species, including metabolites and lipids, within the tissue were identified and compared with respective histological tubulointerstitial fibrosis level and traditional serum markers of kidney function, plasma creatinine and blood urea nitrogen. A 2D-COSY spectrum can be found in Figure 1A.

Results: The adenine-supplemented diet induced tubulointerstitial fibrosis, mirrored by increases in serum creatinine and blood urea nitrogen, indicating decreased kidney function. The 2D-COSY analysis demonstrated numerous changes in metabolites with parallel increasing levels of fibrosis that were detected. Increases in metabolites belonging to the glycolysis (D-glucose, glucose-6-phosphate and lactate) and pentose-phosphate (myo-inositol, D-ribose-5-phosphate) pathways were observed, as well as a decrease in lipid. Additionally, increases in creatinine, creatine and a number of amino acids were also observed. These changes are displayed in Table 1 and Figure 1B.

Conclusion: The primary cell type of the kidney cortex is the proximal tubular epithelial cell. Due to its unique function in water and solute transport, this cell has a very high metabolic demand and utilizes fatty acid oxidation as its primary source of energy. However, when these cells are under pathological stress that contributes to tubulointerstitial fibrosis, such as those present within this animal model of chronic kidney disease, metabolic dysfunction occurs. We observed significant decreases in various lipid signals belonging to fatty acids within the cell. These fatty acids are not being utilised and are instead esterified to triglycerides that accumulate in the kidney, causing lipotoxicity. Increased levels of glucose-6-phosphate, lactate and D-glucose, as well as increased myo-inositol, glucuronic acid D-ribose-5-phosphate are indicative of increased utilisation of the glycolysis and pentose phosphate pathway respectively as primary methods of energy metabolism. Here, we provide evidence that in tubulointerstitial fibrosis within the kidneys leads to a shift in the primary energy pathway used by proximal tubular epithelial cells. The study provides new insights into the changes in biochemical pathways that occur in the kidney during the development of CKD and its progression.

#4344
CHANGES IN ENERGY METABOLISM IN THE KIDNEY WITH TUBULOINTERSTITIAL FIBROSIS: AN EX VIVO WHOLE TISSUE 2D-COSY APPROACH
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Background and Aims: Tubulointerstitial fibrosis is the common pathological manifestation in chronic kidney disease (CKD) and can indicate whether a patient will progress to kidney failure. The metabolic consequences of developing fibrosis are not well understood. This project aimed to investigate metabolic changes in the kidney cortex using an adenine-diet murine model of progressive CKD.

Method: C57BL/6 mice were treated with an adenine-supplemented diet (0.2% adenine) or control diet for eight weeks. At the end of treatment, kidney function was assessed (serum creatinine, proteinuria), animals were euthanised, and the kidneys removed. A transverse section of the kidney was prepared for histology. Whole kidney cortical tissue was analysed using two-dimensional correlated spectroscopy (2D-COSY), a form of proton nuclear magnetic resonance (NMR) spectroscopy. Biochemical species, including metabolites and lipids, within the tissue were identified and compared with respective histological tubulointerstitial fibrosis level and traditional serum markers of kidney function, plasma creatinine and blood urea nitrogen. A 2D-COSY spectrum can be found in Figure 1A.

Results: The adenine-supplemented diet induced tubulointerstitial fibrosis, mirrored by increases in serum creatinine and blood urea nitrogen, indicating decreased kidney function. The 2D-COSY analysis demonstrated numerous changes in metabolites with parallel increasing levels of fibrosis that were detected. Increases in metabolites belonging to the glycolysis (D-glucose, glucose-6-phosphate and lactate) and pentose-phosphate (myo-inositol, D-ribose-5-phosphate, glucuronic acid) pathways were observed, as well as a decrease in lipid. Additionally, increases in creatinine, creatine and a number of amino acids were also observed. These changes are displayed in Table 1 and Figure 1B.

Conclusion: The primary cell type of the kidney cortex is the proximal tubular epithelial cell. Due to its unique function in water and solute transport, this cell has a very high metabolic demand and utilizes fatty acid oxidation as its primary source of energy. However, when these cells are under pathological stress that contributes to tubulointerstitial fibrosis, such as those present within this animal model of chronic kidney disease, metabolic dysfunction occurs. We observed significant decreases in various lipid signals belonging to fatty acids within the cell. These fatty acids are not being utilised and are instead esterified to triglycerides that accumulate in the kidney, causing lipotoxicity. Increased levels of glucose-6-phosphate, lactate and D-glucose, as well as increased myo-inositol, glucuronic acid D-ribose-5-phosphate are indicative of increased utilisation of the glycolysis and pentose phosphate pathway respectively as primary methods of energy metabolism. Here, we provide evidence that in tubulointerstitial fibrosis within the kidneys leads to a shift in the primary energy pathway used by proximal tubular epithelial cells. The study provides new insights into the changes in biochemical pathways that occur in the kidney during the development of CKD and its progression.
Figure 1: *Ex vivo* whole tissue NMR spectroscopy of chronic kidney diseased kidneys induced by an adenine-supplemented diet (0.2% adenine). (A) Representative 2D-COSY spectrum of a treatment mouse kidney. Individual peaks indicate hydrogen containing functional groups of different molecules. These peaks were assigned to specific metabolites and lipids and their respective volumes were used to measure the relative concentration of the metabolite within the tissue. (B) Fold change (FC) versus *p*-value of various identified biomolecule peaks with in the tissue. Blue indicates a decrease in the treatment from control, while red indicates an increase in treatment from control. Dotted lines show thresholds of *p*=0.05 and FC=1. Data was normalised for tissue weights, log₂ transformed and auto scaled. P-values were calculated using unpaired *t*-tests with welch correction.
Table 1: Metabolite changes occurring in the kidney with adenine-diet induced tubulointerstitial fibrosis compared to control. The chemical shift of a molecule indicates the “coordinates” of the specific functional group in a 2D-COSY spectrum (see fig. 1A).

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Chemical shift (ppm)-</th>
<th>f2, f1</th>
<th>Fold Change from control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucuronic acid</td>
<td>3.74, 4.02</td>
<td>3.0</td>
<td>0.002</td>
<td></td>
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#4369

**MYELOID CELL-DERIVED HMGB1 AGGRAVATES THE PROGRESSION OF CHRONIC KIDNEY DISEASE INDUCED BY CHRONIC OXALATE EXPOSURE**

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**Background and Aims:** HMGB1, long form High Mobility Group Box 1, a highly conserved DNA chaperone stabilizes chromatin in the nucleus, regulates gene transcription, and supports DNA repair. In the cytosol, it regulates mitochondrial function, autophagy, and apoptosis. In addition, when secreted or passively released into the extracellular space during cell necrosis, it acts as danger signal (DAMP). As such HMGB1 amplifies necroinflammation in ischemic and toxic acute kidney injury. In contrast, little is known about the contribution of HMGB1 release from infiltrating immune cells in this context. We hypothesized that HMGB1 from resident and infiltrating myeloid cells would contribute to the progression of CKD by driving tubular atrophy and tissue remodeling.

**Method:** We generated myeloid deletion of HMGB1 by crossing Hmgb1 floxed mice (Hmgb1flox) with endogenous Lys2 promoter (LysZCre) to investigate the role of myeloid cell HMGB1 in a model of chronic kidney disease induced by sodium oxalate-rich diet (50 μmol/g), i.e., calcium oxalate nephropathy. The LysZCre mice were on a C57BL/6J background and crossed with mice homozygous for the floxed Hmgb1 gene in all myeloid cells. We used littermates of 6- or 8-week-old males for all experiments. Mice with no LysZCre but the homozygous of floxed Hmgb1 gene served as wildtype controls (LysZCre−Hmgb1flox WT) and mice with LysZCre and the homozygous of floxed Hmgb1 gene were used as LysZCre Hmgb1flox KO. The primary endpoint for the comparison between LysZCre Hmgb1flox KO and WT mice was glomerular filtration rate at 21 days of oxalate feeding, assessed by FITC-sinistrin clearance. Plasma samples were collected only on day 21 before sacrifice by cervical dislocation. Urine samples were collected as well and as GFR was measured from all experimental groups on day 0, day7, day14 and before sacrifice by caval dislocation on day 21. Kidneys were harvested after sacrifice. The kidney was divided into two equal parts. One part was kept in RNA later solution at −80°C for RNA isolation and the second part was kept in 4% formalin to be embedded in paraffin for histology analysis.

**Results:** KO animals did not reveal any abnormalities within an observation phase of 6 months. Healthy mice showed normal kidney function parameters in urine and blood. Observation is continued and will be supplemented by histopathological analyses at the age of 12 months. Primary endpoint: Deletion of HMGB1 from myeloid cells attenuated the decline of GFR as compared to WT control mice. Secondary endpoints: The difference in GFR was consistent with the respective levels of serum creatinine at day 21 upon oxalate-rich diet compared with controls. The ablation of HMGB1 in myeloid cells was associated with less tubulointerstitial fibrosis at day 21 after oxalate-rich diet.

**Conclusion:** Our data suggest that HMGB1 release from myeloid cells promotes crystal-induced chronic kidney injury, which is consistent with the role of HMGB1 as an extracellular DAMP and persistent inflammation in CKD. However, this effect may also relate to the intracellular role of HMGB1 as a transcriptional regulator.
Figure 1: The deletion of intracellular HMGB1 mitigated chronic kidney injury at day 21 after oxalate-rich diet. (A) The renal glomerular filtration from day 0 to day 21 in crystal-induced nephrocalcinosis. (B) The mice serum level of creatinine in crystal-induced nephrocalcinosis at day 21. (C) The renal tubular damage was quantified on periodic acid-Schiff (PAS), sirius red staining represented tubular fibrosis, crystal deposition indicated by pizzolato staining. MC (Lyz2^{cre}^{−}/Hmgb1^{f/f} control mice) and MH (Lyz2^{cre}^{+}/Hmgb1^{f/f} knockout mice). *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.
IDENTIFICATION AND CHARACTERIZATION OF URINARY AND SERUM AMINOACIDS IN DIABETIC KIDNEY DISEASE PATIENTS USING MS-HPLC

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Background and Aims: Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease, but few biomarkers of early identification of DKD are available. The aim of the study was to assess new urinary and plasma biomarkers in early stages of DKD, especially in normoalbuminuric type 2 diabetes mellitus (DM) patients.

Method: This cross-sectional pilot study performed an integrated metabolomic profiling of blood and urine in 90 patients with type 2 DM, classified into 3 stages (30 normo-, 30 micro-, and 30 macroalbuminuric, respectively) and 30 age- and gender-matched healthy controls through high-performance liquid chromatography and mass spectrometry (UPLC-QTOF-ESI* MS). Metabolites were discovered and processed by the advanced MetaXaminer 5.0. online software using multi- and univariate untargeted analysis. Both multivariate and univariate bioinformatics confirmed the relevance of certain amino acids as biomarkers to be responsible for the occurrence of early renal involvement in the course of type 2 DM.

Results: A total of 5 metabolites, namely Taurine, Tiglylglycine, Tryptophan, Kynurenic acid, and L-acetylcarnitine were discovered as potential biomarkers for the early identification of DKD. UPLC-QTOF-ESI* MS revealed that: (1) the urinary amino acids levels were increased in normoalbuminuric type 2 DM patients as compared with healthy control subjects; (2) a number of key biomarkers have been identified in the urine, which reflect kidney injury at specific sites in the nephron, including glomerular injury and tubular damage, oxidative stress, inflammation, and activation of the intrarenal renin-angiotensin system.

Conclusion: High-performance liquid chromatography coupled with mass spectrometry showed that the urinary amino acids levels were increased in normoalbuminuric type 2 DM patients. The results of the study provide a particular metabolomic profile related to blood and urine metabolites which could impact both the glomeruli and the tubules, even in the early stages of DKD.

#5736

IMPACT OF SYMBIOTICS ON UREMIC TOXINS PRODUCTION, RENAL FUNCTION AND PEW SYNDROME IN SHIME AND CKD MICE MODELS

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1Laboratoire CarMeN, INSERM U1060, INRA 1397, Université Claude Bernard Lyon 1, Pierre Benite, France, 2Lyon Sud Hospital Center, Pierre-Bénite, France, 3Ghent University Hospital, Nephrology Section, Department of Internal Medicine and Pediatrics, Gent, Belgium and 4Nestlé Health Science SA, Lausanne, Switzerland

Background and Aims: Alterations in gut microbiota in CKD patients have been linked to CKD progression, cachexia, and mortality. Gut dysbiosis is associated by modification of gut-microbiota-derived metabolites, including a decrease of short-chain fatty acids (SCFAs), an increase in gut-derived uremic toxins. Therefore, modulation of gut microbiota seems to be an attractive therapeutic approach. In silico studies led to the selection of bacterial species able to increase SCFAs production, improve gut function without having the enzymatic machinery for producing uremic toxins. The propose of this study is to indentify the impact of two different symbiotics containing the selected bacteria: 1) on both uremic toxins and SCFAs production using a Simulator of the Human Intestinal Microbial Ecosystem (SHIME) colonized with fresh feces from CKD or healthy controls (HC) and subsequently 2) on renal function, metabolic parameters, intestinal microbiota and gut-microbiota-derived metabolites in a mouse model of CKD (5/6 nephrectomy).

Method: 1) The SHIME® system manufactured by ProDigest (Ghent, Belgium) consists of systems comprising five double-wall biowessels simulating the stomach (ST), small intestine (SI), ascending colon (AC), transverse colon (TC), and descending colon (DC). The supernatant of the homogenized fecal slurry was inoculated into the AC (25 mL), TC (40 mL), and DC (30 mL), respectively. After fecal inoculation, SHIME system were fed in ST twice day with two different symbiotics (P1 or P2) for 10 days. After 7 days, we applied a diet amino acid (AA) challenge to all the groups. SCFAs and uremic toxins were quantified every day. 2) CKD mice received either P1 or P2 admix for 6 weeks. We measured food intake, body composition and renal function including renal fibrosis quantification. Plasma metabolomic and feces metagenomic analyses were performed.

Results: In vitro, the concentration of precursor of uremic toxins (indols and p-cresol) tended to be higher in DC colonized by feces from CKD patients and AA challenge increased uremic toxins production more significantly in CKD compared to HC. CKD microbiome showed a lower butyrate concentration at baseline and higher propionate and acetate production. Both P1 and P2 significantly limited uremic toxins production during AA challenge and increase SCFA production. In vivo, both symbiotics increased body weight (+14%) and food intake (+31%) compared to CKD mice on chow diet. Treatment did not impact lipid or glucose metabolism but fat accretion in epididymal was restored with P1. Both diets, but particularly P1, significantly reduced plasmatric urea, proteinuria, and kidney fibrosis. Symbiotics improved intestinal barrier with a greater expression of Occludin in the ileum. Metagenomic analyses of the gut microbiota indicated that the alpha-diversity was different across groups while the beta-diversity was similar to the sham group if CKD mice were treated with symbiotics. Both symbiotics reduced significantly plasma levels of deleterious uremic toxins such as p-cresyl sulfate and indoxyl sulfate and symbiotics reduce fecal module of tryptophan degradation and other modules related to AA metabolism. Both diets increased fecal bacteria modules related to SCFAs production.

Conclusion: We have shown both in vitro and in vivo that a symbiotic association can reduce uremic toxins production and increase SCFA production by inducing a significant change in gut microbiota composition and function. These metabolic changes are associated with improved appetite, decreased uremic cachexia, and preserved renal function. This data needs be confirmed in a human clinical trial.
HOW WELL INFORMED ARE PATIENTS ABOUT DIALYSIS INITIATION?

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1Karolinska University Hospital, Rosenlund Hospital/PD-unit, Stockholm, Sweden, 2Netherlands, 3United Kingdom, 4Italy, 5Germany, 6Germany, 7Poland and 8Sweden, for the EQUAL study group

Background and Aims: Studies indicate that 30% of patients on dialysis feel inadequately informed about various dialysis options and also lack involvement in the decision-making process surrounding dialysis initiation. The aim of this study was to 1) describe the provision of information to older patients with chronic kidney disease before KRT and 2) to study the association between the perceived amount of information received before dialysis and patients satisfaction with treatment post dialysis initiation.

Method: The EQUAL study is a multicenter, prospective cohort study in six European countries (Germany, Italy, Netherlands, Poland, Sweden, and United Kingdom). Inclusion criteria are older adults >65 years with an incident eGFR < 20 ml/min/1.73 m². Patients were followed up every 3-6 months and received routine medical care as provided by the nephrology clinic in each country. Standardized data were collected at each visit, including demographics, lifestyle, comorbidities, uremic signs and symptoms, quality of life, treatment satisfaction according to renal treatment satisfaction questionnaire (RTSQ-11), nutritional status, medication and routine blood and urine biochemistry. We described patient characteristics and perceived information provision at different time points (incident eGFR<20, eGFR<15, eGFR<10 ml/min/1.73 m²). Subsequently, we compared patient characteristics between those who reported receiving more versus less information at the last eGFR before start of KRT (or end-of follow-up in patients with eGFR <10 ml/min/1.73 m²).

We used multivariable logistic regression models to investigate if perceived information provision before start of dialysis was associated with a treatment satisfaction.

Results: We included 1372 patients at baseline with a median age of 76 (IQR 70–81), 34% (n = 462) women. Over follow-up, 997 of these patients progressed to an eGFR<15, and 573 to an eGFR<10 ml/min/1.73 m². The proportion of patients who reported having received enough information about the decision on when to start dialysis increased with decreasing eGFR (53.2% at baseline to 61.2% (eGFR<15) and 70.9% (eGFR<10)). Among the 638 patients progressing to KRT or eGFR <10 ml/min/1.73 m², the mean eGFR was 8.9 ml/min/1.73 m² (SD 3.4) at their last pre-dialysis visit. Patients who reported that they had received sufficient information regarding dialysis timing were in general younger, where median age was 74 (IQR 69.4-79.3) years for those receiving information and 76 (IQR 70.7-81.4) years for those perceiving not having enough information, but there were otherwise no major differences in patient characteristics. Among these patients, 32% had still not decided on which dialysis modality to start with. There was not any statistically significant difference in RTSQ-11 score associated with type of dialysis modality (hemodialysis versus peritoneal dialysis) post dialysis initiation. Among 302 patients who started dialysis, those reporting to have received more information (highest quartile) before start of dialysis also reported being more satisfied with their treatment post dialysis (OR: 1.22; 95% CI 1.05-1.37).

Conclusion: Although most patients report having received pre-dialysis information, many patients with low kidney function still perceive not having received enough information to make an informed decision. Patients who are well informed are more satisfied with their treatment.
Background and Aims: Cellular senescence is associated with renal disease progression. Accelerated tubular cell senescence promotes the pathogenesis of renal fibrosis no matter caused by natural aging or disease. However, the underlying mechanism is unknown.

Method: Proteomic analysis of natural aging kidney from 20-week mice was used to find potential target protein which is acyl-CoA synthetase medium chain family member 3 (Acsm3). After finding it, two Acsm3 inhibitor (4-Methylsalicylic acid and 2-hydroxyoctanoic acid) were used separately to treat natural aging and pathological aging (unilateral ureteral obstruction induced renal fibrosis) mice. Renal histological injury was measured by HE and Masson's trichrome staining. SA-β-gal staining was used to check cellular senescence. Renal tissues of the mice were analysed by western blot and qPCR assay for the expression of Acsm3, fibrosis and cellular senescence related proteins and genes. In order to avoid drug toxicity, tubular epithelial cells were treated with Acsm3 SiRNA to explore the effects of Acsm3 in vitro.

Results: Firstly, we confirmed that cellular senescence happened in both elderly mice and UUO mice and found SA-β-gal positive cells were mainly tubular epithelial cells. After analysing proteomic sequencing data, Acsm3 is the protein which increased dramatically as the top one protein in elderly mice. We also found Acsm3 increased in tubular cells specifically in adult mice compared with fetal mice from KIT single cell database, which suggested that Acsm3 might have effects for kidney development. After validating changes and location of Acsm3, we treated natural aging and UUO mice with two Acsm3 inhibitor to check the function of Acsm3, separately. Administration of Acsm3 inhibitor (no matter 4-Methylsalicylic acid or 2-hydroxyoctanoic acid) could induce renal histological injuries, renal fibrosis, with significantly increased COL6, α-SMA and FN expression in both natural aging and UUO induced renal fibrosis. The cellular senescence was also observed to increase after Acsm3 inhibitor treatment with growth P21 and P16 expression. In addition, pro-inflammatory senescence-associated secretory phenotype (SASP) including IL6 and MCP1 increased as well. In order to avoid kidney injury induced by drug toxicity instead of by inhibition of Acsm3, we transfected Acsm3 SiRNA in tubular epithelial cells to check in vitro. Similarly, the inhibition of Acsm3 augmented cellular senescence and SASP of tubular epithelial cells as what we found in vivo. It supported that inhibition of Acsm3 could induce senescence of tubular epithelial cells and thus to promote kidney fibrosis.

Conclusion: These findings suggested that Acsm3 could be an important protector for renal fibrosis by inhibiting cellular senescence of tubular epithelial cells. The underlying mechanism needs to explore more.
TUBULE CELL-DERIVED ANGIOPOIETIN-2 EXACERBATES INFLAMMATION AND IS DETRIMENTAL TO RENAL FIBROSIS
AN Jie Luo¹, Fan-Chi Chang² and Shuei-Liong Lin¹,²
¹National Taiwan University College of Medicine, Graduate Institute of Physiology, Taipei, Taiwan, R.O.C. and ²National Taiwan University Hospital, Renal Division, Department of Internal Medicine, Taipei, Taiwan, Rep. of China

Background and Aims: Our previous studies have shown that angiogenic growth factors are dysregulated in fibrotic kidneys. In murine models of progressive renal disease, angiopoietin-2 (Angpt2) was upregulated in injured tubule epithelial cells. We hypothesize that overexpression of Angpt2 in tubule epithelial cells would exacerbate renal fibrosis and inflammation.

Method: The unilateral ureteral obstruction (UUO) and unilateral ischemia-reperfusion injury (UIRI) are used as the murine model of chronic kidney disease. We use the tetracycline/doxycycline-controlled Tet-on system to induce tubule cell-specific overexpression of Angpt2 before the induction of renal fibrosis. Transgenic mice carrying both Pax8-rtTA and pTetos-hAngpt2 genes (double transgenic mice) are used for Angpt2 overexpression. Littermates that inherit single or no transgene serve as experimental controls. Doxycycline is administered to adult (8 weeks) mice to overexpress Angpt2 in tubule epithelial cells.

Results: Doxycycline administration induce overexpression of human Anp2 in the tubule epithelial cells of both sham and fibrotic kidneys. Compared to littermate controls after the UUO and UIRI surgery, the expression of fibrosis-related genes, Col1a1, Col3a1, and Acta2 are higher in the kidneys of double transgenic mice. Deposition of picrosirius red-stained collagen fibrils is significantly higher in double transgenic mice. Inflammatory cell infiltration is also significantly higher in double transgenic mice.

Conclusion: Overall, these findings suggest that increased Angpt2 in tubule epithelial cells deteriorate renal fibrosis through detrimental inflammation. Further studies are necessary to explore the participating cellular components and pathogenic mechanisms.

TRANSGENIC INDUCTION OF EPITHELIAL SENESCENCE PROMOTES RENAL FIBROSIS INDEPENDENT OF INJURY
Marie-Helena Docherty¹, Ross Campbell¹, Laura Denby³, David Baird¹, Katie Mylonas¹ and David Ferenbach¹
¹Queens Medical Research Institute, University of Edinburgh, Centre for Inflammation Research, United Kingdom and ²Queens Medical Research Institute, Centre for Cardiovascular Sciences, United Kingdom

Results: Doxycycline administration induce overexpression of human Anp2 in the tubule epithelial cells of both sham and fibrotic kidneys. Compared to littermate controls after the UUO and UIRI surgery, the expression of fibrosis-related genes, Col1a1, Col3a1, and Acta2 are higher in the kidneys of double transgenic mice. Deposition of picrosirius red-stained collagen fibrils is significantly higher in double transgenic mice. Inflammatory cell infiltration is also significantly higher in double transgenic mice.

Conclusion: Overall, these findings suggest that increased Angpt2 in tubule epithelial cells deteriorate renal fibrosis through detrimental inflammation. Further studies are necessary to explore the participating cellular components and pathogenic mechanisms.
Background and Aims: Chronic Kidney Disease (CKD) affects over 850 million people worldwide. Progressive renal fibrosis is a hallmark of CKD, irrespective of the initiating aetiology. Any episode of acute kidney injury (AKI) significantly increases the risk of development of CKD, even after apparent complete resolution of the initiating injury. This risk is exacerbated by age and pre-existing CKD. This implies that factors persist within damaged/aging kidneys which drive functional loss, impair complete repair and promote ongoing fibrosis. Senescent cells (SCs) are metabolically active, permanently growth arrested cells produced in response to stress and DNA damage. SCs accumulate with age and persist at the sites of previous disease and injury. Their depletion in animal models is safe and extends organ function and healthspan. We have shown that pharmacological SC depletion in kidneys significantly improves kidney function and reduces fibrosis post injury. However, models of renal injury induce changes in multiple cell lineages, and pharmacological depletion is non-specific both in terms of cell lineage (i.e. epithelial vs mesenchymal vs leukocyte) and characteristics of senescent cell (i.e. acute vs chronic, primary vs secondary). We hypothesised that induction of epithelial senescence in the absence of other renal injuries is sufficient to initiate renal fibrosis. We developed a transgenic mouse allowing selective senescence induction in renal epithelia in the absence of injury, with tdTomato labelling of induced cells.

Method: By crossing existing strains, we produced a triple transgenic Pax8\textsuperscript{CreERT2}/mdm2\textsuperscript{flfl}/tdTom\textsuperscript{LSL} mouse allowing conditional senescence induction by tamoxifen via mdm2 deletion in Pax8 expressing renal epithelia, alongside tdTomato expression. Levels of renal fibrosis, p21cip1 and tdTomato induction were quantified by picrosirius red staining, immunofluorescence and flow cytometry, with downstream image analysis on QuPath 0.3.2. \textit{CDKN1A} gene expression was quantified by qPCR.

Results: Examination of kidneys and livers from young mice ± tamoxifen demonstrated that tdTomato induction was tissue specific and restricted to renal epithelia (Fig 1A-C). Administration of Tamoxifen resulted in increased expression of tdTomato and \textit{CDKN1A} expression at day 7 in transgenic but not in WT mice. (Fig. 1C, 2 A-F). We observed a rapid induction of fibrosis in the first 7 days after tamoxifen induction in both young (Fig. 3A,C) and old mice (Fig 3C). This persists to day 42 (Fig. 3B). This demonstrated that epithelial senescence alone was sufficient to induce renal fibrosis in young mice, and exacerbate fibrosis in old mice. Further studies assessed the longer-term impact of acute senescence induction, with fibrosis stabilising in both young and old mice at 6 weeks post induction (Fig. 3D).
Conclusion: Using a novel transgenic mouse line, we demonstrate for the first time that induction of renal epithelial senescence in the absence of injury is sufficient to induce renal fibrosis in the early aftermath of SC induction. The evolution and/or clearance of senescent cells over time is the focus of on-going study and will be presented at the ERA.

#3627
PHOSPHATIDYLSERINE EXPOSURE AND SHORTENED LIFE SPAN OF ERYTHROCYTES IN RENAL ANEMIA
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Background and Aims: The lifespan of erythrocytes in patients with renal anemia is shortened (~70 days) compared to that of healthy erythrocytes (120 days), but the pathological mechanisms and causes are unclear. Senescent erythrocytes express phosphatidylserine (PS) on their outer membrane, which is a signal for being removed by macrophages. The PS localization in the cellular membrane is mainly regulated by two transporters: flippases and scramblases. Flippases, type IV P-type ATPases (P4-ATPases), maintain PS localization in the inner leaflet by transporting PS from the outer leaflet of the cell membrane. When scramblases are activated, they facilitate equal distribution of phospholipids between the inner and outer lipid bilayers, resulting in the exposure of PS on the outer leaflet. Recently, we have revealed that reduced flippase activity contributes to PS exposure in healthy senescent erythrocytes [1]. In this study, we examined the percentage of PS-exposed cells and the transporter activity in erythrocytes from renal anemia to elucidate the mechanism of the shortened lifespan.

Method: This study was approved by the Ethics Committee of Tokyo Women’s Medical University (#3835, #4822R2). Erythrocytes from the renal anemic patients undergoing maintenance hemodialysis were separated with the centrifugation using Percoll-density gradient according to our previous report. Resultant heavy and light fractions were used as senescent and young erythrocytes, respectively. We analyzed the percentage of PS-exposed cells (n = 12), flippase/scramblase activities (n = 7), and the factors involved in those enzymatic activities such as intracellular K+ (n = 10) and ATP concentration (n = 9). We also measured protein 4.1a/b and HbA1c as an index of erythrocytes’ age.

Results: The cells from renal anemia were separated to heavy (senescent) and light (young) fractions, which was similar to the distributions previously performed on healthy erythrocytes. The PS-exposed erythrocytes in the heavy fraction were slightly more than those of the light fraction (p < 0.01, Wilcoxon test), and the flippase activity of the heavy fraction decreased more than that of the light fraction (p < 0.01, paired t-test). Intracellular K+ concentration decreased in the heavy fraction more than in the light fraction similar to the healthy senescent erythrocytes, but there was no statistical difference in the intracellular ATP concentration between the heavy and light fractions. The measurement of protein 4.1a/b and HbA1c in these fractions is still in progress.

Conclusion: Similar to healthy erythrocytes, reduced flippase activity contributes to PS exposure in senescent erythrocytes of renal anemia, maybe due to the decreased intracellular K+ concentration. This may occur in an earlier stage of senescence than the healthy ones, which may explain the mechanism of the shortened life span.

REFERENCE

#5554
ROLE OF THE TUBULAR EPITHELIAL CELL NLRP3 INFLAMMASOME DURING HYPERGLYCEMIA AND GLUCOSURIA IN DIABETES
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Background and Aims: Diabetes is a prominent risk factor for the progression of CKD because hyperglycemia and glucose filtration increase the hemodynamic and metabolic workload to the nephrons, which imposes adaptive mechanisms. Tubules adapt to diabetes by enlargement and epithelial cell hypertrophy but an exceeding metabolic workload promotes oxidative stress, cytokine signaling and tubular epithelial (TEC) cell demise leading to tubular atrophy and interstitial fibrosis. Several studies propose a role of the NLRP3 inflammasome in tubulointerstitial inflammation in diabetic and non-diabetic kidney disease. The NLRP3 inflammasome is a sensor of cellular damage responsible for regulating the IL-1β and IL-18 production, playing important role during the progression of CKD. However, the role of NLRP3 in diabetes-induced tubular adaptation is unknown.

Method: scRNAseq analysis showed previously that the TECs do not express NLRP3 or inflammasome components. However, a group of patients diagnosed with Cryopyrin-Associated Autoinflammatory Syndromes, have a mutation that overexpress NLRP3, which is associated with chronic and systemic inflammation. To investigate the role of NLRP3 in tubular cells under diabetes conditions, we generated a mouse line by crossing mice bearing LoxP-target A350V allele with Pax8-driven Cre transgenic mice. Animals carrying the A350V allele have overexpression of NLRP3 in tubular cells. The combination of unilateral nephrectomy and treatment with multiple low doses of streptozotocin (60 mg/Kg) accelerate the kidney injury caused by hyperglycemia. Kidney function, histology and gene expression were evaluated at the end of 16 weeks of diabetes. In vitro experiments carried out using TECs isolated from Pax8-A350V, and stimulated with LPS (1μg/ml) and/or ATP (20 mM).

Results: In silico analysis showed TECs do not express NLRP3 or inflammasome components. A350V-TECs under inflammasome activation did not produce IL-1β or IL-18. However, the Nlrp3 overexpression upregulated kidney injury markers, as well IL-6 and TNF. Moreover, the increase in kidney inflammation was associated with significative upregulation of fibrosis markers (Tgfβ1, Asma, and Fni1) and extracellular molecules (Ctgf, AnxaII, and Chd2). Diabetic mice carrying the A350V mutation did not have significative differences in blood glucose, albuminuria, or body weight when compared with diabetic control mice. The overexpression of NLRP3 in tubular cells was associated with significative reduction in GFR and BUN when compared with controls mice, even though no differences in tubular injury markers observed. Furthermore, Pax8-A350V diabetic mice expressed significantly more Nlrp3 and Il1b than control group. Although, no differences observed in cryopyrin staining.

Conclusion: Our data suggest the NLRP3-associated damage in tubular epithelial cells occurs in a non-canonical manner.

#4158
URINE DERIVED STEM CELL AMELIORATES RENAL FIBROSIS VIA KLOTHO ACTIVATION
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Background and Aims: After renal IRI, regeneration and recovery of the renal tubular cell occurs. However, if the renal repair process is maladaptive, it progresses to renal fibrosis. The role of stem cells in kidney regeneration or fibrosis has not been fully elucidated. we evaluated the urine derived stem cells (UDSC) for renal inflammation and fibrosis after renal ischemia reperfusion (IR).

Method: 10 week old babie nude male mice were used. sham, sham with UDSC, IR, IR with UDSC. UDSC were infused 3 times via tail vain at 6, 7, 8th day after renal IR. Urine NGAL/creatinine (Cr) were checked. The kidneys
tissue were harvested at day 14 day. In vitro, TGF-β treated HK2 cell were co-cultured with UDSC. Klotho siRNA silencing was performed in UDSC.

**Results:** Urinary NGAL/Cr were significantly increased in IR mice after 14 day IR, compared to sham mice. Urinary NGAL/Cr significantly decreased in UDSC treated IR mice, compared to IR mice. In H&E stain, renal tubulo-interstitial injury were significantly decreased in UDSC treated IR mice, compared to IR mice. In Masson trichrom stain, renal fibrosis area were significantly decreased in UDSC treated IR mice, compared to IR mice. The renal expression of TGF-β, α-SMA, and collagen IV were significantly decreased in UDSC treated IR mice, compared to IR mice. The renal expression of Klotho were increased in UDSC treated IR mice, compared to IR mice. In vitro, UDSCs were stem cells that expressed Klotho protein more strongly than other mesenchymal stem cells (MSCs). UDSCs also suppressed fibrosis by inhibiting transforming growth factor (TGF)-β in HK-2 human renal proximal tubule cells in an in vitro model. Klotho siRNA silencing reduced the TGF-β-inhibiting ability of UDSCs.

**Conclusion:** UDSC attenuate renal fibrosis after renal IR. Klotho-secretion of UDSC play a role in these anti-fibrotic effects.

#6562
**ITGAM PROMOTES MACROPHAGE ALTERNATIVE ACTIVATION IN HYPERURICEMIA-RELATED CHRONIC KIDNEY DISEASE**
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**Background and Aims:** Hyperuricemia is an essential risk factor in chronic kidney disease (CKD), while urate-lowering therapy to prevent or delay CKD progression is controversial. Alternatively activated macrophages in response to local microenvironment play diverse roles in kidney injury, repair, and fibrosis. Here, we aim to investigate whether and how macrophage ITGAM contributes to hyperuricemia-related CKD.

**Method:** In vivo, we explored dynamic characteristics of renal tissue in hyperuricemia-related CKD. By incorporating mRNA and protein sequencing data, we analyzed gene expression profile, hub genes and potential pathways responsible for disease development, which was further confirmed using qPCR, western blotting, and immunofluorescent stainings. In vitro, we validated bioinformatic findings under different conditions of macrophages with interventions corresponding to core nodes in pathway.

**Results:** Hyperuricemia-related CKD was characterized by the rise in serum uric acid, decline in renal function, macrophage alternative (M2) polarization, and kidney fibrosis. Integrated bioinformatic analyses revealed ITGAM as the potential core gene mediating disease progression which was associated with FAK/Akt1/β-catenin signaling. Notably, we confirmed the upregulated macrophage ITGAM, activated pathway, and macrophage M2 polarization in injured kidneys and Raw 264.7 macrophages. In vitro, we verified ITGAM/FAK/Akt1/β-catenin pathway participated in promoting macrophage M2 polarization through silencing Itgam and inhibiting FAK or Akt1 phosphorylation, where the expression of M2 phenotype macrophage markers and downstream molecules in pathway were down-regulated.

**Conclusion:** In hyperuricemia-related CKD, ITGAM promotes macrophage M2 polarization contributing to renal fibrosis through FAK/Akt1/β-catenin signaling pathway. Targeting macrophage ITGAM might be a promising therapeutic approach for preventing or delaying CKD.

**Figure 1:** Progressive renal dysfunction and kidney fibrosis in hyperuricemia-related CKD mice.
Figure 2: Bioinformatic analyses revealed ITGAM as the hub gene associated with downstream FAK pathway.

Figure 3: ITGAM expression and macrophage M2 polarization in vivo.
Figure 4: Interventions of ITGAM, FAK, and Akt verified the participation of pathway ITGAM/FAK/Akt/β-catenin in macrophage M2 polarization in hyperuricemia-related CKD.

#4359

LOSS OF GASDERMIN D LEADS TO AN EXACERBATION OF KIDNEY DAMAGE IN NEPHROCALCINOSIS-RELATED CHRONIC KIDNEY DISEASE

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Background and Aims: Gasdermin D (GSDMD) is a membrane-targeting and pore-forming protein that is primarily expressed in immune cells. In the proinflammatory cell death process known as pyroptosis, cleaved GSDMD plays a crucial role through cell membrane pore formation, leading to the release of proinflammatory cytokines and membrane rapture. Despite this, the majority of GSDMDs other physiological functions remain to be elucidated. Previous reports have implicated GSDMD in the pathogenesis of kidney disease, utilizing some acute kidney injury (AKI) animal models and a few chronic kidney disease (CKD) animal models. However, it remains uncertain if GSDMD contributes to the pathogenesis of nephrocalcinosis-related CKD. Therefore, this study aimed to investigate the role of GSDMD in this context.

Method: In our study, 8-week-old GSDMD-knockout (KO) mice and wildtype (WT) mice received an oxalate-rich diet (50 μmol/g sodium oxalate) for three weeks. All mice were sacrificed on day 21 and kidneys were harvested after the sacrifice. Plasma and urine samples were collected at different time points before the sacrifice. The glomerular filtration rate (GFR) was measured on day 0 and day 20 to assess kidney excretion function. Histological analysis was performed using Periodic Acid-Schiff (PAS) staining to assess renal injury, Sirius Red staining to check renal fibrosis, Pizzolato staining to evaluate calcium crystal deposition, F4/80 staining to evaluate the infiltration of macrophages, TUNEL staining to check for cell death, RIPK3 and phosphorylated MLKL (pMLKL) staining to detecting necroptosis. And GSDMD staining was also performed to examine the expression of GSDMD in the kidney.

Results: Pizzolato staining showed no differences in calcium crystal deposition between WT mice and KO mice. GFR was decreased in both WT mice and KO mice after the oxalate-rich diet (day 0 WT: 199.5±40.1 μl/min vs KO 175.0±44.8 μl/min, day 20 WT: 156.5±37.9 μl/min vs KO: 73.0±48.1 μl/min), and ΔGFR was much greater in KO mice (WT: −22.4±26.5% vs KO: −59.4±19.3%). The level of blood urea nitrogen was significantly higher in KO mice (WT: 41.9±3.90 mg/dl vs KO: 58.7±22.5 mg/dl) in accordance with the result of the GFR. PAS staining revealed more severe kidney injury in KO mice, and Sirius Red staining indicated a higher degree of renal fibrosis in KO mice. Furthermore, F4/80 staining showed greater infiltration of macrophages in KO mice. Although TUNEL staining showed no significant differences in positive cells between WT and KO mice showed greater positive areas implicating more necroptosis in RIPK3 and pMLKL staining. GSDMD staining revealed that injured tubular cells during the chronic phase express GSDMD (Fig. 1). In vitro experiments, we evaluated the functionality of macrophages such as phagocytic ability and migratory ability using bone marrow-derived macrophages (BMDMs), but we didn’t find any significant disparities between BMDMs from WT mice and those from KO mice.

Conclusion: Genetic deletion of GSDMD resulted in more severe kidney injury, macrophage infiltration and fibrosis in mice with nephrocalcinosis-related CKD. Our results suggest a potential role for pyroptosis, especially GSDMD, in contributing to renal tubular cell necroptosis, a process downstream of calcium-oxalate crystal formation and deposition, in the progression of nephrocalcinosis-related CKD, similar to previous reports in mouse models of AKI.
glomerulopathy caused by mutations in the genes encoding the α-chains of type IV collagen, the most abundant component of the glomerular basement membrane (GBM). Alport patients lack effective therapies beyond blockade of the renin-angiotensin system. This work describes the repurposing of two FDA-approved chemical chaperones (4-PBA and TUDCA) to rescue two AS mouse models: a knock-in and a compound heterozygous model bearing the Col4a3-p.Gly1332Glu mutation, recapitulating the most common mutation in Cypriot patients. Samples were collected after therapy and histological effects of chaperones on treated mice, kidney, blood, and urine (WT) mice received chaperones or vehicle daily. To examine the biochemical reduction of lesions and a decline of the lesions-severity in the GBM of 4-PBA treated AS mice. No adverse effects were noted in the GBM of the control and TUDCA groups. The lack of GSDMD, it shows more severe kidney injury.

**Method:** In either a short-term or long-term treatment, AS and wild type (WT) mice received chaperones or vehicle daily. To examine the biochemical and histological effects of chaperones on treated mice, kidney, blood, and urine samples were collected after therapy.

**Results:** Electron microscopy studies showed that the GBM of the 4-PBA treated AS mice after the long-term treatment has a considerable improvement in morphology, compared with vehicle-treated or TUDCA-treated AS mice. Importantly, EM measurements displayed a significant (p-value <0.0001) reduction of lesions and a decline of the lesions-severity in the GBM of 4-PBA treated AS mice. No adverse effects were noted in the GBM of the control and TUDCA groups. The lack of GSDMD, it shows more severe kidney injury.

**Conclusion:** Together, these results suggest a therapeutic potential for the 4-PBA agent in combating renal dysfunction in AS.

**#5441**

**EVIDENCE THAT CHAPERONE 4-PBA TREATMENT ALLEVIATES THE RENAL PHENOTYPE IN ALPORT SYNDROME MOUSE MODELS**

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**Background and Aims:** Alport Syndrome (AS) is a severe inherited glomerulopathy caused by mutations in the genes encoding the α-chains of type IV collagen, the most abundant component of the glomerular basement membrane (GBM). Alport patients lack effective therapies beyond blockade of the renin-angiotensin system. This work describes the repurposing of two FDA-approved chemical chaperones (4-PBA and TUDCA) to rescue two AS mouse models: a knock-in and a compound heterozygous model bearing the Col4a3-p.Gly1332Glu mutation, recapitulating the most common mutation found in Cypriot patients.

**Method:** In either a short-term or long-term treatment, AS and wild type (WT) mice received chaperones or vehicle daily. To examine the biochemical and histological effects of chaperones on treated mice, kidney, blood, and urine samples were collected after therapy.

**Results:** Electron microscopy studies showed that the GBM of the 4-PBA treated AS mice after the long-term treatment has a considerable improvement in morphology, compared with vehicle-treated or TUDCA-treated AS mice. Importantly, EM measurements displayed a significant (p-value <0.0001) reduction of lesions and a decline of the lesions-severity in the GBM of 4-PBA treated AS mice. No adverse effects were noted in the GBM of the control and TUDCA groups. The lack of GSDMD, it shows more severe kidney injury.

**Conclusion:** Together, these results suggest a therapeutic potential for the 4-PBA agent in combating renal dysfunction in AS.

**#3976**

**THE ROLE OF GENDER DIFFERENCES AND MENOPAUSE IN OBESITY-RELATED RENAL DISEASE, RENAL INFLAMMATION AND LIPOTOXICITY**

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**Background and Aims:** The pathogenesis of obesity related-renal disease is unknown. Gender differences may have a role in renal damage in obesity. In particular, menopause can promote renal disease in obese women. In a previous study we observed that obese male and female mice developed albuminuria, hyperfiltration and glomerulomegaly, and these changes were more severe in those obese ovariectomized females. In this study we evaluated renal inflammation and lipotoxicity in that model.

**Method:** Twenty-two males and 57 females C57BL6/J mice were randomized to standard diet (SD) or high fat diet (HFD) for six months. A group of female animals on SD o HFD was ovariectomized to induce menopause. In renal tissue we evaluated cytokines: NF-κβ, IL-1β, MCP-1, TNF-α and total lipid content, lipid classes, fatty acid profile and fatty acids in lipid classes. Part of the lipidomic analysis was performed in urine.

**Results:** Obese males and females showed higher NF-κβ, IL-1β, MCP-1, TNF-α and TUDCA treated AS mice. No adverse effects were noted in the GBM of the control and TUDCA groups. The lack of GSDMD, it shows more severe kidney injury.

**Conclusion:** Obese males and females showed higher NF-κβ, IL-1β, MCP-1 and TNF-α compared with obese female not-ovariectomized (Fig. 1B). Obese animals showed lower pro-inflammatory fatty acids (16:0, 16:1n-7 and 18:2n-6) and higher anti-inflammatory fatty acid (22:6 n-3) (Fig. 2A). This pattern was also observed in specific lipid classes and urine. Finally, obese females ovariectomized had a more exacerbated pattern, with high 18:0 in phosphatidylethanolamine and low 16:0 in triglycerides (Fig. 2B-D).

**Conclusion:** Obese females ovariectomized had a more exacerbated pattern, with high 18:0 in phosphatidylethanolamine and low 16:0 in triglycerides (Fig. 2B-D).

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Figure 1: Quantitative analysis of each inflammation marker in males and females. A) Males in HFD showed higher NF-κβ, TNF-α, MCP-1 and IL-1β in renal tissue. B) Females in HFD showed higher NF-κβ, TNF-α and MCP-1 in renal tissue; and obese females ovariectomized (HFD-OVX) had higher IL-1β and TNF-α compared to females in HFD. Data are represented as mean ± standard deviation. * M-SD vs. M-HFD p≤0.01. M-SD: male standard diet; M-HFD: male high fat diet. a, F-SD vs. F-SD-OVX p≤0.01; b, F-HFD vs. F-SD p≤0.0001; c, F-HFD-OVX vs. F-HFD and vs. F-SD-OVX p≤0.0001; d, F-SD vs. F-HFD p≤0.01; e, F-HFD-OVX vs. F-SD-OVX p≤0.0001. F-SD: female standard diet; F-HFD: female high fat diet; F-SD-OVX: female standard diet ovariectomized; F-HFD-OVX: female high fat diet ovariectomized.
CALCIUM ISOTOPE RATIOS IN SERUM ARE THE STRONGEST PREDICTOR OF BONE CALCIUM BALANCE IN PATIENTS ON DIALYSIS

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**Background and Aims:** Dysregulated mineral homeostasis is common in chronic kidney disease (CKD) and associated with bone demineralization and vascular calcification. The balance between bone formation and resorption, which reflect the bone calcium (Ca) balance (BCaB), cannot be determined without bone biopsy which is invasive and not easily repeatable. Recently, we have shown that stable (i.e. non-radioactive) Ca isotopes, 42Ca and 44Ca, can be measured in serum and bone and arterial biopsy samples using a multi-collector inductively-coupled plasma mass spectrometer (Thermo Fisher Scientific, Germany).

**Method:** Adults receiving chronic dialysis who underwent bone and arterial biopsies at the time of kidney transplantation were recruited. Patients who had parathyroidectomy or received cinacalcet or anti-resorptive agents were excluded. All participants had Dual Energy X-ray Absorptiometry (DXA) of the hip and lumbar spine. Ca44 and Ca42 measurements were performed in serum and bone and arterial biopsy samples using a multi-collector inductively-coupled plasma mass spectrometer (Thermo Fisher Scientific, Germany).

**Results:** Nineteen patients, median age 59.8 years, 84% male, median time on dialysis 3.3 years were included. δ44/42Ca was significantly higher in serum compared to bone or arterial biopsy samples (p < 0.0001), with the lowest isotope ratios in bone (Fig. 1A). δ44/42CaBone was significantly lighter than δ44/42CaArtery (p = 0.0002; Fig. 1B), δ44/42CaArtery correlated positively with the osteoblastic markers BAP and P1NP (p = 0.0006, R² = 0.51 and p = 0.009, R² = 0.31) and inversely with PTH and the osteoclastic marker RANKL (p = 0.0017, R² = 52 and p = 0.02, R² = 0.29 respectively; Fig. 2). Both the DXA hip and lumbar spine T-scores and z-scores correlated positively with δ44/42CaBone. δ44/42CaSerum showed an inverse correlation with the osteoid area (p = 0.04, R² = 0.22) and a positive correlation with the absolute mineralized area and the trabecular thickness (p = 0.0004, R² = 0.58 and p = 0.013, R² = 0.34 respectively). The were no significant correlations with δ44/42CaArtery. On multivariable linear regression analysis significant predictors of 44/42CaSerum were 44/42CaBone (p = 0.018, 95%CI = −1.35 to −0.15), age (p = 0.02, 95%CI = 0.02 to 0.02) and BAP (p = 0.019, 95%CI = 0.04 to 0.38), together predicting 71% of the variability in δ44/42CaSerum. The only significant predictor of 44/42CaBone was the δ44/42CaSerum: p = 0.004, 95%CI = −1.6 to −0.37, model R² = 69%.

**Figure 2:** Lipidomic analysis in renal tissue. A) Total fatty acids profile in renal tissue of male and female animals in percentage relative area (RA %). a, M-SD vs. M-HFD p < 0.001; b, F-HFD vs. F-SD p < 0.001 and vs. F-SD-OVX p < 0.05; c, F-HFD-OVX vs. F-SD p < 0.001 and vs. F-SD-OVX p < 0.01. B) Percentage Relative Area (RA %) of fatty acid profile from phosphatidylcholine; C) phosphatidylethanolamine and triglycerides in renal tissue. Data are represented as mean ± standard deviation. g, F-HFD vs. F-HFD-OVX and vs. F-SD-OVX p ≤ 0.05, h, F-HFD-OVX vs. F-HFD and vs. F-SD-OVX p ≤ 0.05, i, F-HFD-OVX vs. F-HFD and vs. F-SD-OVX p ≤ 0.05, j, F-HFD vs. F-SD p ≤ 0.05, k, F-HFD vs. F-SD and vs. F-SD-OVX p ≥ 0.05, l, F-HFD-OVX vs. F-SD-OVX and vs. F-SD p ≥ 0.05 and vs. F-HFD p = 0.052. n, F-HFD-OVX vs. F-SD-OVX and vs. F-SD p = 0.058. M-SD: male standard diet (white square), M-HFD: male high fat diet (hard grey square), F-SD: female standard diet (white circle), F-HFD: females high fat diet (hard grey circle), F-HFD-OVX: female high fat diet ovariectomized (light grey circle), F-HFD-OVX: female high fat diet ovariectomized (black circle).
Figure 1: 

Figure 2: 

Conclusion: $\delta^{44/42}\text{Ca}_{\text{serum}}$ is a significant and independent maker of BCaB, correlating with bone histology measures, and may provide a more sensitive measure than DXA or bone biomarkers. Further studies are required to determine the clinical utility of using $\delta^{44/42}\text{Ca}_{\text{serum}}$ to guide management of mineral bone disease in CKD.

REFERENCES


#4032

RAPAMYCIN AGGRAVATES KIDNEY LESIONS IN RATS FED HIGH PHOSPHATE

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Background and Aims: Rapamycin is currently used to prevent rejection after kidney transplantation. mTOR blockade by rapamycin may slow the progression of diabetic kidney disease. Rapamycin promotes phosphaturia by inhibiting renal tubular transport of phosphate. Excessive tubular load of phosphate produces kidney damage by inducing tubular injury and interstitial fibrosis. The aim of this work is to evaluate the effect of rapamycin on kidney pathology in rats fed different phosphate levels.

Method: Thirty four female Wistar rats were used in this experiment. Rats, aged 2 months at the beginning of the studies, were allotted to 6 groups (n = 4-6). Rats with intact renal function were fed a standard diet containing either normal (0.6%, NP), low (0.2%, LP) or high (1.2%, HP) phosphate. Half of the groups received placebo treatment (NP, LP, HP) and the other half were treated with rapamycin (NP-Rapa, LP-Rapa, HP-Rapa) at a dose of 1.3 mg/kg/day, for 22 days. Plasma concentrations of urea, creatinine, and phosphate as well as urine creatinine and phosphate were measured by spectrophotometry. Microscopic evaluation of the kidneys was performed in tissue sections fixed with formaldehyde solution and embedded in paraffin. Kidney sections were stained with hematoxylin-eosin, Masson Trichrome, periodic acid Schiff, and Von Kossa staining. Thirty non overlapping fields were evaluated. Chronic interstitial fibrosis and renal calcification were measured with a point counting grid and the result was expressed in percentage. Atrophic tubules were counted and the result was expressed as number of atrophic tubuli/field. Values are expressed as the mean ± standard error (SE). The difference between means was assessed by ANOVA. Fisher LSD test was used as a post-hoc procedure. A correlation study was carried out using the Pearson test. p < 0.05 was considered significant.

Results: Kidney lesions were more severe in rats treated with rapamycin and fed high phosphate diet. Areas of chronic interstitial fibrosis, with interstitial fibrosis and lymphoplasmacytic infiltrate, as well as atrophic tubules with thickened and wrinkled tubular basement membrane, loss of the brush border and flattening of the tubular cell cytoplasm, were observed. Calcification foci, mainly located in the corticomedullary junction, were identified with Von Kossa staining. Thirty non overlapping fields were evaluated. Chronic interstitial fibrosis and renal calcification were measured with a point counting grid and the result was expressed in percentage. Atrophic tubules were counted and the result was expressed as number of atrophic tubuli/field. Values are expressed as the mean ± standard error (SE). The difference between means was assessed by ANOVA. Fisher LSD test was used as a post-hoc procedure. A correlation study was carried out using the Pearson test. p < 0.05 was considered significant.

Fractional excretion of P was higher in all the groups treated with rapamycin, and the differences reached significance in HP-Rapa rats. Fractional excretion of P showed an excellent correlation with kidney lesions: chronic interstitial fibrosis ($r = 0.822$), calcification ($r = 0.827$) and tubular atrophy ($r = 0.855$).

Conclusion: The phosphaturic action of rapamycin aggravates renal lesions in rats fed high phosphate diets. Thus, rapamycin could be deleterious for the kidneys in the context of high phosphorus intake.
Table 1: Renal histopathology and biochemical parameters in rats fed different P levels with and without rapamycin. * p < 0.05 vs its non-rapamycin (placebo) control.

<table>
<thead>
<tr>
<th></th>
<th>LP</th>
<th>LP-Rapa</th>
<th>NP</th>
<th>NP-Rapa</th>
<th>HP</th>
<th>HP-Rapa</th>
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<tr>
<td>Chronic interstitial fibrosis (%)</td>
<td>0.09±0.08</td>
<td>0.05±0.03</td>
<td>0.25±0.10</td>
<td>0.76±0.40</td>
<td>8.28±3.62</td>
<td>13.98±3.85*</td>
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<tr>
<td>Calcification (%)</td>
<td>0±0</td>
<td>0±0</td>
<td>0.15±0.12</td>
<td>0.45±0.30</td>
<td>5.29±2.01</td>
<td>7.71±1.73</td>
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<tr>
<td>Tubular atrophy</td>
<td>0.05±0.03</td>
<td>0.04±0.04</td>
<td>0.37±0.26</td>
<td>1.92±1.03</td>
<td>6.80±1.82</td>
<td>12.48±2.10*</td>
</tr>
<tr>
<td>Plasma P (mg/dl)</td>
<td>6.99±0.26</td>
<td>6.24±0.48</td>
<td>6.10±0.39</td>
<td>5.33±0.34</td>
<td>5.56±0.27</td>
<td>5.24±0.09</td>
</tr>
<tr>
<td>Fraccional excretion P (%)</td>
<td>0.15±0.02</td>
<td>0.99±0.041</td>
<td>29.04±3.23</td>
<td>34.99±2.13</td>
<td>66.73±9.79</td>
<td>103.07±11.41*</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>30.99±1.61</td>
<td>26.33±2.30</td>
<td>32.10±1.74</td>
<td>28.59±1.95</td>
<td>39.59±4.78</td>
<td>54.95±15.77*</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.53±0.01</td>
<td>0.55±0.02</td>
<td>0.56±0.02</td>
<td>0.52±0.01</td>
<td>0.51±0.01</td>
<td>0.61±0.06*</td>
</tr>
</tbody>
</table>

#4544
THE ASSOCIATION OF TAMOXIFEN TO THE CONSERVATIVE CKD TREATMENT PROMOTED ADDITIONAL ANTIFIBROTIC EFFECTS IN A MODEL OF HYPERTENSIVE NEPHROSCLEROSIS
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Background and Aims: Chronic kidney disease (CKD) is an insidious, progressive and highly debilitating condition, which leads to the loss of renal function and to the need of life-sustaining renal replacement therapy. The conservative treatment of CKD is mainly based in the blockade of the renin-angiotensin-aldosterone system (RAAS), which can be associated to immunosuppressant drugs, according to the etiology of the renal injury. However, this pharmacological approach is not able to prevent CKD progression completely. Until the present moment, medical community still lack of a specific drug to effectively stop the progression of renal fibrosis associated to CKD, which once triggered became irreversible. Tamoxifen (TAM) is an estrogen receptor antagonist, widely employed for the clinical treatment of breast cancer, and responsible for saving a number of lives worldwide, in the past decades. This well-tolerated and cost-effective drug have been reported to exert antifibrotic effects in both experimental and human peritonedal fibrosis. Moreover, our research group already demonstrated that TAM efficiently prevented albuminuria, glomerulosclerosis, and interstitial fibrosis in a model of CKD. In the present study, we investigated if the association of TAM to the classic conservative treatment of CKD, here obtained by the association of Losartan (LOS) and Micofenolate Mofetil (MMF), could promote further renoprotection in an experimental model of hypertensive nephrosclerosis, induced by the chronic nitric oxide synthase blockade, obtained by the oral administration of L-NAME (NAME), associated to a high sodium (HS) diet, in rats.

Method: The experimental protocol was approved by the local Research Ethics Committee (CAPPesq) and was developed in strict conformity with the international standards for care and manipulation of laboratory animals. Thirty male Wistar rats were kept with a 3.2% HS diet for 15 days of adaptation, before the protocol start. After this period, the animals continued to receive the HS diet and were divided among 5 groups. CONT: receiving no further drugs or treatments, NAME: treated with 70 mg/kg/d of L-NAME, diluted in drinking water, LOS: NAME rats treated with 50mg/Kg/d of LOS, also diluted in drinking water, MMF: NAME rats treated with 10 mg/Kg/d of MMF given by gavage, TAM: NAME rats treated with 10 mg/Kg/d also by gavage, and LOS+MMF+TAM: NAME rats treated with all the drugs simultaneously. Systolic blood pressure (SBP), urinary albumin excretion (24 h uAE), glomerulosclerosis (GS), glomerular ischemia (GI), interstitial fibrosis (INT), tubulointerstitial infiltration of macrophages (CD68) and T-cells (CD3), as well as renal cortical interstitial collagen I (COLL1) and fibronectin (FIBRO) accumulation were evaluated after 30 days of treatment.

Results: The association of TAM to the classic treatment of CKD improved the renoprotection obtained by LOS+MMF. The triple combined treatment significantly reduced hypertension, albuminuria, glomerular structural damage, renal macrophage and T-cell infiltration in NAME rats, compared to the animals treated with the respective monotherapies. Moreover, both TAM alone or the association, were equally effective in reducing interstitial collagen and fibronectin accumulation, in NAME rats. Data are presented as Mean ± SE. For One-way ANOVA statistical analysis, we considered: p<0.05 vs.*CONT, #NAME, †LOS, §MMF, &TAM.

Conclusion: Our preliminary results shown TAM to be effective in reducing renal inflammation and fibrosis in the chronic nitric oxide synthase blockade model and to exert additional renoprotective effects when associated to LOS and MMF in all the analyzed parameters. Although further studies with different nephropathy models are still required in order to confirm our findings, here we suggest TAM to be a potential adjuvant in the conservative management of CKD.

#5904
COMPARATIVE TRANSCRIPTOMICS OF THREE CANONICAL MOUSE MODELS OF CHRONIC KIDNEY DISEASE
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Gubra aps, Denmark

Background and Aims: A range of mouse models are available in preclinical chronic kidney disease (CKD) research but differ in their disease etiology and pathological hallmarks. To enable better selection of the mouse CKD model optimal for preclinical drug discovery studies, we characterized the kidney transcriptome signature of three well-established models of CKD induced by unilateral ureter obstruction (UUO), unilateral ischemic reperfusion injury (uIRI) and adeno-supplemented diet feeding (ADI).

Table 1:
Method: Male C57BL/6J mice were used in all studies. UUO or sham surgery was performed in 9 weeks old mice, which were terminated two weeks post-surgery. uIRI or sham surgery was performed in 10 weeks old mice terminated 6 weeks post-surgery. 12 weeks old mice received an adenine-supplemented diet or a control diet for 6 weeks. Endpoints included plasma biochemistry, kidney histology and RNA sequencing on kidney samples.

Results: Compared to corresponding controls, plasma urea was only increased in ADI mice. All three models presented with increased inflammation (F4/80, UUO > ADI > uIRI) and fibrosis (Col1A1, UUO = uIRI > ADI) in the histological analysis. Compared to corresponding controls, all three models demonstrated substantial increases in differential expressed genes (DEGs, UUO, n = 12,046; uIRI, n = 12,236; ADI, n = 11,468), with significant overlap in transcriptome signatures between the models. Three models presented with a substantial increase in differential expressed genes (DEGs, UUO, n = 12,046; uIRI, n = 12,236; ADI, n = 11,468), with significant overlap in transcriptome signatures between the models. Gene expression markers of inflammation (e.g., Ccl2, Cd68 and Il1b), fibrogenesis (e.g., Tgfb1, Serpine1 and Col1a1) and kidney injury (e.g., Htrc1, Lcn2 and Spp1) supported histological findings in the three models. Interestingly, several molecular targets pursued in CKD drug discovery were significantly regulated, however with different directionality, in UUO (upregulated Atg7, Bax, Ednrb/a, Gli2, Fshr, Shh; downregulated Glp1r, Nr3c2, Pth1r, Scl5a2), uIRI (upregulated Edf1r, Glu2, Glp1r, Fshr, Nr3c2; downregulated Agrp, Egfr, Scl5a2), and ADI mice (upregulated Agrp, Atg7, Bax, Ednrb; downregulated Ednrb, Egfr, Fhr1, Nr3c2, Pth1r, Scl5a2).

Conclusion: UUO, uIRI and ADI mouse models demonstrate histopathological hallmarks of CKD, characterized by increased macrophage infiltration and fibrosis, which was corroborated by their individual transcriptome signatures. Despite similarities in histological phenotype, the models were distinguished based on kidney transcriptome changes, with several current drug targets regulated in a model-specific fashion. In conclusion, the current work will enable researchers to select the mouse model optimal for profiling individual preclinical test drugs with therapeutic potential in CKD. Also, our data may serve to enable further development of CKD mouse models with improved clinical translatability.

MIR-451B AND CHRONIC KIDNEY DISEASE: A NOVEL TARGET TO MODULATE RENAL VEGF SIGNALING

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Background and Aims: Chronic kidney disease (CKD) is a progressive disorder that affects over 15% of adults worldwide. A major component of CKD pathophysiology is renal microvascular rarefaction and loss that pairs the progression of the disease and complications. We developed a translational swine model of CKD and showed that loss of renal function associates with a significant decrease in renal vascular endothelial growth factor (VEGF) signaling and progressive microvascular (MV) rarefaction. VEGF is a key endogenous cytokine for MV proliferation and repair, but underlying mechanisms of renal VEGF downregulation in CKD are unknown. We hypothesized that micro-RNA (miRNA)-mediated processes contribute to the downregulation of renal VEGF signaling in CKD.

Method: Unbiased renal micro-RNA (miRNA)-seq was performed in a swine model of CKD stage 3 (14 weeks of bilateral renal artery stenosis + atherogenic diet) and normal controls (n = 5/group). Micro-RNAs up (≥1.4 FC, p < 0.05) and down-regulated (<0.7 FC, p < 0.05) were identified, followed by target prediction analysis (miRwalk 3.0, Target Scan 7.2). Renal gene and protein expression of VEGF was measured by qPCR and western blot, respectively, and renal MV architecture was studied by 3D micro-CT.

Results: Unbiased miRNA-seq and target prediction analysis identified four miRs upregulated in the kidney of CKD pigs vs. controls, of which miR-451b (validated by qPCR), broadly conserved among species, was capable of downregulating VEGFA (FC = 4.46, p = 0.04). Renal gene and protein expression of VEGF was downregulated in CKD vs. controls, associated with significant cortical and medullary microvascular rarefaction (Figure 1).

Conclusion: Our data suggest that post-transcriptional modulation of renal VEGF signaling may serve as a prominent mechanism of VEGF downregulation, which leads to MV rarefaction and disease progression in CKD. Furthermore, this work in progress identified a novel candidate (miR-451b) and may set the stage for its targeted modulation to preserve VEGF signaling as a potential strategy to protect the renal microvasculature in CKD.
DI(2-ETHYLHEXYL) PHTHALATE INDUCES RENAL PROXIMAL TUBULAR CELLS TO UNDERGO EPITHELIAL-MESENCHYMAL TRANSITION VIA AHR SIGNALING

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1Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, Division of Nephrology, Department of Internal Medicine, Kaohsiung, Taiwan, Rep. of China and 2Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, Department of Emergency Medicine, Kaohsiung, Taiwan, Rep. of China

Background and Aims: Environmental factors account for the majority of identified risks associated with CKD of uncertain etiology (CKDu). Among the various environmental factors, plasticizer di(2-ethylhexyl) phthalate (DEHP) is widely used in modern life. The exposure to DEHP is extensive but mostly underestimated in the general population. The link between DEHP exposure and renal injuries has been scarcely reported but the underlying mechanisms are largely unknown. This study aimed to examine the mechanisms by which DEHP causes renal tubular injuries.

Method: Human proximal tubular cells (PTC), HK2 cells, were used as a cellular model to test the central hypothesis of this study. Cells were treated with various concentrations of DEHP at different time points. WST-1 assay was used to examine the impacts of DEHP on cell viability. Bright field microscopy and immunofluorescence were used to analyze the morphological evidence of epithelial-mesenchymal transition (EMT). Western blots were used to investigate the changes in the expression of EMT-related proteins and arylhydrocarbon receptor (AhR) signaling. Inhibitors of AhR signaling were employed to investigate the crucial roles of AhR signaling in DEHP-induced EMT in HK2 cells.

Results: By using WST-1 assay, we found that DEHP did not affect cell viability when the examined concentration was below 50 μM, which resembled the low-level environmental exposures. However, when the concentration was higher than 100 μM, DEHP reduced the cell viability in a dose-dependent manner. In response to DEHP, HK-2 cells changed from cuboid to spindle shape when cultured with DEHP (25 μM). This morphological evidence became evident when the treatment time was longer than 48 hours. At the protein levels, DEHP resulted in down-regulation of e-cadherin and upregulation of vimentin and α-SMA. DEHP also lead to upregulation of AhR. The inhibitor of AhR signaling, CQDP (chloroquine diphosphate) reversed the DEHP-induced EMT, which were evidenced by morphology and by the expression patterns of EMT-related proteins.

Conclusion: At cellular level, our results suggested that low-level environmental exposures of DEHP led to EMT in renal PTC via AhR signaling.
#2724

THROMBO-INFLAMMATORY BIOMARKERS OF CARDIORENAL SYNDROME IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS IN END STAGE RENAL DISEASE

Vinod Bansal1, Pranathi Karumanchi2, Jawed Fareed2, Fakiha Siddiqui2 and Debra Hoppensteadt2

1Loyola University Medical Center, Nephrology, Maywood, United States of America and 2Loyola University Medical Center, Pathology, Maywood, United States of America

Background and Aims: Cardiovascular disease is a highly common complication in patients with end stage renal disease (ESRD) on maintenance hemodialysis. In the ESRD patient population, cardiovascular mortality is 20 times higher compared to the general population. The strong relationship of both illnesses can be explained through cardiorenal syndrome (CRS). CRS encompasses a spectrum of disorders involving both the heart and kidneys in which acute or chronic dysfunction in one organ may induce similar effect in the other organ. The diagnosis, prognosis and risk stratification of CRS is poorly understood. Current literature reveals that inflammation and thrombosis are integral to CRS development and key cardiac and renal biomarkers are elevated in CRS patients. Hence, this study aims to demonstrate that thrombo-inflammatory biomarkers and laboratory parameters give a telling narrative of ESRD progression to CRS.

Method: Plasma samples were collected from 95 ESRD patients which were recruited with an approved IRB protocol at Loyola University Medical Center hemodialysis unit. Normal human plasma (NHP) was obtained from a commercial source (George King Biomedical, Overland Park, KS). Thrombo-inflammatory biomarkers, including Annexin V, MPO, Troponin, L-FABP, VEGF, D-dimer, TNF-alpha, IL-6, CRP, eNOS, Nitrotyrosine, MDA, NEFA, NO, vWF and MCP-1 were measured using commercially available ELISA methods. Cardiovascular comorbidities and laboratory parameters were obtained from EPIC chart analysis. Results were then statistically analyzed using GraphPad Prism v.9; the results were compiled into mean ± SEM, percent change comparison to NHP, analyzed for significance.

Results: Several cardiovascular comorbidities were seen in the 95 ESRD patient samples including AF (22%), PAD (29%), HF (24%), CAD (22%), DVT (15%), COPD (6.5%), and PE (5.3%). Overall, 25% of the ESRD patients have CRS. Laboratory parameters, ferritin (521.99 ±289.33) and PTH (442.91 ±1.50) were elevated in ESRD patients. Most of the thrombo-inflammatory CRS biomarkers were elevated in ESRD patients. Biomarkers including Annexin V (ESRD 7.57 ±5.24, 23.64% vs. 6.12 ± 8.29, p < 0.001), L-FABP (106599.4 ±1676.28, 1983% vs. 5116.3 ± 1767.88, p < 0.0001), D-dimer (ESRD 14477.0 ±142.91 ±1.06, 35.87% vs. 1.85 ± 1.20, p < 0.0001), IL-6 (ESRD 5.211 ± 10.36, 317.21% vs. 1.25 ± 1.24, p < 0.0001), CRP (ESRD 14.53 ± 14.11, 22.44% vs. 0.63 ± 0.99, p < 0.0001), NO (ESRD 34.74 ± 19.74, 151.74% vs. 13.8 ± 5.60, p < 0.0001), vWF (ESRD 200.7 ± 25.89, 183.03% vs. 70.91 ± 23.13 p < 0.0001) and MCP-1 (148.4 ± 56.09, 67.49% vs. 88.6 ± 27.25, p < 0.0001) showed significant increase when compared to NHP.

Conclusion: This study suggests that thrombo-inflammatory biomarkers and laboratory parameters may be helpful in indicating CRS in ESRD patients. Ultimately, these biomarkers can now be readily used to correlate against other biomarker findings and studied further to determine their accuracy in prognosis and diagnosis of CRS.

#4845

EFFECT OF OMEGA-3 FATTY ACID ON MITOCHONDRIAL MEMBRANE FATTY ACID AND COMPARISON WITH ERYTHROCYTE MEMBRANE IN ADENINE INDUCED UREMIC RATS

Dong Eun Yang1, Su Mi Lee2, Jun Chul Kim3 and Won Suk An2

1Dong-A University Hospital, Internal Medicine, Rep. of South Korea, 2Dong-A University, College of Medicine, Internal Medicine, Busan, Rep. of South Korea and 3CHA Gumi Medical Center, CHA University, Internal Medicine, Rep. of South Korea

Background and Aims: The kidney has the second highest mitochondrial content in the human body. Fatty acids (FAs) are one of the important energy sources and main constituents of cell membranes. Higher erythrocyte membrane oleic acid contents are related to acute coronary syndrome and omega-3 FA can reduce oleic acid contents. We investigated whether omega-3 FA modifies not only erythrocyte membrane FA but also mitochondrial membrane FA of kidney in adenine-induced uremic rats.

Method: Male Sprague-Dawley rats were fed diets containing 0.75% adenine and 2.5% protein for three weeks. Next, rats were randomly divided into six groups that were fed diets containing 2.5% protein and saline with cholecalciferol (3000 IU/kg/week) or omega-3 FAs (300 mg/kg/day) with cholecalciferol were supplemented by gastric gavage for four weeks: normal control (n = 7), adenine control scarified at 3 weeks (n = 6), adenine control scarified at 5 weeks (n = 5), adenine control scarificated at 7 weeks (n = 5), omega-3 FAs group scarificated at 7 weeks (n = 5), and omega-3 FAs group scarificated at 7 weeks (n = 5). The mitochondrial isolation kit was used for renal mitochondria extraction. The mitochondrial and erythrocyte membrane FA contents were measured using gas chromatography.

Results: Compared to the normal control group, serum creatinine levels in adenine control group was significantly increased and improved in omega-3 FA group. Compared with adenine control, erythrocyte and mitochondrial membrane monounsaturated FA contents including oleic acid and arachidonic acid (AA) levels were significantly decreased in omega-3 FA group. FA compositions were similar between erythrocytes and mitochondrial membranes in each group. Monounsaturated FA contents including oleic acid, and eicosapentaenoic acid were higher and saturated FA was lower in the mitochondrial membrane than erythrocyte membrane in adenine control group.

Conclusion: Omega-3 FA affects not only erythrocyte membrane FA but also mitochondrial membrane FA in uremic rats. Erythrocyte membrane FA contents can reflect mitochondrial membrane FA contents of the kidney.

Table 1:

<table>
<thead>
<tr>
<th>Cardiovascular Disease</th>
<th>Percentage of ESRD patients with Cardiovascular Comorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation (AF)</td>
<td>22%</td>
</tr>
<tr>
<td>Peripheral Artery Disease (PAD)</td>
<td>29%</td>
</tr>
<tr>
<td>Heart Failure (HF)</td>
<td>24%</td>
</tr>
<tr>
<td>Coronary Artery Disease (CAD)</td>
<td>22%</td>
</tr>
<tr>
<td>Deep Vein Thrombosis (DVT)</td>
<td>15%</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease (COPD)</td>
<td>6.5%</td>
</tr>
<tr>
<td>Pulmonary Embolism (PE)</td>
<td>5.30%</td>
</tr>
<tr>
<td>Cardiorenal Syndrome (CRS)</td>
<td>25%</td>
</tr>
</tbody>
</table>
Table 1: Changes of erythrocyte and mitochondrial membrane fatty acids content.

<table>
<thead>
<tr>
<th></th>
<th>Normal control</th>
<th>AC_3W</th>
<th>AC_5W</th>
<th>AC_7W</th>
<th>AC_5W+O</th>
<th>AC_7W+O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated (E)</td>
<td>44.7±2.4</td>
<td>47.0±1.0a</td>
<td>47.0±0.9</td>
<td>48.2±0.2abc</td>
<td>48.6±0.6abc</td>
<td>46.7±0.7abc</td>
</tr>
<tr>
<td>Saturated (M)</td>
<td>45.9±1.3</td>
<td>41.1±1.9a</td>
<td>40.4±1.8a</td>
<td>40.6±1.0a</td>
<td>41.3±1.0abcd</td>
<td>41.6±0.5abcd</td>
</tr>
<tr>
<td>Mono (E)</td>
<td>11.3±1.3</td>
<td>10.1±0.3a</td>
<td>11.5±1.0b</td>
<td>11.1±0.1b</td>
<td>9.4±0.4abcd</td>
<td>9.5±0.4abcd</td>
</tr>
<tr>
<td>Oleic (E)</td>
<td>10.4±1.3</td>
<td>9.4±0.2a</td>
<td>10.3±0.4b</td>
<td>10.3±0.0b</td>
<td>8.8±0.3abcd</td>
<td>9.0±0.4abcd</td>
</tr>
<tr>
<td>Mono (M)</td>
<td>9.8±0.9</td>
<td>12.9±0.5a</td>
<td>13.9±1.5a</td>
<td>15.6±1.2ab</td>
<td>12.7±0.4abcd</td>
<td>14.2±1.0abcd</td>
</tr>
<tr>
<td>Oleic (M)</td>
<td>9.1±0.8</td>
<td>12.3±0.5a</td>
<td>13.2±1.4a</td>
<td>14.6±1.2ab</td>
<td>12.0±0.4abcd</td>
<td>13.3±0.9abcd</td>
</tr>
<tr>
<td>AA (E)</td>
<td>24.1±1.6</td>
<td>21.9±0.7a</td>
<td>21.7±0.7a</td>
<td>21.4±0.4a</td>
<td>18.2±0.2abcd</td>
<td>19.1±1.0abcd</td>
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<tr>
<td>EPA (E)</td>
<td>0.3±0.1</td>
<td>0.4±0.1</td>
<td>0.4±0.1</td>
<td>0.4±0.1</td>
<td>2.3±0.3abcd</td>
<td>2.5±0.4abcd</td>
</tr>
<tr>
<td>AA (M)</td>
<td>32.6±1.4</td>
<td>26.9±1.1a</td>
<td>28.4±3.2a</td>
<td>26.9±1.0a</td>
<td>23.6±0.4abcd</td>
<td>21.8±1.1abcd</td>
</tr>
<tr>
<td>EPA (M)</td>
<td>0.3±0.1</td>
<td>0.7±0.5</td>
<td>1.3±0.8a</td>
<td>1.5±0.8a</td>
<td>2.2±0.2abcd</td>
<td>2.6±0.4abcd</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SD. E; Erythrocyte membrane, M; Mitochondrial membrane, Mono; Monounsaturated fatty acid, AA; Arachidonic acid, EPA; Eicosapentaenoic acid

\( ^a P \text{ value} <0.05 \) (mean values are significantly different from normal control)

\( ^b P \text{ value} <0.05 \) (mean values are significantly different from AC_3W)

\( ^c P \text{ value} <0.05 \) (mean values are significantly different from AC_5W)

\( ^d P \text{ value} <0.05 \) (mean values are significantly different from AC_7W)

#4966

CELLULAR PRION PROTEIN ACTIVATES THE TBK1-IRF3 SIGNALING PATHWAY TO AGGRAVATE RENAL FIBROSIS

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Background and Aims: Chronic kidney disease (CKD) is an irreversible degenerative disease characterized by gradual loss of renal function, contributing to high morbidity and mortality as well as heavy economic cost to society. Clinically, there are few available strategies to slow CKD progression. Because the uremic phenotypes include many features of aging, CKD is considered as a premature aging syndrome. Neurodegenerative diseases, such as Alzheimer’s disease, and Parkinson’s disease are extensively studied aging-related diseases, in which cytotoxic proteins misfolding and aggregation in neural cells is the main characteristic. The misfolding and aggregation of the prion protein is tightly linked to the development of prion diseases. Interestingly, a remarkable elevation of cellular prion protein (PrPC) in the urine and plasma of CKD patients was reported. However, the role of PrPC in the pathogenesis of kidney diseases remains largely unknown. The aim of the current study is to investigate the role of PrPC in renal fibrosis.

Methods: Immunohistochemistry staining was conducted to evaluate the expression of PrPC in renal biopsies from CKD patients. Enzyme linked immunosorbent assay (ELISA) was performed to detect urinary PrPC of CKD patients. Animal model of renal fibrosis was induced by unilateral ureteral occlusion (UUO). Western blot, real time PCR and immunofluorescence staining were performed to evaluate the expression and distribution of PrPC. Proximal tubular epithelial cells (PTCs) overexpressed PrPC were collected for RNA-seq analysis. TBK1 inhibitor amlexanox, and IRF3 siRNA were used to block TBK1-IRF3 pathway in rat tubular epithelial cells (NRK-52E), respectively. Amlexanox was administered orally to UUO mice. H&E, Masson and Sirius red staining were used to estimate renal pathology.

Results: The protein expression levels of PrPC both in renal biopsies and urine from CKD patients were elevated and significantly correlated with the severity of interstitial fibrosis and the decline of eGFR. PrPC proteins were significantly increased, and aggregated in proximal renal tubules in fibrotic renal tissues induced by UUO. Compared with wild-type littermates, PEPCK-Prnp-KO mice had significantly lower levels of PrPC in the kidneys, indicating a protective role of PrPC in renal fibrosis.

Figure 1: Schematic illustration of how PrPC triggers the production of profibrotic genes, ultimately aggravating renal fibrosis.
mice showed reduced extracellular matrix accumulation and interstitial inflammation at day 7 after UUO. PrPC provokes profibrotic response of renal tubular cells via the TBK1-IRF3 pathway. TBK1 inhibitor amlexanox or silencing endogenous IRF3 significantly inhibited PrPC-induced profibrogenic phenotypic transformation in NRK-52 cells. Amlexanox attenuated interstitial fibrosis induced by UUO.

Conclusion: Our experimental results indicate that PrPC-TBK1-IRF3 pathway plays a detrimental role in profibrogenic transformation of renal tubular cells and thus contributes to interstitial fibrosis. Blocking TBK1 activation is a plausible strategy for therapeutic intervention of chronic kidney disorders.

#5978
SUBCAPSULAR INJECTION OF EXTRACELLULAR VESICLES FROM MESENCHYMAL STEM CELLS, PROMOTED ADDITIONAL RENOPROTECTION IN AN EXPERIMENTAL MODEL OF CKD
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1University of São Paulo Medical School, Laboratory of Cellular, Genetic, and Molecular Nephrology, Renal Division, São Paulo, Brazil; 2University of São Paulo Medical School, Laboratory of Cellular, Genetic, and Molecular Nephrology, Renal Division, São Paulo, Brazil; 3University of São Paulo Medical School, Laboratory of Cellular, Genetic, and Molecular Nephrology, Renal Division, São Paulo, Brazil

Background and Aims: Chronic kidney disease (CKD) is considered a public health concern worldwide, both due to its insidious and highly debilitating feature and to its high global prevalence. Clinical management of CKD is often achieved by the blockade of the renin-angiotensin-aldosterone system (RAAS). However, this treatment alone is not efficient to prevent CKD progression completely, motivating the scientific community to search for alternative treatments to control CKD progression and to detain its evolution to the end-stage renal failure. In this context, we have recently shown that the association of a single renal subcapsular injection of 2 × 10^6 adipose-derived mesenchymal stem cells (ASC) to RAAS blockade with the AT1RB Losartan (LOS) promoted greater renoprotection when compared to LOS monotherapy, leading to the normalization of urinary protein excretion (UPE) and to the regression of established glomerulosclerosis (GS), in experimental CKD. Since there are methodological limits for the number of ASC that can be injected under the renal capsule, and based on the current literature, which suggests the main beneficial effects of ASC are not due to direct in situ cell differentiation, but to paracrine factors produced and released by the ASC, in the present study we aimed to investigate if the association of a renal subcapsular injection of extracellular vesicles (EV) derived from ASC, to the oral treatment with LOS would promote additional renoprotective effects in a model of experimental CKD.

Method: The present experimental protocol was approved by the Ethics Committee for the Use of Experimental Animals of the University of São Paulo Medical School (CEUA-FMUSP No 1761/2022). EV were obtained from ASC isolated from gonadal adipose tissue of 5 male Wistar rats. Cells were cultured until P4, characterized by flow cytometry and in vitro differentiation, and kept under serum deprivation for 24 h. The conditioned culture media, containing the EV released by these cells, was ultracentrifuged and the resulting EV pellets were diluted in 100 μL of sterile PBS and used for the renal subcapsular injections. Experimental CKD was induced in 25 male Wistar rats through the surgical ligation of 2 from the 3 branches of the left renal artery, followed by the total nephrectomy of the right kidney, resulting in a 5/6 renal ablation. Additional 10 Sham-operated rats were used as control. After 15 days from surgery, the animals submitted to renal ablation were stratified into 3 groups, with closely similar mean values of body weight (BW), systolic blood pressure (SBP), UPE and urinary albumin excretion (UAE), before the start of the different treatments. Animals from CKD group were kept untreated, LOS and LOS + EV animals received diary 50 mg/Kg/d of Losartan, diluted in drinking water and LOS + EV rats underwent a second surgery for the renal subcapsular application of EV. All animals were followed until 30 days after CKD induction, when BW, SBP, UPE and UAE were analyzed again. Animals where then euthanized for the assessment of serum creatinine (Scr) and blood urea nitrogen (BUN) concentration, as well as for histological studies to determine the percentage of GS and the renal interstitial infiltration by macrophages (CD68).

Results: The association of a single subcapsular injection of EV derived from ASC, to the oral treatment with the AT1RB LOS, significantly improved the effects of this antihypertensive drug. CKD + LOS + EV animals exhibited normal SBP, in spite of having only 1/6 of functioning renal mass. Moreover, the combined treatment significantly reduced UAE and numerically diminished the percentage of glomerulosclerosis, compared to LOS alone. Detailed obtained results are presented in Table 1. Data are presented as Mean ± SE. Differences among groups were analyzed by one-way ANOVA: p < 0.05 vs. CONT. *CKD, †LOS, ‡CKD + LOS; as Mean ± SE.

Conclusion: Despite the small number of animals in the association group, our preliminary results suggest EV from ASC to exert additional renoprotective effects when associated to LOS, especially regarding the control of SBP and the protection of the glomerular filtration barrier integrity.

Table 1:

<table>
<thead>
<tr>
<th></th>
<th>Sham (n=10)</th>
<th>CKD (n=10)</th>
<th>CKD + LOS (n=10)</th>
<th>CKD + LOS + EV (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW (g)</td>
<td>362 ± 16</td>
<td>313 ± 8*</td>
<td>306 ± 8*</td>
<td>314 ± 8</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>143 ± 5</td>
<td>216 ± 5</td>
<td>187 ± 7*</td>
<td>152 ± 9</td>
</tr>
<tr>
<td>24h UPE (mg/24h)</td>
<td>22 ± 3</td>
<td>302 ± 51*</td>
<td>150 ± 30</td>
<td>145 ± 55*</td>
</tr>
<tr>
<td>24h UAE (mg/24h)</td>
<td>1 ± 1</td>
<td>154 ± 23*</td>
<td>104 ± 27*</td>
<td>78 ± 39</td>
</tr>
<tr>
<td>Scr (mg/dL)</td>
<td>0.57 ± 0.06</td>
<td>0.95 ± 0.07*</td>
<td>0.92 ± 0.10</td>
<td>0.90 ± 0.11*</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>50 ± 3</td>
<td>103 ± 7*</td>
<td>96 ± 4*</td>
<td>93 ± 6*</td>
</tr>
<tr>
<td>GS (%)</td>
<td>2 ± 1</td>
<td>37 ± 6*</td>
<td>31 ± 6</td>
<td>25 ± 13</td>
</tr>
<tr>
<td>CD68  (cell/mm²)</td>
<td>27 ± 5</td>
<td>177 ± 22*</td>
<td>128 ± 19*</td>
<td>130 ± 37*</td>
</tr>
</tbody>
</table>
POST-BURNS PERSISTENT INFLAMMATION LEADS TO KIDNEY PROGRAMMED CELL DEATH THROUGH ACTIVATION OF THE CASPASES SIGNALING PATHWAY

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Background and Aims: The underlying mechanism for the increased incidence of chronic kidney disease (CKD) in burn patients discharged from hospital remains unclear. Recent studies have shown that burn patients are discharged from the hospital with chronic inflammation despite normalization of all physiological parameters. We hypothesized that severe burns accelerate the onset and progression of CKD by activating persistent inflammation. This study aimed to investigate the long-term effects of severe burns on kidney and its possible mechanisms.

Method: The study was divided into three parts. First, to understand the effect of burns on the general population and the CKD population, 4-month-old C57BL/6 mice were divided into a blank control group (Blank) and an adenine-induced CKD group. Some mice were established by burns in a 10% total body burn surface area model at 5-month-old. Experiments were terminated at 7-month-old. The function, morphology, inflammatory response and oxidative stress of the kidney were assayed. Second, the effect of activated macrophages on podocytes was studied by in vitro experiments.

Results: In the Blank group, burns did not cause kidney function and weight alterations, but caused a small amount of organic lesions, glomerular atrophy, apoptosis, and macrophage infiltration. In the CKD group, burns not only significantly reduced kidney function, but also caused kidney atrophy, organic lesions, glomerular atrophy, apoptosis and macrophage infiltration. In addition, burns significantly increased Caspase-1 and -3 pathway expression in all mice. Electron microscopy showed that burns significantly aggravated glomerular injury in the CKD group, including podocyte injury, cell membrane blubbing and rupture. In vitro studies showed that polarized M1 macrophages increased MPCS podocytes death.

Conclusion: Severe burns cause programmed cell death through activation of inflammation-induced Caspase-dependent pathways leading to kidney injury in mice. This phenomenon has a small effect on normal populations and a larger effect on CKD populations. This study has important implications for determining the prognosis of kidney function in burn patients and provides a promising therapeutic strategy.

Figure 1: Model exploration and characteristics.
Figure 2: Burns cause subclinical kidney injury in normal mice and aggravate kidney injury in CKD mice.
Figure 3: Burns increase inflammation in the kidney.
Figure 4: Post-burns inflammation increases Caspases expression.

Figure 5: Burns increase Caspases-dependent programmed cell death.
DEPLETED HDAC3 ATTENUATES HYPERURICEMIA-INDUCED RENAL INTERSTITIAL FIBROSIS VIA MIIR-19B-3P/SF3B3 AXIS
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Background and Aims: Hyperuricemia (HN) is a threat for the occurrence of renal interstitial fibrosis (RF). Dysfunctional histone deacetylase 3 (HDAC3) elicits renal fibrosis and damage. This study aimed to explore the role of HDAC3 in HN-induced RF from microRNA-19b-3p/splncing factor 3b subunit 3 (miR-19b-3p/SF3B3) axis.

Method: 1. The HN model was established on rats to induce RF by oral administration of adenine and potassium oxalate; 2. HN rats were injected with related vectors (sh-HDAC3, mimic-miR-19b-3p, sh-HDAC3+miR-19b-3p inhibitor) to suppress and/or promote HDAC3 and/or miR-19b-3p; The detection indicators are listed as follows: (1) Blood samples and urine samples were collected for UA, BUN, Scr and 24 h urine protein measurement; (2) Renal pathological damages, RF index and renal cell apoptosis were measured by HE, Masson and TUNEL staining; (3) α-SMA, TGF-β1 and FN contents in renal tissues were detected by IHC staining; (4) mRNA and protein levels of HDAC3, miR-19b-3p and SF3B3 in renal tissues were detected by RT-qPCR and/or WB. (5) Interaction of HDAC3 and miR-19b-3p was detected by ChIP and dual luciferase reporter gene assay; (6) Interaction of miR-19b-3p and SF3B3 was predicted/detected by bioinformatics website/dual luciferase reporter gene assay.

Results: 1. HN induced renal dysfunction, renal pathological damages, RF and renal cell apoptosis of rats; HN rats showed elevated HDAC3, SF3B3 and reduced miR-19b-3p in renal tissues. 2. Suppressed HDAC3 or promoted miR-19b-3p relieved HDAC3-induced renal dysfunction, renal pathological damages, RF and renal cell apoptosis; HDAC3 bound to the promoter of miR-19b-3p; miR-19b-3p negatively regulated SF3B3; miR-19b-3p depletion abrogated down-regulated HDAC3-induced effects on HN-induced RF.

Conclusion: HDAC3 bound to the promoter of miR-19b-3p to regulate SF3B3. Depressed HDAC3 relieved HN-induced RF by restoring miR-19b-3p and knocking down SF3B3. Targeting HDAC3 and miR-19b-3p/SF3B3 axis may be a promising therapeutic strategy for preventing HN-induced RF.

ENDOTHELIAL CELL PROTEOME AND SECRETOME ALTERATION UNDER CHRONIC UREMIC EXPOSURE
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Medical University of Vienna, Wien, Austria

Background and Aims: Dialysis therapies including peritoneal dialysis (PD) are described to lead to premature vascular aging, atherosclerosis and associated cardiomyopathies, which are associated with high cardiovascular morbidity and mortality. Chronic inflammation, incomplete clearance of uremic toxins, and dyslipidaemia, are factors affecting the vasculature system. However, how these factors affect the endothelium, the fist cell layer in contact with these molecules, and the molecular mechanisms triggered by uremic toxins remain poorly understood. In vitro and in vivo studies have shown that cytotoxic and secretory additives (e.g. dipeptide alanyl-glutamine (AlaGln) or kinase inhibitor lithium chloride (LiCl)) to PD fluids reduce peritoneal damage in mesothelial and endothelial (EC) cells. Their potential systemic effects were not studied so far. Here, we demonstrate, in a newly developed model system, the changes induced by chronic exposure to serum of PD patients in the proteome and secretome of endothelial cells, and the effects of cytoprotective additives.

Method: For modelling systemic conditions of PD patients, primary EC were cultured for 5 passages in medium containing 10% serum collected from PD patients (n = 26) during regular PET tests, or from healthy donors (n = 12). Cytoprotective additives were added in parallel experiments. Cells were stably labelled (SILAC) to differentiate cell and donor serum proteins and the cellular proteome and secretome profiles were analysed by quantitative mass spectrometry. Prior to analysis of the secretome, equalizer beads, to enrich low abundant and deplete high abundant proteins, were used. ECIS (Electric Cell-substrate Impedance Sensing), was used to measure barrier function, growth rate, and permeability.

Results: Proteome analysis revealed perturbation of major cellular processes by serum of PD patients including inflammatory related processes such TLR regulation and complement activation, as well membrane related processes such as extracellular matrix interactions and junctions, and plasma lipoprotein remodelling. Addition of LiCl counteracted cell-adhesion related proteins. ECIS analysis showed that in uremic conditions the EC monolayer has a decreased barrier function compared to healthy conditions, and LiCl partially restores the tightness of the membrane. Secretome analysis showed differentially regulated proteins related to oxidative stress, senescence-associated secretory phenotype (SASP) and apoptosis. Interestingly, in the secretome, LiCl addition counter regulated INHBA and tissue factor pathway inhibitor 2, both proteins related to vascular calcification.

Conclusion: Surprisingly few studies have analysed uremic effects on EC using proteomics approaches, and no reports of chronic settings, modelling the patient situation, are available. Our data demonstrates that EC react to serum factors of PD patients with increased inflammation, permeability and a senescence profile. Interestingly, our model reflects many of the known effects on the vasculature, but unravels the molecular mechanism that may induce these processes. We have also identified potential mechanisms by which the addition of cytoprotective additives may counteract some of the uremic effects systemically. Secretomics data identified several proteins secreted by EC that are regulated in uremia with potential for cellular crosstalk with other cells of the vasculature, showing the potential to identify therapeutic targets to reduce the cardiovascular risk of PD patients and current limitations of the therapy.

AGING-RELATED RENAL FIBROSIS WAS ALLEVIATED VIA CONSERVING MITOCHONDRIAL FUNCTION AND AUTOPHAGY IN NLRP3 KO MICE
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Background and Aims: Nod-like receptor family, pyrin domain containing-3 (NLRP3) activation in kidney diseases contributes to aggravating disease progression and fibrosis. However, the role of NLRP3 in renal aging is not clear. This study was designed to identify whether the NLRP3 KO mice could be protected from renal aging.

Method: NLRP3 KO and counterpart wild-type (WT) mice were used at different ages (3 months, 12 months, and 24 months). Plasma, urine, and kidneys were collected.

Results: Plasma creatinine and blood urea nitrogen (BUN) increased with aging, while BUN was significantly decreased in NLRP3 KO old mice (24M) compared with WT old mice. NLRP3 ablation contributed to decreasing tubular vacuolization, tubulointerstitial fibrosis, and atypical autophagosomes with aging. In line with it, renal fibrosis markers, such as connective tissue growth factor, and fibronectin were alleviated in RT-PCR tests. Immunoblot results showed that autophagy with mitochondrial biogenesis increased in old NLRP3 KO mice. In addition, phosphorylated AMP-activated protein kinase and peroxisome proliferator-activated receptor gamma coactivator 1α were increased in old NLRP3 KO mice. Transcriptional expression data using kidney RNA bulk sequencing showed augmentation of autophagy and mitochondrial biogenesis in old NLRP3 KO mice.

Conclusion: NLRP3 absence prevented aging-related renal fibrosis via maintaining renal mitochondrial biogenesis and autophagy.

IDENTIFICATION OF GLYCOSYLATED IGF2 IN HUMAN URINARY PEPTIDOME AND ITS ASSOCIATION WITH CKD
Sonnal Lohia1, Agnieszka Latosinska2, Jerome Zoidakis3, Manoussos Makridakis1, Harald Mischak3, Griet Glorieux1, Antonia Vlahou1 and Vera Jankowski4

1Biomedical Research Foundation, Academy of Athens, Centre of Systems Biology, Athens, Greece, 2Mosaïques Therapeutics GmbH, Hannover, Germany, 3Ghent University Hospital, Gent, Belgium and 4RWTH Aachen University, Institute for Molecular Cardiovascular Research, Aachen, Germany

Background and Aims: Chronic kidney disease (CKD) is prevalent in 10% of world’s adult population, with estimated glomerular filtration rate (eGFR) and albuminuria employed in its diagnosis. Role of protein glycosylation in causal mechanisms of CKD progression is largely unknown. Aim of this study was to identify urinary O-linked glycopeptides in association to CKD for better characterization of CKD molecular manifestations.

Method: Urine samples from eight CKD and two healthy subjects were analyzed by Capillary Electrophoresis-Tandem Mass Spectroscopy (CE-MS/MS) and glycopeptide analysis using Proteome Discoverer 1.4 was performed. Distribution of identified glycopeptides and correlation with Age, eGFR and Albuminuria were evaluated in 3810 datasets from the Human Urinary Proteome database using Spearman’s rank correlation test and multiple linear regression.
regression analysis by statistical software R. The quantification of Insulin-like growth factor-II (IGF2) protein (7.5 kDa) was performed by enzyme-linked immunosorbent assay (ELISA) in two matched (for age, sex, no diabetes and no cardiovascular history) groups of 12 plasma samples each (eGFR < 30 ml/min/1.73m² and eGFR > 90 ml/min/1.73m²). An open-source tool “Proteasix” was used to predict proteases involved in cleavage of the identified glycopeptides. The transcriptomics database and analysis tool “Nephroseq v4” were utilized to investigate the expression of predicted proteases in existing human transcriptomics CKD datasets.

Results: In total, 17 O-linked glycopeptides from 7 different proteins were identified, derived primarily from Insulin-like growth factor-II (IGF2) (n = 6). Glycosylation occurred at the surface exposed IGF2 Threonine 96 position. Further Investigation of the human proteome database containing 3810 datasets, showed that only three unglycosylated urinary peptides of IGF2 were identified, at significantly lower abundance and frequency (0-2.5% in the database) in comparison to the glycosylated forms (frequency of 23-90%). Interestingly, all identified IGF2 peptides belonged to E-domain of IGF2, i.e., 92 – 180 aa; which cleaves after undergoing O-linked glycosylation during the post-translational process yielding the “mature IGF2” (25-91 aa) protein. Results of multiple linear regression analysis indicated that three IGF2 glycopeptides, DVStPPTVLPDNFPRYPVGK [β(1024) = 0.08, p = 1.42*10⁻⁴], DVStPPTVLPDNFPRYP [β(560) = 0.01, p = 5.22*10⁻⁵] and DVStPPTVLPDNFPRYP [β(290) = 0.02, p = 1.07*10⁻⁴], exhibited positive correlation with Age and the glycopeptide tPPTVLPDNFPRYP showed strong negative association with eGFR [β(177) = -0.01, p = 4.21*10⁻⁹]. Along the same lines, the latter urinary IGF2 glycopeptide tPPTVLPDNFPRYP was found at increased [p < 2.2*10⁻¹⁶] abundance in CKD (n = 686) in comparison to healthy control (n = 229) datasets. In addition, IGF2 increased [p = 0.042] plasma levels were observed in CKD patients (eGFR < 30 ml/min/1.73m² group) as supported by ELISA measurements. Protease predictions, considering also available transcriptomics data, suggest activation of cathepsin S with CKD potentially involved in the cleavage of the CKD-associated glycopeptide of IGF2.

Conclusion: Collectively, this study indicates that with aging and deteriorating kidney function, alterations in IGF2 proteoforms take place; which may be reflective of respective changes in the mature IGF2 protein abundance and function; as well as associated protease activity. Further, correlation analyses of the levels of the CKD-associated urinary IGF2 glycopeptide with the plasma IGF2 levels with CKD progression is planned.

* Results of multiple linear regression where regression Co-efficient is β; degree of freedom is stated in (brackets); and p-value <0.05 was considered statistically significant.
Background and Aims: Beta trace protein (BTP) is a low molecular weight protein that has been proposed as an earlier biomarker of decreased
glomerular filtration rate (GFR) and renal damage, than the traditional biomarkers, particularly in the creatinine blind range. Early biomarkers of renal (dys)function are needed to allow, in due time, the detection and treatment, to prevent worsening of the disease. To the authors’ knowledge, neither urine nor serum BTP has been assessed in animals with kidney disease. In the present study, we aimed to concomitantly evaluate BTP and creatinine circulating levels, to compare their value as early biomarkers of renal dysfunction, by performing the studies in rat models of mild and moderate chronic renal failure (CRF) induced by nephrectomy.  

**Method:** Male Wistar rats, 12 weeks old, were randomly divided in three groups: Sham (n = 8, subjected to surgical process without kidney mass reduction), Mild CRF (n = 8, subjected to 1/2 nephrectomy), and Moderate CRF (n = 7, subjected to 5/6 nephrectomy). After five weeks, rats were sacrificed, blood and kidneys were collected. We analysed the circulating levels of BTP and creatinine and studied the association of BTP concentration with the glomerular and tubulointerstitial lesions, and with the traditional biomarkers of renal (dys)function, eGFR and creatinine.

**Results:** The serum levels of BTP were correlated with serum levels of creatinine (r = 0.575, p = 0.004) and also with eGFR (r = -0.453, p = 0.030); additionally, we found positive correlations with the total score of mild and advanced tubular lesions (r = 0.610, p = 0.02 and r = 0.517, p = 0.011, respectively), observed in kidney sections. The circulating levels of BTP increased with disease severity; Mild CRF showed a higher value of BTP than Sham group, although without statistical significance that was reached in Moderate CRF group, as observed for serum creatinine. The combined use of BTP and creatinine did not improve the discriminatory power in early disease detection. Though, the combination showed stronger correlations with the total score of tubular lesions (r = 0.849, p < 0.001 for mild tubular lesions and r = 0.774, p < 0.01 for advanced tubular lesions).

**Conclusion:** In rat models of mild and moderate CRF induced by nephrectomy, serum BTP levels increased with kidney function worsening, and correlated with disease severity, assessed by GFR and the degree of histopathological alterations. However, the earlier diagnostic value of BTP does not outperform serum creatinine in this model.

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**#4425**  
**EZH2 PROMOTES RENAL INTERSTITIAL FIBROSIS THROUGH DOWNREGULATION OF PHOSPHOENOLPYRUVATE CARBOXYKINASE 1 MEDIATED GLUCONEOGENESIS**  
Yanfang Bai, Ming Wu, Chaoyang Ye and Dongping Chen  
Shanghai Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, P.R. China, Department of Nephrology, Shanghai, P.R. China

**Background and Aims:** Renal fibrosis is the common pathological pathway of various chronic kidney diseases progressing to the end stage of renal failure. The methyltransferase enhancer of zeste homolog 2 (EZH2) has been identified as a therapeutic target to inhibit renal interstitial fibrosis. However, the mechanism underlying the role of EZH2 in renal fibrosis is not completely understood.

**Method:** Unilateral ureteral obstruction (UUO), unilateral ischemia-reperfusion injury (UIRI) mouse models were established. PCR, cleavage under targets and tagmentation (CUT&Tag) and Western blotting was performed to evaluate the expression of EZH2 and phosphoenolpyruvate carboxykinase 1 (PCK1).

**Results:** Using EZH2 inhibitor 3-DZNNeP and Ezh2 conditional knockout mice, we confirmed the pro-fibrotic effect of EZH2 in unilateral ureteral obstruction (UUO). Through RNA sequence and cleavage under targets and tagmentation (CUT&Tag) sequence analysis, we found that the phosphoenolpyruvate carboxykinase 1 (PCK1), a critical enzyme in gluconeogenesis, is negatively regulated by EZH2 in fibrotic kidneys, which was further confirmed by quantitative PCR, CUT&Tag and Western blotting. We further showed that deletion or inhibition of EZH2 inhibited renal fibrosis and enhanced PCK1 expression and activity in unilateral ischemia-reperfusion injury (UIRI) and folic acid induced mouse nephropathy. Moreover, the dysregulated production of renal glucose and lactate in mouse UUO kidneys was restored after EZH2 inhibition by 3-DZNNeP. Finally, inhibition of PCK1 by 3-mercaptopropionic acid (3-MPA) abrogated the anti-fibrotic effect of 3-DZNNeP in UUO kidneys.

**Conclusion:** We conclude that EZH2 promotes renal interstitial fibrosis through inhibition of PCK1 mediated gluconeogenesis.

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**#4884**  
**DISRUPTION OF THE INTESTINAL MUCOSAL BARRIER IN CHRONIC KIDNEY DISEASE IS RELATED TO REDUCED EXPRESSION OF THE TIGHT JUNCTIONS’ COMPONENTS**  
Georgia Andriana Georgopoulou1, Marios Papasotiriou1, Pinelopi Bosgana2, Anne-Lise Delastic3, Evangelos Papachristou1, Dimitrios Goumenos1, Vasiliki Zolota1, Konstantinos Thomopoulos4 and Stelios Assimakopoulos5
1 Patras University Hospital, Nephrology and Transplantation, Rio, Greece, 2 Patras University Hospital, Pathology, Rio, Greece, 3 Patras University Hospital, Hematology, Rio, Greece, 4 Patras University Hospital, Gastroenterology, Rio, Greece and 5 Patras University Hospital, Internal Medicine and Infectious Diseases, Rio, Greece

**Background and Aims:** Patients with chronic kidney disease (CKD) present evidence of systemic inflammation without clinical infection. This is partly attributed to intestinal barrier dysfunction resulting in increased gut permeability with microbial and endotoxin translocation. However, the potential mechanism(s) implicated in increased gut permeability remain unclear. In this study, we investigated several parameters of the intestinal barrier in patients with CKD of various stages.

**Methods:** Thirty-three patients with CKD were prospectively enrolled. Patients were divided in stage 1-IV CKD (group A, n = 17, 9 of them with IgA nephropathy) or end-stage kidney disease (ESKD) (group B, n = 16) and were compared with 11 healthy controls (group C). Duodenal biopsies from all subjects, obtained by endoscopy, were examined histologically for evaluation of the villous length and apoptotic bodies in crypt epithelium. Intraepithelial CD3+ T-lymphocytes, expression of occludin and claudin-1 in the intestinal epithelium were evaluated by immunohistochemistry. Circulating endotoxin concentration was measured by enzyme-linked immunosorbent assay and cytokine levels [interleukin (IL)-1β, IL-6, IL-8, IL-10, TNF-α] by flow cytometry.

**Results:** Patients in groups A and B presented significantly higher serum endotoxin, IL-6 and IL-10 levels compared to controls (p < 0.01, both groups). Patients in group B presented additionally significantly higher IL-6 levels compared to controls (p < 0.01). Occludin expression was significantly decreased in groups A and B compared to group C (p < 0.0001 and p < 0.001, respectively). Interestingly, in CKD patients (groups A and B) a gradient of occludin expression along the length of the villi, from crypt to tip was recorded with greater loss of its expression at villous tip. Claudin-1 expression was significantly decreased in crypts in groups A and B compared to group C (p < 0.0001 and p < 0.01 respectively). Endotoxin concentrations were inversely correlated with intestinal occludin (p < 0.0001) and claudin-1 (p < 0.01) expression and positively correlated with serum IL-6 (p < 0.05) and IL-8 (p < 0.001) levels. Subgroup analysis for patients with IgA nephropathy showed similar histological findings for occludin and claudin-1 expression as well as for serum endotoxin levels.

**Conclusion:** Decreased enterocytes’ occludin and claudin-1 expression, might represent an important mechanism of intestinal barrier disruption and increased gut permeability in patients with CKD.

**Table 1:** (%) of occludin (+) enterocytes.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group A (n = 17)</th>
<th>Group B (n = 16)</th>
<th>Group C (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>75.3 ± 6.2***</td>
<td>77.5 ± 10**</td>
<td>93.6 ± 5</td>
</tr>
<tr>
<td>Tip of the villi</td>
<td>44.7 ± 25**</td>
<td>53.7 ± 29**</td>
<td>91.8 ± 7.5</td>
</tr>
<tr>
<td>Middle of the villi</td>
<td>84.7 ± 6.2**</td>
<td>86.3 ± 7.2*</td>
<td>97.3 ± 4.7</td>
</tr>
<tr>
<td>Crypts</td>
<td>97.5 ± 5.9</td>
<td>93.1 ± 11.3</td>
<td>99.3 ± 3.9</td>
</tr>
</tbody>
</table>

*p < 0.01, **p < 0.001, ***p < 0.0001, compared to controls."
Dietary Magnesium Supplementation Reduces Renal and Cardiac Fibrosis in an Experimental Model of Type 4 Cardiorenal Syndrome

Juan R. Muñoz-Castañeda, Andrés Carmona Muñoz, Julio Manuel Martínez-Moreno, Teresa Obrero, Rodrigo López-Baltanas, Fatima Guerrero, Ana Torralbo Romero, Cristina Membrives, María Encarnación Rodríguez Ortiz, Cristian Rodelo Haad, Cayetana Moyano Peregrín, M. Victoria Pendón-Ruiz de Mier and Mariano Rodríguez

Maimónides Institute for Research in Biomedicine of Córdoba IMIBIC, Nephrology Service, Reina Sofía University Hospital. University of Córdoba, Córdoba, Spain

Background and Aims: In chronic kidney disease (CKD) patients, high serum phosphate (HP) levels are associated with the development of a cardiorenal syndrome type 4 (CRS4). In this syndrome, the heart is damaged by oxidative stress, inflammation, and fibrosis in renal tissue. In this study we have evaluated if dietary Mg supplementation could reduce CRS4.

Method: The in vivo studies were performed in 5/6Nx rats fed a high (0.9%) phosphate diet with high or low dietary content of Mg to evaluate: 1) The effect of dietary Mg supplementation (0.3%) on oxidative stress, inflammation and fibrosis of kidney and heart. 2) The contribution of hypomagnesemia (using a low Mg diet (0.03%)) to the progression of CRS4 in Nx rats and normal rats as controls. 3) Whether dietary Mg supplementation (8 weeks) reduces renal and cardiac fibrosis in Nx rats with established CRS4. In vitro, we evaluated the effects of Mg (MgCl₂) on mesangial and tubular cells and also cardiomyocytes cells exposed to TGF-β.

Results: Dietary Mg supplementation (0.3%) improved renal function, decreased oxidative stress, FGF23 levels, hypertension, renal and cardiac fibrosis and recovered renal expression of Klotho. A low Mg diet increased FGF23 and renal fibrosis but a subsequent switch to dietary Mg supplementation did not significantly improve CRS4 parameters although it reduced the values of blood pressure. In HK2 and rat mesangial cells treated with TGFβ (100 ng/ml), high Mg levels (1.4- and 2.8-times basal levels in the medium) reduced the amount of pro-fibrotic proteins such as α-smooth muscle actin, fibronectin, or renin, recovering Klotho expression and decreasing Smad3 phosphorylation.

Conclusion: Dietary Mg supplementation is a useful tool to improve renal function and prevent CRS4, by reduction the progression of renal and cardiac fibrosis.
#3257

EFFECTS OF CKD ASSOCIATED GENETIC VARIATION ON TRANSCRIPTOMIC REGULATION OF RENAL CELLS

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Background and Aims: Chronic kidney disease (CKD) is an universal health problem characterized by a decline of renal function. This progressive disease leads to kidney failure and CKD patients have a high risk of cardiovascular diseases, including endothelial dysfunction in the heart. Genetic variability in the general population has a strong impact on the risk of CKD development. Genome wide association studies (GWAS) already identified more than 250 single nucleotide polymorphisms (SNPs) associated with renal function. These SNPs are studied in relation with their location in the genome in protein coding regions, however, genetic variability in the genome could also affect the function of DNA regulatory elements (DREs). These non-protein coding regions regulate transcriptional expression of genes by transcription factor binding. These elements are ubiquitously present in the genome and can regulate promotor activity from a long distance (> 100 kb from the start site) via 3D chromatin folding. DRE activity is cell type dependent and also changes in different conditions (e.g. disease). Therefore, genetic variability e.g. SNPs located in DREs and their regulation of gene transcription could play a key role in the development and progression of CKD. Previous studies identified more than 30 DREs localized SNPs in renal cells which could be important in CKD development. We focus on SNP rs881858, a CKD associated SNP region without a protein coding sequence. Moreover, vascular endothelial growth factor (VEGF) is identified as target gene of this SNP which could therefore impact renal cell-endothelial cell interaction. Six possible active DREs were identified in this rs881858 DNA region. We hypothesize that the CKD associated SNP rs881858 induce DRE mediated transcriptional changes that contribute to the development and progression of CKD. We aim to study the effect of the DREs in DNA region rs881858 on transcriptional gene regulation in renal cells.

Method: All variations of the genetic variability in 6 identified DREs in DNA region rs881858 were introduced by site-directed mutagenesis. These variations including the reference variant, were cloned into a luciferase reporter plasmid with a minimal promoter and subsequently transfected in human embryonic kidney (HEK) cells. Luciferase activity was measured using spectrophotometry and represent DRE regulation of transcription. A decline in luciferase activity of one of the variants in a DRE imply a reduced activity of that specific variant compared to the reference variant. To assess the impact of the DREs in the genome, a CRISPR/Cas9 construct was made to knockout each individual DRE on the risk locus rs881858.

Figure 1: Dietary Mg supplementation reduces the development of renal and cardiac fibrosis in uremic rats. 5/6Nx rats were fed a normal (0.6%) P and (0.05%) Mg diet (Nx+0.6%P+0.05%Mg) or received a high dose of P (0.9%) and normal Mg diet (0.05%) (Nx+0.9%P+0.05%Mg) or Mg dietary supplementation (0.3%) (Nx+0.9%P+0.3%Mg). Sham-operated rats fed a normal P and Mg diet (Sham+0.6%P+0.05%Mg) served as controls. (A) Renal content of lipid peroxides (MDA). (B) Klotho positive area quantified by Image J software. (C) Representative images of renal Klotho immunohistochemistry. (D) Representative images of siriusred staining from renal (D) and cardiac (E) tissues. Scale bar represents 200 μm. ap<0.05 vs Sham+0.6%P+0.05%Mg; bp<0.05 vs Nx+0.6%P+0.05%Mg; cp<0.05 vs Nx+0.9%P+0.05%Mg.
Results: We considered a DRE functional if (almost) all variants within this DRE demonstrated a change in luciferase activity. Based on this, we identified 3 DRE DNA regions in which SNPs gave a decline in luciferase activity. CRISPR/Cas9 mediated knockout of DRE in the HEK cells was validated using PCR and qPCR analysis of SNP rs881858 associated genes is planned to confirm the DRE mediated transcriptomic regulation of these genes.

Conclusion: These primary results show that CRISPR associated SNP rs881858 has a negative impact on DRE function compared to the reference variant. Next we will study the effect of DRE mediated gene transcription in the DRE knockout lines using qPCR. Furthermore, CRISPR/Cas9 mediated DRE-knockout will be performed in an iPSC derived renal organoid model. Since this in vitro model consists of both renal and vascular cell types, the interaction between these cell types can be evaluated in a background of epigenetic variability. This study provides new knowledge in the effect of genetic variant in the development of CKD. Results could lead to identification of novel pathways and therefore personalized strategies for intervention. This method is a stepping stone for studying other known genetic variants in other diseases, including renal and cardiovascular diseases.

#3635
THERAPEUTIC STRATEGIES TARGETING RAGE IMPROVES RENAL OUTCOME IN LUPUS NEPHRITIS
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Background and Aims: Lupus nephritis (LN) occurs in up to 60% of patients with systemic lupus erythematosus (SLE). Despite of current development of immunosuppressant agents, LN still impairs the survival and quality of life in SLE patients. Receptor for advanced glycation endproducts (RAGE) is a multi-ligand receptor that belongs to the immunoglobulin superfamily, which is strongly associated with innate immune system. In the present study, we examined whether RAGE is involved in the development of LN. Further, we explored the therapeutic impact of DNA-aptamer directed against RAGE on lupus-related kidney injury.

Method: [Protocol 1] RAGE expression in kidneys and urinary RAGE excretion (uRAGE) were determined at 8, 12, 16, 18, 20-week-old by real-time PCR and ELISA, respectively in MRL/lpr, SLE-prone mice. [Protocol 2] LN was induced by peritoneally injecting pristane in wild type and RAGE globally knockout mice. [Protocol 3] MRL/lpr mice were subcutaneously administrated with DNA-aptamer raised against RAGE (RAGE-apt) or Control-aptamer (Ctrl apt) for 10weeks.

Results: [Protocol 1] uRAGE, but not urinary protein excretion, was increased in 8-week-old MRL/lpr mice when compared to that of the control of MRL/MpJ mice. uRAGE is positively correlated with urinary NAG, a tubular injury marker, suggesting that uRAGE can predict the onset and the progression of LN. Immunofluorescence staining demonstrated that RAGE was upregulated in distal tubules but not in glomerulus in early stage, meanwhile RAGE started to be extensively expressed in nephron at late stage of LN. Not only tubules, but RAGE was also found in infiltrated macrophages in glomerulus. In proximal tubules (PTC), RAGE was co-localized with cathepsine D, a lysosomal aspartyl protease, and Rab7, a marker of late endocytosis, suggesting that PTC RAGE is involved in endosome-related protein degradation. [Protocol 2] Pristane-induced the increase in systolic blood pressure was reduced with improvement of renal dysfunction in RAGE knockouts. RAGE knockouts also showed less fibrosis with the decrease in macrophage infiltration when compared to wild type mice in pristane-induced lupus nephritis. [Protocol 3] Similar to RAGE knockouts, administration of RAGE-apt reduced systolic blood pressure and attenuated the renal dysfunction. RAGE-apt also ameliorated mesangial expansion, crescent formation, and macrophage infiltration into glomerulus in MRL/lpr mice. The level of pro-inflammatory cytokines gene expression including IL-6, TNF-a, and MCP-1 was reduced by RAGE-apt, but not Ctrl apt, in MRL/lpr mice.

Conclusion: RAGE could be involved in the pathogenesis of LN, and RAGE-DNA aptamer might be one of the promising therapeutic strategies for preventing the development of LN.

#1448
UPEREGULATION OF ADIPOSE TISSUE FATTY ACID-BINDING PROTEIN 4 IN PATIENTS WITH CHRONIC KIDNEY DISEASE: IMPLICATIONS FOR DYSFUNCTIONAL VASCULAR CELLS
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Background and Aims: FABP4, a fatty acid-binding protein, is predominantly expressed in adipose tissue (AT) and has been shown to be elevated in patients with chronic kidney disease (CKD). Although elevated levels of FABP4 have been linked to cardiovascular disease in end-stage renal disease (ESRD) patients, the cause of this increase is unclear. The aim of this study was to evaluate the expression of AT FABP4 under uremic conditions and its impact on the function of macrophages and vascular smooth muscle cells (VSMC).

Method: We measured the levels of FABP4 in the blood and urine of CKD patients. The expression of AT FABP4 under uremic conditions was analyzed using omental AT obtained from healthy kidney donors and patients with ESRD who received peritoneal catheter insertion. The effect of FABP4 on the function of macrophages and VSMC was also assessed.

Results: The levels of FABP4 in the blood and urine of CKD patients were inversely correlated with their estimated glomerular filtration rate (eGFR). An increase in plasma FABP4 was detected in the blood before its increase in the urine. FABP4 expression was found to be higher in mature adipocytes in visceral AT compared to the stromal vascular fraction (SVF). Adipocytes treated with p-cresol and adipocytes isolated from CKD patients showed higher levels of FABP4 expression compared to healthy individuals. Single-cell RNA sequencing of SVF showed increased FABP4 expression in progenitor cells and macrophages from CKD patients. In THP-1 cells, FABP4 induced more foam cells and increased levels of inflammatory mediators in the presence of palmitic acid. VSMC treated with p-cresol or VSMC isolated from CKD mice induced by an adenine diet showed a pro-calcific phenotype, as indicated by increased calcium content and bone-related gene expression, which was further enhanced by FABP4.

Conclusion: The elevated levels of FABP4 in CKD patients are not solely a result of increased renal clearance but also due to increased production in AT. These higher levels of circulating FABP4 may be associated with dysfunction in vascular cells.

#2728
THROMBOINFLAMMATORY BIOMARKERS AND THEIR RELATIONSHIP WITH CIRCULATING GLYCOSAMINOGLYCANS IN END-STAGE RENAL DISEASE PATIENTS
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Background and Aims: End stage renal disease (ESRD) is a complex progressive medical condition that affects multiple organ systems. Given the high risk of morbidity and mortality of ESRD as well as its rising incidence, it is critical to understand the relevance of thromboinflammatory biomarkers in disease development and progression of kidney dysfunction. The purpose of this study is to profile the levels of thromboinflammatory biomarkers in ESRD patients including D-Dimer, C-reactive protein (CRP), von Willebrand factor (vWF), plasminogen activator inhibitor 1 (PAI-1), and thrombin activatable fibrinolysis inhibitor (TAFl). In addition, the levels of anti-F4 IgG and endogenous circulating glycosaminoglycans (GAGs) were measured.

Method: Citrated plasma samples were collected from seventy-three ESRD patients. Control plasma samples (NHP) from healthy, non-smoking adults aged 19 to 53 were obtained commercially. Validated ELISA methods have been used to profile each of the biomarkers. The levels of endogenous GAGs were determined (Redprobes UG, Germany). To compare the levels of thromboinflammatory biomarkers, anti-F4 IgG, and endogenous circulating glycosaminoglycans (GAGs) were measured.

Results: All of the biomarkers and GAGs were significantly elevated, with the exception of TAFI, in ESRD patients. The ESRD patients exhibited varying levels of increase in the D-Dimer, CRP, vWF, PAI-1, anti-F4 IgG, and GAGs as shown in Figure 1 (p < 0.05). D-Dimer showed the most pronounced increase (1075%) followed by PAI-1 (361.31%), anti-F4 IgG (209.78%), CRP (101.77%).
and endogenous GAGs (17.29%). The correlation analysis revealed varying degrees of association among these biomarkers (Figure 2).

**Conclusion:** These results suggest that thromboinflammatory biomarkers offer the potential utility of identifying inflammation in end-stage renal disease. Marked increase in thromboinflammatory mediators due to endothelial damage may result in the upregulation of glycosaminoglycans and anti-PF4 IgG antibodies in the ESRD patients.

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**#5403**

**PTEN-INDUCED KINASE 1 HAS ASSOCIATION WITH RENAL AGING PROCESS THROUGH THE CGAS-STING PATHWAY**

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**Background and Aims:** The global increase of an aging population has encouraged the research on renal aging, as the kidney is one of the organs that shows the greatest change as aging progresses. Although the mechanism of renal aging has not been clearly identified, dysfunctional mitochondria has been suggested as one of the factors that induce inflammation of the kidney, which is the major mediator of the pro-aging process of chronic kidney disease. PTEN-induced kinase 1 (PINK1) is a protein involved in the quality control of mitochondria and regulates mitochondrial dysfunction. Although it is known that the mitochondrial DNA release promoted by PINK1 deficiency stimulates cyclic GMP–AMP synthase (cGAS) - stimulator of interferon genes (STING) pathway eventually resulting in the inflammatory response, the role of PINK1 and cGAS-STING pathway in renal aging has not yet been clarified. This study aimed to investigate the relationship between PINK1 and renal aging, especially through the cGAS-STING pathway.

**Method:** To determine the role of PINK1 on the renal aging process, renal fibrosis, and tubular injury were compared in 4- and 24-month-old wild-type (Pink1+/+) and PINK1 knockout (PINK1-/-) mice. To establish in vitro senescence model, hydrogen peroxide (H2O2) treatment on human renal proximal cells (HKC-8) was used. The changes in gene expression levels related to PINK1 were analyzed by RNA sequencing, applying transcriptomic and metabolomic analyses. To validate the results of RNA sequencing, we measured mitochondrial oxygen consumption rate (OCR) by Seahorse Mito Stress Test. To investigate the relationship between PINK1 and renal aging through the cGAS-STING pathway, we explored the change of cGAS-STING expression on senescence-induced HKC-8 cells and additionally used H-151 treatment, a specific STING inhibitor.

**Results:** The renal fibrosis and tubular injury were significantly aggravated in 24-month-old Pink1-/- mice compared to 24-month-old Pink1+/+ mice. Western blot and RT-qPCR confirmed remarkably increased senescence markers and senescence-associated secretory phenotype (SASPs) in 24-month Pink1-/- mice and senescence-induced HKC-8 cells. The RNA sequencing of mice kidneys showed that inflammation-related pathways significantly increased in 24 months Pink1-/- mice and transcriptional and metabolomic analyses showed that PINK1 has an association with mitochondrial metabolism dysregulation. On OCR measurement, the basal respiration, maximal respiration, ATP production, and respiratory capacity significantly declined in H2O2-treated siPINK1 cells, suggesting that PINK1 deficiency might have effects on mitochondrial dysfunction. Finally, the STING pathway was significantly activated in 24-month Pink1-/- mice and senescence-induced HKC-8 cells, which was inhibited by a specific inhibitor of STING, H-151.

**Conclusion:** In conclusion, PINK1 is associated with renal aging, and the dysregulation of mitochondria caused by PINK1 deficiency might lead to aging-related inflammatory responses through the cGAS-STING pathway.
**Conclusion:** Here, we show that enhanced levels of ROS and oxidative DNA damage due to glucose induced TXNIP expression could be diminished using ROS scavengers. These findings show that further antioxidative substances may be potential drugs, which could also be potential drug candidates for use in clinical practice to treat PD patients.

**#3937 URINARY EXCRETION OF LIVER-TYPE FATTY ACID-BINDING PROTEIN DETECTS KIDNEY HISTOLOGICAL ALTERATIONS DURING PROGRESSIVE RENAL FIBROSIS**

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**Background and Aims:** Subclinical sequelae of acute kidney injury (AKI) are commonly associated with the development of chronic kidney disease (CKD). Despite extensive investigation on AKI to CKD transition on different experimental models, the underlying mechanisms of this transition remain unclear, and there are no known biomarkers monitoring this transition to CKD. The liver-type fatty acid-binding protein (L-FABP) is expressed in the kidney under normal and pathological conditions, and seems to play an important role on kidney injury and repair. We evaluated the efficacy of urinary L-FABP excretion as a prognostic indicator of the progression of renal damage in our AKI to CKD experimental model.

**Method:** 8 week old male Wistar rats were divided in two experimental groups: "Control" group (n = 8): SHAM-operated rats, which received saline solution i.p.; and Cpt-IR2 group (n = 8): 5 mg/kg cisplatin i.p and 2 weeks after renal function normalization, 60 min ischemia-reperfusion on the left kidney. Blood and urine samples were collected at day 0 (basal), day 4 (AKI development), day 8 (normalized renal function), day 24 (1 day after ischemia), and 2 (M2) and 3 (M3) months after first AKI induction. Renal function was estimated analysing by colorimetric methods plasma and urinary creatinine concentrations (pCr and uCr) and creatinine clearance. Animals were sacrificed at days 56 and 90. Tissue samples were stained with haematoxylin-Eosin, periodic acid Schiff and Masson’s Trichrome for histological analysis. Enzyme-linked immunosorbent assay was used to measure urinary L-FABP concentration.

**Results:** Cpt-IR2 rats showed a reduction in renal filtration with respect to control rats even though this decrease does not indicate a severe decline in renal function. This group also presented multiple histological alterations such as fibrosis, loss of brush border membrane, inflammatory infiltrates, basement membrane thickening, tubular dilatation, cellular debris and hyaline casts that worsened markedly from M2 to M3. ul-FABP was greater in Cpt-IR2 rats (52,299 ± 8,407 ng/g uCr M2 and 23,427 ± 4,778 ng/g uCr M3) than in control rats (16,657 ± 2,322 ng/g uCr M2 and 10,636 ± 1,395 ng/g uCr), but this urinary excretion does not correlate with the histological alterations in the last month of the study.

**Conclusion:** Urinary L-FABP may be a potential biomarker for the detection of the presence of histological damage although it is not correlated with the extent and degree of the damage in our AKI to CKD transition model. This research was funded by grants from Instituto de Salud Carlos III (ISICII) P121/00548 and P121/01226 co-funded by the European Union and Red de Investigación Renal RICORS2040 (Kidney Disease), RD21/0005/0004 co-funded by the European Union – NextGenerationEU, Mecanismo para la Recuperación y la Resiliencia (MRR). Joana Mercado-Hernández is recipient of a predoctoral fellowship from the Junta de Castilla y Leon (Spain) and the European Social Fund from the European Commission.

**#5865 BET INHIBITION DIMINISHES CELLULAR SENESCENCE IN CULTURED TUBULAR EPITHELIAL CELLS**

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**Background and Aims:** Chronic kidney disease (CKD) can be considered an age-related disorder. Recent studies have shown the involvement of the activation of cellular senescence mechanisms in the kidney and aging. Intensive research to develop pharmacological approaches targeting cellular senescence is under investigation. Among novel therapeutic options, epigenetic drugs, such as bromodomain and extra terminal BET inhibitors, are being widely explored in proliferative, immune and chronic inflammatory diseases, including CKD. These drugs regulate the transcription activation of cell cycle control and proinflammatory factors. There are not studies about the potential effect of BET inhibitors on cellular senescence in the kidney despite the fact that tubular epithelial cells are frequently implicated in kidney senescence.

**Method:** To study this, we evaluate the effect of JQ1, a BET inhibitor, on cellular senescence in primary cell culture of murine tubular epithelial cells (TECs) using Adriamycin as a senescence inducer verified by B-galactosidase assay. Next, we evaluated the effect of JQ1 on gene expression levels of cell cycle markers, components of senescence-associated secretory phenotype (SASP) as well as anti-apoptotic and antioxidant markers, all of them related to senescence program.

**Results:** Our results indicated that JQ1 significantly decreased Adriamycin-induced p21 gene upregulation, a primordial cell cycle arrest factor. This BET inhibitor also downregulated SASP genes, such as Tgfb1, Il1b, Ctgf, Cu2 and Il6 overexpression in Adriamycin-treated tubular cells. Likewise, anti-apoptotic Bcl-xl and antioxidant factors Cat, Hmox-1, Nos-4 and Nrf2 mRNA levels were significantly restored by JQ1.

**Conclusion:** In conclusion, the present study highlights the use of JQ1 as a therapeutic option to ameliorate tubular cellular senescence-associated markers. These data support the potential use of BET inhibitors in chronic kidney diseases.

**#4161 DELETION OF PROTEIN TYROSINE KINASES 4A1 AMELIORATE RENAL FIBROSIS INDUCED BY UUO IN MICE**

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**Background and Aims:** Inhibitors of protein tyrosine kinases has been investigated as potential anti-fibrotic agents. protein tyrosine kinases 4A1 belongs to a sub-class of three prenylated protein tyrosine kinases. protein tyrosine kinases 4A1 has been shown to be involved in the promotion of growth, migration and tumor cells. The role protein tyrosine kinases 4A1 has little known in kidney. We evaluated whether the protein tyrosine kinases 4A1 could be target of renal fibrosis.

**Method:** 10 weeks old male background protein tyrosine kinases 4A1 KO mice and wild type mice were divided into 4 groups; wild, protein tyrosine kinases 4A1 KO with unilateral ureteral obstruction. Mice were sacrificed at 7 days after surgery and kidney tissue were collected. Molecular study and Histologic examination were performed.

**Results:** Protein tyrosine kinases 4A1 KO with unilateral ureteral obstruction mice showed decrease of renal tubule-interstitial damage and fibrosis compared to wild type unilateral ureteral obstruction mice. protein tyrosine kinases 4A1 KO with unilateral ureteral obstruction reduced the renal expression of α-SMA and TGF-β in unilateral ureteral obstruction kidney, compared to wild type with unilateral ureteral obstruction mice. Wild type with unilateral ureteral obstruction kidney showed decrease of renal expression of E-cadherin, compared to sham mice. However, protein tyrosine kinases 4A1 KO unilateral ureteral obstruction showed increase of renal expression of E-cadherin, compared to Wild type unilateral ureteral obstruction mice. In vitro, silencing of protein tyrosine kinases 4A1 in TGF-β treated HK2 cell showed increase of E-cadherin and decrease of phosphorylation of AKT and GSK3β.

**Conclusion:** Protein tyrosine kinases 4A1 KO ameliorate renal fibrosis in unilateral ureteral obstruction kidney.

**#5040 UNTARGETED METABOLOMIC ANALYSIS IDENTIFIES A SPECIFIC METABOLIC PROFILE IN PATIENTS WITH EARLY CHRONIC KIDNEY DISEASE**

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Background and Aims: Chronic kidney disease (CKD) has become one of the most challenging diseases of the twenty-first century and is characterized by increased mortality and morbidity. The pathogenesis of CKD is heterogeneous and the evaluation of renal function is performed with biomarkers such as serum creatinine and blood urea, which have low specificity and sensitivity. Metabolomics, one of the omics sciences, has become of interest in the nephrology field of research. Metabolic pathways can impact both glomerular and tubular structures and can offer a better understanding of the pathogenic mechanisms of CKD. Also, metabolomics provides more sensitive biomarkers for an early detection of CKD. The aim of this study was to perform metabolic profiling of serum and urine in CKD patients by means of targeted metabolomics in relation with the glomerular filtration rate (eGFR) and to identify potential serum and urinary biomarkers of early CKD.

Method: In this cross-sectional study were included 99 patients with CKD, staged by eGFR in six subgroups, according to the KDIGO Guidelines and 20 healthy control subjects. Serum and urinary metabolomic profiling were performed by using ultra-high-performance liquid chromatography coupled with electrospray ionization-quadrupole-time of flight-mass spectrometry. Blood and urine samples were evaluated by multivariate analysis, followed by univariate analysis. First, the PLSDA score plot and VIP score were applied. By using the cross-validation algorithm for the first 4 molecules identified, a high accuracy, high R² values, and a significant Q² value were obtained. Therefore, the model could be considered predictive. Biomarker analysis and prediction by Random Forest analysis was performed. The specificity and sensibility of the molecules identified as potential biomarkers were evaluated by applying the Receiver Operating Characteristic (ROC) curve and the area under the curve (AUC).

Results: Significant direct correlations with eGFR were demonstrated for serum levels of Oleoyl glycine ($p < 0.05$, Log2 = 0.773), alpha-lipoic acid ($p < 0.05$, Log2 = 0.505), and L-cysteine ($p < 0.05$, Log2 = 0.363). Interestingly, serum levels of 5-Hydroxyindoleacetic acid, Phenylalanine, Pyridoxamine, Cysteinylglycine, Propenoylcarnitine, and Uridine increased gradually from G1 group to subgroups G5. Also, 5-Hydroxyindoleacetic acid, Phenylalanine, Pyridoxamine, Cysteinylglycine, Propenoylcarnitine, Uridine, and All-trans retinoic acid levels correlated negatively with eGFR ($p < 0.05$). Moreover, in urine samples the majority of molecules were increased in group G4 and G5 versus G1-G3b and C groups, respectively. Urinary levels of Inositol sulfate, Glycophospholipins, and Butenylcarnitine correlated negatively with eGFR ($p < 0.05$).

Conclusion: Amino acids, antioxidants, uremic toxins, and acylcarnitines are increased in all CKD stages. The impact of this metabolites on the glomerular and tubular structures, even in the early stages of CKD, can be explained by their dual serum and urinary variation. The study provided a particular metabolic profile that can offer new biomarkers useful for the evaluation of early CKD and its progression, as well as potential therapeutic targets.

Conclusion: The urinary metabolome of kidney transplant recipients with chronic allograft injury and who experienced severe IRI was significantly enriched with long chain fatty acids (FA). We identified a renal FA-related gene signature with low levels of Cpt2 and Acsm5 and high levels of Acsl4 and Acsm5 associated with IRI, transition to chronic injury, and established CKD in mouse models and kidney transplant recipients. The findings were consistent with the presence of Cpt2−, Acsl4−, Acsm5−, PTC− lacking recovery from IRI as identified by single nucleus RNA sequencing. In vitro experiments indicated that endoplasmic reticulum (ER) stress contributes to CPT2 repression, which, in turn, promotes lipids accumulation, drives profibrogenic epithelial phenotypic changes, and activates the unfolded protein response.

Conclusion: ER stress through CPT2 inhibition and lipid accumulation, engages an auto-amplification loop leading to lipotoxicity and self-sustained cellular stress. Thus, IRI imprints a persistent FA metabolism disturbance in the proximal tubule sustaining the progression to chronic kidney allograft injury.

**Figure 1: Novel cell intrinsic model of lipotoxicity.**

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**#3971**

**INJURY INDUCED RENAL FIBROSIS PROMOTES CYSTGENESIS AND CYST GROWTH IN ADULT MICE WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE**

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**Background and Aims:** Acute kidney injury (AKI) is not a merely transient event, which can lead to a subsequent progression to chronic kidney disease (CKD). Autosomal dominant polycystic kidney disease (ADPKD) is the most frequent inherited kidney disease caused by mutations in PKD1 or PKD2 gene. Previous studies showed that acute kidney injuries promote cystogenesis in adult mice with ADPKD. Fibrosis is a hallmark of AKI to CKD (AKI-CKD) transition, and positively correlated with renal cyst growth in humans. All these data imply a role of AKI-CKD transition in ADPKD. In this study, we aimed to determine the role of AKI-CKD transition in ADPKD.

**Method:** We established AKI-CKD transition model by toxic or surgical injuries, and Pkd gene inactivation in adult mice was performed in different time point of AKI-CKD transition. The progression of renal fibrosis was shown.
by Western blotting analysis in toxic or surgical injury induced AKI-CKD transition model.

**Results:** We showed that renal injury before or after Pkd gene inactivation can both induce renal cyst formation in adult Pkd1 or Pkd2 mice, and the extent of cyst formation was correlated with the initial fibrosis level of three hits (injury and gene inactivation). Inactivation of Pkd1 gene at fibrosis recovery stage in adult Pkd1 mice. Enhanced renal fibrosis by repeated toxic injuries before gene inactivation accelerated renal cyst growth in Pkd1 mice. We further showed that the speed of cyst growth at the early stage in adult Pkd1 mice was decided by the baseline of renal fibrosis. Finally, we showed that conditional knockout of Ezh2 gene attenuated renal fibrosis and cyst growth in adult Pkd1 mice with established renal fibrosis.

**Conclusion:** Fibrotic responses in AKI-CKD transition is a driving force for renal cyst formation and growth in adult kidneys and inhibition of renal fibrosis through targeting EZH2 might be a new therapeutic strategy for adult ADPKD.

**#6744**

**SELF-ASSEMBLED FISETIN NANOPARTICLES WITH ENHANCED BIOACTIVITIES FOR EFFECTIVE HYPERURICEMIC NEPHROPATHY THERAPY**

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**Background and Aims:** The prevalence of hyperuricemia is rising rapidly around the world, and increasing evidence demonstrates that hyperuricemia is the independent risk factor for chronic kidney diseases (CKD) development and progression. Hyperuricemia-induced renal injury, namely hyperuricemic nephropathy (HN), is characterized by urate crystal formation, tubulointerstitial fibrosis and glomerulosclerosis, which would eventually progress into end-stage renal disease (ESRD). Up to now, the mechanism of HN remains unclear and the treatment still needs further exploration. Fisetin is a natural flavanol with potent antioxidative and anti-inflammatory properties and showed therapeutic effects in mice with HN. However, the poor water solubility, rapid metabolism, and low bioavailability of fisetin largely hampered its clinical application. Herein, we reported the simple and efficient preparation of fisetin-EGCG nanoparticles (EG/FIS NPs) based on a solvent-mediated disassembly/reassembly strategy.

**Method:** The fisetin nano-formulation (FIS/EG NPs) was prepared based on a general solvent-mediated disassembly/reassembly strategy. The physicochemical properties of FIS/EG NPs including morphology, specific surface area and pore size distribution, drug encapsulation rate and loading rate, intracellular distribution were characterized. The potential toxic effects of FIS/EG NPs on RAW264.7 and TCMK-1 cells were investigated by CCK-8. Meanwhile, the anti-oxidative and anti-inflammatory effects of FIS/EG NPs were detected in vivo and in vitro. In vivo small animal imaging was employed to assess the kidney accumulation of FIS/EG NPs. And finally, HN was induced to measure the effect of FIS/EG NPs in mice and PAS staining, Masson staining, RT-qPCR were used to explore underlying mechanisms.

**Results:** EG/FIS NPs with stable water dispersion was prepared by using a general solvent-mediated disassembly/reassembly strategy. EG/FIS NPs contains both features of fisetin and EG NPs, and displayed more potent free radical scavenging ability than fisetin and EG NPs. Meanwhile, it was found that both RAW264.7 and TCMK-1 cells were able to uptake EG/FIS NPs and no proliferation toxicity was observed in these two cell types after incubation with various concentrations of EG/FIS NPs. By in vivo and in vitro experiments, fisetin and EG NPs were shown to have synergistic effects in inhibiting LPS-stimulated NO production after encapsulation. Moreover, fluorescence imaging revealed that EG/FIS NPs preferentially accumulated in the injured kidney of HN mice. Finally, it was observed that EG/FIS NPs exhibited enhanced therapeutic efficiency against HN due to the combined antioxidative, anti-inflammatory, and antifibrotic activities of fisetin and EG NPs.

**Conclusion:** Collectively, these results suggested that EGCG-based nanocarriers might be a novel strategy for the development of therapeutic drugs for HN.
BACKGROUND AND AIMS: Hyperphosphatemia in chronic kidney disease (CKD) is closely linked to medial vascular calcification. Phosphate is able to induce pro-inflammatory effects in vascular smooth muscle cells (VSMC), which could actively augment calcification processes. This study investigated the role of the IL-6 family member leukemia inhibitory factor (LIF) during vascular calcification.

METHOD: Experiments were performed in primary human aortic VSMCs, ex vivo mouse aortic rings and cholecalciferol treated mice, as well as serum samples from CKD patients and healthy controls.

RESULTS: Phosphate exposure induced LIF release in VSMCs, while supplementation of LIF aggravated calcification and expression of pro-calcific markers in VSMCs. Silencing of LIF by siRNA decreased calcification (40.4 ± 1.3 μmol/L, p < 0.05) and were found to be higher in PKD-male rats than in their female counterparts (p < 0.0001). Compared to Control-male rats, PKD-male rats showed decreased maximum relaxation to acetylcholine (55.2% ± 7.7 ±1%, p < 0.05), indicating impaired endothelial function. Contractile responses to phenylephrine (3.0±0.1 g vs. 3.4±0.1 g, p < 0.05) and high potassium (3.3±0.1 g vs. 3.7±0.1 g, p < 0.05) were reduced in the PKD-male compared to Control-male. Additionally, in PKD-male aortas, the concentration-response curve to sodium nitroprusside, an endothelium-independent vasodilator, was shifted to the right compared to Control-male. Morphometric analysis revealed that wall thickness and wall cross-sectional area normalized to body weight, and the wall/lumen area ratio were significantly higher in PKD-male aortas compared to Control-male. Additionally, PKD-male showed increased cleaved PARP-1 immunoreactivity confined to endothelial level compared to Control-male. All these parameters were unchanged in PKD-female rats compared to Control-female.

CONCLUSION: Six month-old PKD-male, not female, rats show endothelial dysfunction, impaired smooth muscle contraction and relaxation, pathological changes in aortic morphometry, and apoptosis in a non-renal vasculature. The rat model of autosomal dominant PKD in males can be used to identify novel targets for the treatment of this disease.

C2 - PATHOPHYSIOLOGY, RISK FACTORS & PROGRESSION

HEART FAILURE IN ASCEND-ND AND ASCEND-D

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BACKGROUND AND AIMS: Heart failure (HF) is a common cardiovascular (CV) complication in chronic kidney disease (CKD) [1]. Two CV outcome trials (ASCEND-ND [NCT02878635][2] and ASCEND-D [NCT02879035][3]) have provided the principal assessment of CV risk with daprodustat in CKD: both studies showed noninferiority of daprodustat to erythropoiesis-stimulating agent (ESA) in patients with anaemia of CKD not on (ASCEND-ND) or on (ASCEND-D) dialysis. Time-to-first adjudicated major adverse CV event (MACE) was the primary endpoint. Time-to-first MACE or hospitalisation for heart failure (HHF) was assessed as a principal secondary endpoint, and time-to-first HHF was analysed as an additional secondary endpoint. To better understand HF-specific outcomes, post-hoc analyses accounting for competing risk of death were conducted via the composite endpoint of all-cause mortality (ACM) + HHF – more typically employed to evaluate HF-specific outcomes and to assess “hospitalisation-free survival”. Post-hoc subgroup analyses of patients identified as having a baseline HF history were also conducted.

RESULTS: Overall, 3872 and 2964 patients were randomised in ASCEND-ND and ASCEND-D respectively. All key prespecified and post-hoc CV endpoints in ASCEND-ND and ASCEND-D are shown in the Table, and the composite endpoint of ACM + HHF is shown in the Figure. In summary, for components of MACE for daprodustat vs ESA, respectively, ACM and HHF were similar between treatment arms in both studies: ASCEND-ND: 11.6% vs 12.2%; ASCEND-D: 14.8% vs 14.6%. For HHF alone in both studies, event rates for daprodustat vs ESA, respectively, were: 7.2% vs 5.8% (hazard ratio [HR] 95% confidence interval [CI] = 1.22 [0.95, 1.56]) in ASCEND-ND; and 7.5% vs 6.8% (HR [95% CI] = 1.10 [0.84, 1.45]) in ASCEND-D. In post-hoc analyses using the composite endpoint of ACM + HHF in ASCEND-ND, the event rate for daprodustat was 20.3% (n = 393/1937), and the event rate for ESA was 19.0% (n = 368/1935) (HR [95% CI] = 1.09 [0.94, 1.26]). More HHF events were
observed in patients with a history of HF (daprodustat: 20.4% [n = 54/265]; ESA: 13.4% [n = 34/254]). In ASCEND-D, ACM + HHF events were similar for daprodustat (24.4% [n = 363/1487]) and ESA (24.8% [n = 366/1477]; HR [95% CI] = 0.98 [0.85, 1.14]). In this composite endpoint in patients with a history of HF in ASCEND-D, there were also more HHF events in those treated with daprodustat (18% [n = 47/267]) vs ESA (13% [n = 32/254]), but there were fewer deaths with daprodustat (21% [n = 56/267]) than ESA (28% [n = 71/254]). For subgroup analyses of daprodustat vs ESA, the proportion of patients with a history of HF at baseline was greater in ASCEND-D (18.0% vs 17.2%) than ASCEND-ND (13.7% vs 13.1%). Incidence of MACE + HHF was similar between treatment arms in both studies.

**Conclusion:** Our findings showed that there was a higher HHF risk in daprodustat-treated patients who had a history of HF compared to ESA-treated patients. While HF risk was similar between treatments in patients on dialysis (ASCEND-D) when combining ACM + HHF in a post-hoc analysis, the risk remained numerically higher for daprodustat vs ESA in patients not on dialysis (ASCEND-ND). The underlying mechanism responsible for these observations and differences is not known, although patients with advanced CKD and comorbid HF who are not on dialysis are recognised to be at underlying risk of HF decompensation.

**REFERENCES**

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**Table. Key prespecified and post-hoc CV endpoints in ASCEND-ND and ASCEND-D**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>ASCEND-ND</th>
<th>ASCEND-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients, N</td>
<td>1937</td>
<td>1935</td>
</tr>
<tr>
<td>First MACE or HHF, n (%)</td>
<td>444 (22.9)</td>
<td>417 (21.6)</td>
</tr>
<tr>
<td>ACM</td>
<td>225 (11.6)</td>
<td>237 (12.2)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>86 (4.4)</td>
<td>81 (4.2)</td>
</tr>
<tr>
<td>Non-fatal stroke</td>
<td>26 (1.3)</td>
<td>17 (0.9)</td>
</tr>
<tr>
<td>Non-fatal HHF</td>
<td>107 (5.5)</td>
<td>82 (4.2)</td>
</tr>
<tr>
<td>First HHF alone, n (%)</td>
<td>140 (7.2)</td>
<td>115 (5.9)</td>
</tr>
<tr>
<td>First ACM or HHF, n (%)</td>
<td>393 (20.3)</td>
<td>368 (19.0)</td>
</tr>
<tr>
<td>ACM</td>
<td>253 (13.1)</td>
<td>253 (13.1)</td>
</tr>
<tr>
<td>No history of HF, N</td>
<td>1671</td>
<td>1679</td>
</tr>
<tr>
<td>First MACE or HHF, n (%)</td>
<td>331 (19.9)</td>
<td>334 (19.9)</td>
</tr>
<tr>
<td>First HHF alone, n (%)</td>
<td>86 (5.1)</td>
<td>81 (4.8)</td>
</tr>
<tr>
<td>ACM</td>
<td>289 (17.3)</td>
<td>292 (17.4)</td>
</tr>
<tr>
<td>ACM</td>
<td>203 (12.1)</td>
<td>211 (12.6)</td>
</tr>
<tr>
<td>All patients, N</td>
<td>113 (42.6)</td>
<td>83 (32.7)</td>
</tr>
<tr>
<td>History of HF, N</td>
<td>104 (39.2)</td>
<td>76 (29.9)</td>
</tr>
<tr>
<td>First MACE or HHF, n (%)</td>
<td>50 (18.9)</td>
<td>42 (16.5)</td>
</tr>
<tr>
<td>ACM</td>
<td>54 (20.4)</td>
<td>34 (13.4)</td>
</tr>
<tr>
<td>ACM</td>
<td>54 (20.4)</td>
<td>34 (13.4)</td>
</tr>
<tr>
<td>First MACE or HHF, n (%)</td>
<td>113 (42.6)</td>
<td>83 (32.7)</td>
</tr>
</tbody>
</table>

For ASCEND-ND, the median duration of follow-up for evaluation of CV events was 1.9 years (IQR=1.0 to 2.7), providing 7210 total PY of follow-up. For ASCEND-D, the median duration of follow-up for evaluation of CV events was 2.5 years (IQR=2.2 to 2.9), providing 7028 total PY of follow-up.

Egolovs, CVD, diastolic dysfunction, MI, comorbid disease, MI, MACCE, major adverse cardiovascular event.
#3974
EFFECTIVE PREDICTION OF NEED FOR CHRONIC DIALYSIS IN CHILDREN, BASED ON RANDOM FOREST ALGORITHMS USING BLOOD CELL COUNT-DRIVEN PARAMETERS

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Background and Aims: Persistent, low-grade inflammation is a significant component of chronic kidney disease (CKD) that plays a pivotal role in its pathophysiology, progression, complications, and all-cause mortality. Previous studies have searched for simple, cost-effective, and universally available markers useful in the systemic inflammation assessment in CKD patients. In the adult population, an increase in neutrophil count, correlated with a reduction in lymphocyte count, indicates the rate of progression to dialysis and predicts mortality in hemodialysis and peritoneal dialysis patients. Due to modulating role of platelets within the inflammatory pathways, a mean platelet volume (MPV) and platelet-to-lymphocyte ratio have also been proposed as markers of inflammation. The systemic immune inflammation index (SII) is a newly defined ratio combining neutrophil, lymphocyte, and platelet counts. It is proposed as a prognostic indicator comprehensively reflecting patients’ inflammatory and immune status. Recently, elevated SII has shown a predictive value for mortality risk among CKD adult patients. SII has not been evaluated in the pediatric CKD population so far.

Thus, the study aimed to analyze complete blood cell count (CBC) driven parameters, including SII, in children with CKD and to assess their potential usefulness in the prediction of the need for chronic replacement therapy with the use of artificial intelligence tools.

Method: The study group consisted of 27 predialysis children with CKD stages 4-5 (stage 4 - 11 patients, stage 5 - 16 children) and 40 patients on chronic dialysis (HD - 21 children, APD - 19 patients). The patients’ age ranged from 5 to 18 years, children under 5 were excluded due to the different CBC profile regarding neutrophil – lymphocyte proportions. The evaluated CBC parameters were: hemoglobin, hematocrit, leukocyte, neutrophil, monocyte, lymphocyte, platelet counts and MPV. Kidney function, standard biochemical parameters, CRP and SII were also analyzed. This database was used for further analysis. The recursively selected subsets of input variables constituted the input of random forest classifier (RFC). Each variant has been optimized, taking into account various features (accuracy, AUROC, precision, recall, MCC), then the best model was saved. The aim was to narrow the set of input parameters so that high predictive power is secured, whereas overfitting or overcomplicating could be avoided. Moreover, the GINI importance was measured in order to define the parameter with the largest share in the prediction.

Results: The best Random Forest Classifier contained neutrophil count, MPV, and SII as input variables, and achieved the following values: AUROC 0.9286, accuracy 93.75%, precision 0.9437, recall 0.9375 and MCC 0.87. The statistics for each class were as follows: precision 0.90, recall 1.00 and f1-score 0.95 for children with CKD 4-5 on conservative treatment; precision 1.0, recall 0.86, and f1-score 0.92 for patients on chronic dialysis. The values of mean GINI importance measured for 40 random splits of the base for MPV, neutrophil count and SII, were 0.28, 0.32 and 0.39, respectively.

Conclusion: RFC built up with the input variables of neutrophil count, MPV, and SII, was the best predictor of progression into pediatric end stage kidney disease requiring chronic dialysis. SII turned out the most important parameter...
#4914
LOW LEAN BODY TISSUE IS AN INDEPENDENT RISK FACTOR FOR KIDNEY DISEASE PROGRESSION AND MORTALITY IN PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE

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Background and Aims: Lean tissue mass is a marker of good health and is associated with a lower risk of death in patients without chronic kidney disease (CKD). A potentially underestimated risk factor for impaired renal function is low serum albumin concentration. Previous studies have shown that even small decreases in serum albumin concentration levels are strongly associated with cardiovascular disease, heart failure, impaired kidney function, and mortality in vulnerable populations. An association between low lean body tissue with mortality in patients with stage 4 and 5 CKD has recently been demonstrated. The aim of this study was to evaluate the effect of lean body tissue index (LTI) measured by multifrequency bioelectrical impedance analysis (BIA) on kidney disease progression and mortality in a cohort of patients with stage 4 and 5 CKD.

Method: We performed a retrospective observational cohort study that included patients with stage 4 and 5 CKD who were referred to the Advanced Chronic Kidney Disease outpatient clinic at our centre between January 2014 and December 2020, in whom a baseline measurement of body composition by using BIA was performed in the first 6 months of follow-up. Baseline clinical and laboratory parameters (serum creatinine, glomerular filtration rate, serum albumin, hemoglobin, cholesterol, triglycerides, calcium, phosphorus, PTH and CRP) were defined as those observed at the time of BIA measurement. Low lean tissue was defined as having LTI values below the 10th centile adjusted by age and sex. Renal survival was defined as the absence of need of renal replacement therapy (RRT) at the end of follow-up.

Results: The study included 145 patients who had a mean age of 72 ± 11.8 years, 69.7% were males, with a mean GFR measured by CKD-EPI of 20.4 ± 4.7 ml/min, mean albumin of 4.1 ± 0.3 g/dl and median urinal albumin-creatinine ratio (uACR) of 413 mg/g (IQR 98-1341). The mean body mass index of the population was 30.1 ± 6.1 kg/m², and BIA showed a mean LTI of 15.4 ± 3.9 kg/m² and fat tissue index (FTI) of 14.1 ± 6.8 kg/m². Nineteen patients (13.1%) had lower LTI. Patients with low LTI were younger (65.9 ± 11.4 years, p = 0.013) and had higher uACR (1444 [484-1815] vs 318 [68-1188] mg/g, p = 0.002) with no differences in sex, GFR, and other laboratory parameters. After a mean follow-up of 27.7 months (IQR 15.3-45.4), 72 (49.7%) showed CKD progression to RRT and 55 patients (37.9%) died. The Kaplan-Meier survival analysis showed that patients with low LTI had a worse renal survival (log-rank 5.5, p = 0.019) and overall survival (log-rank 7.6, p = 0.006).

The multivariable Cox regression analysis showed that low LTI (HR 2.28, 95% CI 1.12-4.62), lower GFR (HR 0.86, 95% CI 0.81-0.92) and higher uACR (HR 1.001, CI 95% 1.001-1.001) were independent risk factors for CKD progression to ESKD, while low LTI (HR 3.16, 95% CI 1.42-7.05), age (HR 1.09, CI 95% 1.05-1.13) and serum albumin (HR 0.31, CI 95% 0.13-0.77) were the factors that were independently associated with mortality.

Conclusion: Low lean body tissue index measured by multifrequency bioelectric impedance analysis is an independent risk factor for CKD progression and mortality in stage 4-5 CKD. Close monitoring of nutritional status by BIA should be followed in these patients to provide timely and adequate nutritional interventions that might help in improving patient outcomes.

#4918
IS THE KIDNEY FAILURE RISK EQUATION VALID IN PREDICTING END STAGE KIDNEY DISEASE IN ADULTS WITH GLOMERULONEPHRITIS?

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Background and Aims: The Kidney Failure Risk Equation (KFRE) is a clinical tool that predicts the 2- and 5-year risk of progression to end stage kidney disease (ESKD) in patients with chronic kidney disease (CKD) stages 3a-5. The equation’s accuracy and its predictive performance in subjects with glomerulopathies were not properly evaluated and validated. The current study examined the 4 variable KFRE in subjects with advanced CKD from glomerulopathy etiologies by evaluating discrimination and calibration at 2 and 5 years.

Method: This retrospective, single-center, cohort study included 558 subjects who were diagnosed by kidney biopsy with primary or secondary glomerulopathies between 1st January 2008 and 31st December 2016 and followed until 31st December 2021 for a mean follow-up time of 85.3 (95%CI 78.9 to 91.8) months. Patients with inadequate biopsy samples, histological findings other than glomerulopathy, those with missing data, and those with eGFR > 60 ml/min/1.73 m² were excluded. The 4-variable KFRE using eGFR, urinary albumin to creatinine ratio (uACR), age, and sex was calculated using the data from the first visit. The primary outcome of the study was the need for renal replacement therapy (RRT) initiation (dialysis or kidney transplant). The area under the receiver operator characteristic curve (AUC) and calibration plots were used to measure discrimination and calibration of the KFRE in specific glomerulopathy etiologies: IgA nephropathy, diabetic nephropathy, amyloidosis, endocapillary and crescentic glomerulonephritis, lupus nephritis, minimal change disease, membranous nephropathy, focal segmental glomerulosclerosis and membranoproliferative glomerulonephritis.

Results: In this cohort, most of the patients were males (57.7%) and the median age was 53 (95% CI 53 to 57) years. The median eGFR was 30.5 (95% CI 28 to 32.6) ml/min/1.73 m² and the median uACR 1932 (95% CI 1633 to 2200) mg/g. The most common glomerulopathies were IgA nephropathy (21.3%), diabetic nephropathy (15.4%), and membranoproliferative glomerulonephritis (9.5%). The median 2-year and 5-year KFRE score was 2.2 (95% CI 1.8 to 2.7) % and 18.9 (95% CI 17.8 to 19.7) % respectively. During the first 2 years of follow-up 154 (27.5%) subjects needed RRT and 93 (16.6%) subjects died, while 218 (39%) started RRT and 108 (19.3%) died within 5 years from the kidney biopsy. The 4-variable KFRE provided good discrimination in the whole cohort with an AUC of 0.728 (95% CI 0.686-0.770) for predicting ESRD at 2-years and 0.725 (95% CI 0.686-0.767) at 5 years (figure 1A). There was also a good to excellent discrimination of 2-years and 5-years KFRE across all glomerulopathy etiologies, with statistically significant p-values (p<0.05), with the exception of diabetic nephropathy and endocapillary GN which had a non-significant AUC (Figure 2). Calibration plots were adequate both overall and across glomerulopathy etiologies; however, the predicted risks for kidney failure were overstated across CKD etiologies, especially in those with low to moderate risk in the 2-years model. Notably the...
calibration plot for the 5-years KFRE showed that the predicted risk was near the observed risk across all glomerulopathies (Figure 1B).

**Conclusion:** The 4 variable-KFRE seems to be a good predictive tool in patients with glomerulopathies both for 2 and 5-years, except for diabetic nephropathy and endocapillary glomerulonephritis.

#3781

**INSULIN RESISTANCE IS ASSOCIATED WITH INCIDENT CHRONIC KIDNEY DISEASE IN POPULATION WITH NORMAL RENAL FUNCTION**

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\(^1\)Gwangju, Rep. of South Korea and \(^2\)Ansan, Rep. of South Korea

**Background and Aims:** Insulin resistance is prevalent in chronic kidney disease (CKD) and may accelerate its progression. This study aimed to investigate whether insulin resistance was associated with the development of incident CKD in a population with normal renal function.

**Method:** A total of 3,331 individuals with normal renal function from a community-based cohort formed the study population. We determined the relationship between insulin resistance indices and incident CKD using Cox proportional hazard model and Kaplan-Meier survival analysis.

**Results:** During a mean follow-up of 11.03 ± 4.22 years, incident CKD occurred in 414 (12.4%) participants. The high homeostasis model assessment-insulin resistance (HOMA-IR) level group had an increased risk of incident CKD (HR, 1.40; 95% CI, 1.13-1.74; \(p = 0.002\)) compared to the normal group after adjusting for confounding factors. The risk of incident CKD also increased with lower quantitative insulin sensitivity check index (QUICKI) levels (HR, 0.62; 95% CI, 0.41-0.92; \(p = 0.018\)) and higher leptin-adiponectin ratio (LAR) levels (HR, 1.23; 95% CI, 1.06-1.42; \(p = 0.006\)).

**Conclusion:** Higher insulin resistance indices were associated with the incidence of CKD. Our data suggests that increased insulin resistance may be involved in the development of incident CKD in individuals with normal renal function.
Figure 1: Kaplan-Meier free-CKD probability curve with the log-rank test between high HOMA-IR group and incident CKD. High group is associated with poor free-CKD probability compared to normal group.

Abbreviations: CKD, chronic kidney disease; HOMA-IR, homeostasis model assessment-insulin resistance.

Figure 2: Restricted cubic spline curve of hazard ratio of HOMA-IR level for incident CKD probability. The HOMA-IR level exhibited a positive correlation with incident CKD risk.

Abbreviations: CKD, chronic kidney disease; HOMA-IR, homeostasis model assessment-insulin resistance.

#4519
CAN WE REPLACE URINE TESTING AND DELIVER A STEP CHANGE IN ACCESS TO RENOPROTECTIVE MEDICATIONS?

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Background and Aims: Albuminuria is a medical condition characterized by leakage of albumin into the urine due to kidney damage. The condition is diagnosed by heightened Albumin to Creatinine ratio in the urine (ACR) and is typically categorized into microalbuminuria (ACR ≥ 30, < 300 mg/g mg/g) and macroalbuminuria (ACR ≥ 300 mg/g). Currently, despite compelling data, only a minority of patients with diabetes, and rarely individuals without diabetes, are screened for albuminuria in a systematic way. ACR tests also present high intra-person variability, making it harder to identify meaningful biologic changes and increasing complexity of clinical trials. In this study we develop a method using machine learning to predict ACR level from Electronic Health Records, excluding urine tests, and validated the model for identifying patients with albuminuria. Identifying patients with undiagnosed
albuminuria could help slow progression of kidney disease and be used to speed up recruitment to, and reduce screen failures in, clinical trials.

**Method:** We developed a Quantile Regression model for ACR using US Limited IBM MarketScan Explorys Claims-EMR Data Set (LCED). We included subjects who had an ACR test (0 < ACR ≤ 5000 mg/g) and was of at least 18 years of age. Patient demographics (age, sex), vital signs (BMI, Blood Pressure) and 8 common blood tests (Albumin, Bilirubin, Creatinine, HbA1C, Triglyceride, Glucose, White Blood Cell count & ALT) were used as covariates. A tree based gradient boosting framework (LightGBM) was used to train the quantile regression models, viz., the 25-, 50-, and 75-percentiles of ACR conditioned on the covariates. The model was then validated on all qualified subjects in Optum’s de-identified Clininformatics® Data Mart Database (2007-2021). We evaluated performance using the metrics Area Under the Curve (AUC), precision (PPV), specificity (TNR), and sensitivity (TPR). Finally, we use Kaplan-Meier estimates to compare the risk of progression to kidney failure as identified by ICD codes (Chronic kidney disease, stage 5; End stage renal disease; Dependence on renal dialysis; Unspecified kidney failure; Kidney transplant) of both the predicted and measured ACR values.

**Results:** A final cohort of 63,459 individuals matched the inclusion and exclusion criteria in LCED and 5,857,385 individuals in Optum. Using the 25% quantile to predict patients at risk, the model consistently reaches a PPV greater than 0.8 and a specificity (TNR) greater than 0.99 (Table 1). The risk of progression to kidney failure increases with both increased predicted and measured ACR (Figure 1).

**Conclusion:** The results show that the models have discriminative power in all datasets. It predicts both micro- and macro-albuminuria with a PPV above 80% for the 25-quantile. However, classification performance is lacking in sensitivity, i.e., subjects suffering from albuminuria may not be classified as such. By using the median prediction of ACR we identify patient subpopulations that have a risk of kidney failure at least on par with the true ACR subpopulation targeted. This means that the method can be used confidently to identify at-risk individuals. Therefore, our model is advantageous in applications such as identifying undiagnosed albuminuria and pre-screening for clinical trials, where high PPV is more important than sensitivity. We intend to validate the model further for outcomes prediction in an upcoming CKD trial.

**Table 1:** Classification performance on datasets with three different quantile predictors.

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Classification</th>
<th>Quantile</th>
<th>AUC (%)</th>
<th>PPV (%)</th>
<th>TNR (%)</th>
<th>TPR (%)</th>
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ASSOCIATION OF SERUM 25-HYDROXYVITAMIN D WITH ALL-CAUSE MORTALITY AND KIDNEY OUTCOME IN PATIENTS WITH EARLY STAGES OF CKD
Lin Yuxin, Yuping Zhang, Sheng Nie and Xu Xin
P.R. China

Background and Aims: Although serum 25-hydroxyvitamin D (25(OH)D) deficiency is prevalent in all stages of chronic kidney disease (CKD), the effects of 25(OH)D deficiency on all-cause mortality and kidney outcomes in patients with early-stage CKD remain incompletely understood.

Method: This nationwide retrospective cohort study included 9840 adults with stages 1–3 CKD from 19 medical centers across China. The study outcomes included all-cause mortality, cardiovascular mortality, and kidney disease progression. The associations between serum 25(OH)D concentrations and the risks of mortality and CKD progression were evaluated using a Cox proportional hazard model. A mixed-effects model was used to estimate the slopes of estimated glomerular filtration rate (eGFR).

Results: Of 9840 adults with stages 1–3 CKD, 26.9% had severe (<10 ng/ml) and 38.7% had moderate (10–20 ng/ml) serum 25(OH)D deficiency. Compared with patients having 25(OH)D >20 ng/ml, patients with serum 25(OH)D <10 ng/ml were at significantly higher risks of all-cause mortality (hazard ratio [HR] 1.87, 95% confidence interval [CI] 1.53–2.28), cardiovascular mortality (HR 1.80, 95% CI 1.33–2.44), and CKD progression (HR 2.28, 95% CI 1.74–2.99), and had a steeper decline in eGFR slope (estimate -0.07; 95% CI -0.10 to -0.05 mL/min/1.73 m² per year). Similar results were obtained in subgroups and by sensitivity analyses.

Conclusion: 25(OH)D deficiency is associated with increased risks of all-cause mortality and CKD progression in patients with early-stage CKD. Studies are needed to determine whether early intervention for 25(OH)D deficiency could improve the prognosis of patients with early-stage CKD.

Figure 1: Associations of baseline 25(OH)D concentrations with (A) all-cause mortality and (B) CKD progression. Model of all-cause death adjusted for Age group, gender, Charlson score, department, hospitals, RAAS inhibitors, vitamin D supplements, calcium channel blockers, glucocorticoids, diabetes agents, chemotherapeutic drugs, statins, eGFR, coronary heart disease, cerebrovascular disease, myocardial infarction, osteoporosis, cirrhosis, peripheral vascular disease, diabetes, heart failure, malignant tumor, hypertension; Model of CKD progression additional adjusted for immunosuppressant, alkaline phosphatase, potassium, triglyceride, uric acid, proteinuria, acute coronary syndrome.

Table 1: Associations of serum 25(OH)D concentrations with all-cause mortality and CKD progression.

<table>
<thead>
<tr>
<th></th>
<th>Crude model</th>
<th>Adjusted model*</th>
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<tr>
<td>Serum 25(OH)D, ng/mL</td>
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<tr>
<td>All-cause mortality</td>
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<td>Continuous, per SD decrease Category</td>
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<td>≥20</td>
<td>2147</td>
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<tr>
<td>10 to 20</td>
<td>3097</td>
<td>271(8.8)</td>
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<tr>
<td>&lt;10</td>
<td>2183</td>
<td>288(15.2)</td>
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<tr>
<td>P for trend</td>
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<td>CKD progress</td>
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<tr>
<td>10 to 20</td>
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<td>214(12.2)</td>
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<tr>
<td>&lt;10</td>
<td>1388</td>
<td>271(19.5)</td>
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<td>P for trend</td>
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</table>

Abbreviations: 25(OH)D: 25-hydroxyvitamin D; CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval; Ref, reference.

* Model of all-cause death adjusted for Age group, gender, Charlson score, department, hospitals, RAAS inhibitors, vitamin D supplements, calcium channel blockers, glucocorticoids, diabetes agents, chemotherapeutic drugs, statins, eGFR, coronary heart disease, cerebrovascular disease, myocardial infarction, osteoporosis, cirrhosis, peripheral vascular disease, diabetes, heart failure, malignant tumor, hypertension; Model of CKD progression additional adjusted for immunosuppressant, alkaline phosphatase, potassium, triglyceride, uric acid, proteinuria, acute coronary syndrome.
REDUCED TUBULAR MIR-190A-5P: A NOVEL BIOMARKER FOR STRATIFICATION OF PATIENTS WITH CHRONIC KIDNEY DISEASE

David Baird1, Jinnan Zang2, Ryan Wong3, Katie Connor4, Carolyn Cairns5, Maximilian Reck1, Jeremy Hughes1, Patrick Mark3, Alexander Peter Maxwell2, Gareth McKay2, David Simpson2, Laura Denby4 and Bryan Conway4

1University of Edinburgh, United Kingdom, 2Queen’s University Belfast, United Kingdom and 3University of Glasgow, United Kingdom

Background and Aims: Circulating microRNA (miRNAs) have been proposed as potential diagnostic and prognostic biomarkers and are functionally important in disease pathogenesis. In this study, we used an unbiased measurement of circulating miRNAs in patients with type 2 diabetes to identify a miRNA differentially expressed in kidney disease before moving to a larger, unselected cohort of patients with CKD to assess its potential to predict progression in CKD.

Method: MiRNA next generation sequencing (NGS) studies were undertaken to measure differential expression of plasma miRNAs in a discovery cohort of 3 groups; individuals with type 2 diabetic kidney disease (T2DKD, n = 9), age and sex matched patients with type 2 diabetes mellitus and normal renal function (T2DNRF, n = 13) and patients without diabetes and with normal renal function (NDNRF, n = 11). Differentially expressed miRs were validated in a separate cohort of the same groups (each n = 10). The prognostic value of miR-190a-5p in a general CKD population was assessed using the seNSOR cohort (n = 395, excluding patients on RRT, with an eGFR < 20 ml/min/1.73 m² or AKI at recruitment). The primary outcome of CKD progression was defined as reaching ESKD (starting RRT or maintaining an eGFR < 15mls/min) or >30% reduction in renal function from eGFR at baseline. Reaching ESKD alone was used as a secondary outcome.

Results: MiR-190a-5p was the only miRNA differentially expressed between T2DKD and both control groups in both the discovery and validation cohorts. In the seNSOR cohort, miR-190a-5p levels correlated positively with eGFR (rho = 0.12, p = 0.04) and inversely with age (rho = -0.12, p = 0.04). MiR-190a-5p levels below the median predicted CKD progression in individuals with minimal and moderate albuminuria (ACR < 3mg/mmol and 3-300mg/mmol respectively) but not in those with severe albuminuria (ACR>300mg/mmol, see figure). In those without severe albuminuria, miR-190a-5p levels predicted CKD progression in multivariate Cox proportional hazards models (HR 0.8, 95% CI: 0.66-0.96, p = 0.015), independently of baseline eGFR, ACR, age, SBP, DBP and sex. When participants with an ACR > 300mg/mmol were included, miR-190a-5p was not predictive of the composite CKD progression endpoint (multivariate HR 0.86, p = 0.064) but was predictive for reaching ESKD alone (multivariate HR 0.68, 95% CI: 0.5-0.93, p = 0.015). Analysis of miR-190 expression in individual renal cell types in the reversible unilateral ureter obstruction mouse model revealed that it is enriched in proximal tubule cells and falls significantly following injury before increasing again the repair phase.

Conclusion: miR-190a-5p is expressed by healthy proximal renal tubular cells and serum miR-190a-5p levels correlate positively with eGFR. Low serum miR-190a-5p levels may predict progression of CKD in patients with low or moderate proteinuria independently of existing risk factors.
#3386
PROTON-PUMP INHIBITORS AND SERUM CONCENTRATIONS OF UREMIC TOXINS IN PATIENTS WITH CHRONIC KIDNEY DISEASE
Carolina El Chamiñel1, Islam Amine Larabi1, Solene Laville1,4, Christian Jacquelinet1,5, Christian Combe6,7, Denis Fouque8,9, Quentin Villejuif, France, 2Department of Pharmacology and Toxicology, Inserm U1173, UFR Medicine Ville Saint André, University Paris-Saclay, Paris, France, 3Raymond Poincaré Hospital, AP-HP, Garches, France, 4MP3CV Laboratory, Jules Verne University of Picardie, Amiens, France, 5Biomedecine Agency, Saint Denis La Plaine, France, 6Service de Néphrologie Transplantation Dialyse Apherèse, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France, 7INSERM, U1062, Univ Bordeaux Segalen, Bordeaux, France, 8Pharmacoepidemiology Unit, Department of Clinical Pharmacology, Amiens-Picardie University Medical Center, Amiens, France, 9MP3CV Laboratory, Jules Verne University of Picardie, Amiens, France, 10Biomedecine Agency, Saint Denis La Plaine, France, 11Service de Néphrologie Transplantation Dialyse Apherèse, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France, 12INSERM, U1062, Univ Bordeaux Segalen, Bordeaux, France, 13Nephrology Dept, Centre Hospitalier Lyon Sud, Université de Lyon, Carmen, Pierre-Bénite, France, 14University of Lyon, CarMeNN INSERM 1060, France, 15Nephrology Department, CHRU de Nancy, Vandouvre-lès-Nancy, France, 16Lorraine University, APEMAC, France, 17United States of America and 18Department of Nephrology, Ambroise Paré University Hospital, APHP, Boulogne-Billancourt, France

Background and Aims: Use of proton-pump inhibitors (PPIs) is common in patients with chronic kidney disease (CKD). PPIs and many uremic toxins (UTs) are eliminated by a kidney tubular organic anion transporter system. In a cross-sectional study, we sought to evaluate the association between PPI prescription and serum concentrations of various UTs.

Method: We studied a randomly selected subgroup of participants in the CKD-REIN prospective cohort (adult patients with a confirmed diagnosis of CKD and estimated glomerular filtration rate (eGFR) <60mL/min/1.73m2) with available frozen samples collected at baseline. PPI prescription was recorded at baseline. Serum concentrations of 10 UTs were measured using a validated liquid chromatography tandem mass spectrometry technique. Multiple linear regression was performed, with the log UT concentration as the dependent variable.

Results: Of the 680 included patients [median age: 68 years; median eGFR: 32 mL/min/1.73 m²], 31% had PPI prescriptions at baseline. Patients using PPIs had higher levels of certain UTs in comparison to other patients, including total and free indoxyl sulfate (IS), total and free p-cresylsulfate, total and free p-cresylsulfonate (PCG), phenylacetylglycine (PAG), free kynurenine, and free hippuric acid. After adjustment for baseline comorbidities, number of co-prescribed drugs and laboratory data including eGFR, associations between PPI prescription and elevated serum concentrations of free and total IS, free and total PCG, and PAG remained significant.

Conclusion: Our results indicate that PPI prescription is independently associated with serum UT retention. These findings indicate a potential mechanism for side effect of PPIs in CKD patients that will need to be confirmed by longitudinal studies.

#5331
MOLECULAR IMAGING OF PDGFR-ß IN KIDNEY FIBROSIS
Barbara Mara Klinkhammer1, Diana Mocek1, Maike Wagner2, Fabian Kiessling2, Twan Lammers2 and Peter Boor1
1RWTH Aachen University Hospital, Institute of Pathology, Aachen, Germany and 2RWTH Aachen University Hospital, Institute for Experimental Molecular Imaging, Aachen, Germany

Background and Aims: Chronic kidney disease affects >10% of the world’s population and is associated with high mortality and morbidity. The best predictor of CKD progression is the extent of fibrosis, e.g., pathological deposition of extracellular matrix (ECM) and loss of functional kidney parenchyma. Currently, there are no specific treatment options and invasive biopsies remain the gold standard for diagnosis. Multiple signaling pathways are involved in fibrosis, including platelet-derived growth factor (PDGF) signaling. Mesenchymal stromal cells express both PDGF receptors PDGFR-α and PDGFR-ß, whose activation drives proliferation, migration and production of extracellular matrix, i.e., key processes involved in fibrosis initiation and progression. Based on these notions, we set out to study the bicyclic PDGFR-ß-binding peptide (BiPPB) for diagnosis, quantitative imaging and treatment monitoring of kidney fibrosis.

Method: The biodistribution and kidney accumulation of Cy7-labeled BiPPB and a scrambled peptide control were visualized and quantified using in vivo computed tomography - fluorescence molecular tomography (CT-FMT), ex vivo fluorescence reflectance imaging (FRI) and microscopy. This was done in three different mouse models of kidney fibrosis: the unilateral ischemia-reperfusion injury (I/R), the adenine-induced nephropathy (Adenine) and a transgenic model with constitutive PDGFR-ß activation specifically in renal mesenchymal cells leading to increased PDGFR-ß expression and expansion of PDGFR-ß+ cells (Mutant). In the latter model, we also monitored pharmacological PDGFR-ß inhibition with imatinib. Kidney fibrosis and therapeutic efficacy findings were verified by immunochemistry (IHC).

Results: In vivo 3D CT-FMT imaging and ex vivo 2D FRI showed strong accumulation in fibrotic kidneys for Cy7-labeled BiPPB, whereas only moderate amounts accumulated in the contralateral (I/R) and healthy (Adenine) kidney over 48 hours after i.v. injection. The accumulation of the scrambled BiPPB was also significantly lower compared to the specific BiPPB. In transgenic Mutant mice with specific activation of mesenchymal cells and primary renal scaring significantly more Cy7-BiPPB accumulated in the kidneys in comparison to healthy wildtype littermates. In combination with imatinib treatment for three weeks (Mutant imatinib) the accumulation of Cy7-BiPPB was decreased (Fig. 1a-c). This was confirmed ex vivo by significantly increased probe accumulation (2D FRI; Fig. 1d) and PDGFR-ß for development of microalbuminuria, randomized to either spironolactone 25 mg per day or placebo. Crude and adjusted Cox models were applied to investigate the association between baseline biomarker levels and development of the primary outcome, persistent microalbuminuria, and development of microalbuminuria in at least one morning void sample, used as a secondary outcome.

Results: In the PRIORITY trial, spironolactone treatment did not prevent progression to microalbuminuria compared to placebo. All biomarkers were measured in 154 participants at baseline and 117 at end-of-study (week 208). Treatment with spironolactone did not affect serum levels of any of the investigated collagen remodeling biomarkers compared to placebo, and there were no differences in delta-biomarker levels between baseline and end-of-study (p ranging 0.277-0.875). In crude analyses, serum endotrophin was associated with both the primary (n = 44) and secondary outcome (n = 74) for a two-fold higher level: 1.58, 95% CI 1.03-2.44, p = 0.037 and 1.62, 1.12-2.35, p = 0.010), whereas serum PRO-C3 was only associated with the secondary outcome (1.89, 1.19-2.99, p = 0.007). After adjustment for sex, baseline age, systolic blood pressure, estimated glomerular filtration rate, urinary albumin-creatinine ratio, and HbA1c, serum endotrophin and PRO-C3 remained significantly associated with the secondary outcome (1.52, 1.03-2.24, p = 0.036 and 1.73, 1.08-2.78, p = 0.022). Levels of PRO-C7, PRO-C8 and CTX-III were not associated with the specified outcomes. Neither baseline levels of serum endotrophin nor PRO-C3 correlated with baseline CKD273 levels (R: 0.00-0.06, p>0.47).

Conclusion: Treatment with spironolactone did not change serum levels of collagen remodeling biomarkers. Serum endotrophin, reflecting collagen type VI formation and the pro-fibrotic molecule endotrophin, and PRO-C3, a biomarker of collagen type III fibrosis, were associated with development of microalbuminuria in at least one urine sample, suggesting that these biomarkers are relevant risk markers for kidney disease development in type 2 diabetes.

#5482
CIRCULATING BIOMARKERS OF COLLAGEN REMODELING AS MARKERS FOR DEVELOPMENT OF MICROALBUMINURIA IN TYPE 2 DIABETES: THE PRIORITY TRIAL
Alexandra Louise Moller1,2, Viktor Rotbas Curovic3, Daniel G. K. Rasmussen1, Federica Genoveze1, Morten A. Karsdal6,7, Tine Hansen1,3 and Peter Rossing1,4
1Nordic Bioscience A/S, Herlev, Denmark, 2Copenhagen University, Department of Biomedical Sciences, Faculty of Health and Medical Sciences, Copenhagen, Denmark, 3Copenhagen Diabetes Center, Copenhagen, Herlev, Denmark and 4Copenhagen University, Department of Clinical Medicine, Faculty of Health and Medical Sciences, Copenhagen, Denmark

Background and Aims: Kidney disease progression is characterized by extensive deposition of extracellular matrix components such as collagen. Therefore, we assessed the effect of spironolactone on collagen remodeling biomarkers and investigated the association between the markers and development of microalbuminuria in serum of persons with type 2 diabetes and normoalbuminuria.

Method: We measured collagen type III (PRO-C3), VI (PRO-C6; endotrophin), VII (PRO-C7), and XVIII (PRO-C28) formation, and a fragment of degraded crosslinked collagen type III (CTX-III) in serum of persons with high-risk (stratified by a urinary proteomics classifier, CKD273)
expression (immunohistochemistry (IHC) Fig. 1e) in fibrotic kidneys, which was diminished by imatinib treatment.

**Conclusion:** Our findings demonstrate the potential of PDGFR-β-based imaging agents for non-invasive and quantitative monitoring of renal fibrosis progression and therapy response.

**Figure 1:** Imaging biomarker and mouse models for diagnosis and staging of kidney fibrosis with molecular imaging of PDGFR-β using BiPPB. a) Examples of biodistribution of Cy7-BiPPB in a transgenic model with PDGFR-β overexpression (Mutant), with imatinib treatment (Mutant Imatinib) or wildtype littermate (WT) quantified by hybrid CT-FMT. The results of the 3D CT-FMT quantification for Cy7-BiPPB in kidneys are shown as bar at 24h (b) and 48h (c) post injection presented as percentage of the injected dose per gram (%ID/g). d) Example 2D FRI of one mouse per group are shown 48h p.i. for all organs (L = Liver; Lu = Lungs; S = Spleen; P = Pancreas; A = Aorta; H = Heart; K = Kidneys; SK = Skin; B = Bone; M = Muscle; I = Intestine; St = Stomach). e) Representative pictures from immunohistochemical stains of PDGFR-β, Collagen III and F4/80 in WT, Mutant, and Mutant Imatinib mice. Bar graph = 50 μm.

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**DISCOVERY AND VALIDATION OF NOVEL RENAL EPITHELIAL SENECESSCE ASSOCIATED BIOMARKERS**

**David Baird**1, **Maximilian Reck**1, **Ross Campbell**1, **Eoin O'Sullivan**1, **Marie-Helena Docherty**1, **Carolyn Cairns**1, **Cyril Carvalho**1, **Matthieu Vermeren**1, **Jeremy Hughes**1, **Patrick Mark**2, **Laura Denby**1, **Bryan Conway**1, **Katie Mylonas**1 and **David Ferencbach**1

1University of Edinburgh, United Kingdom and 2University of Glasgow, United Kingdom

**Background and Aims:** Cellular senescence is characterised by irreversible cell cycle arrest and marked changes in transcriptional and secretory activity. It can occur as a physiological component of healthy organismal development or in response to a range of cellular insults including DNA damage, oncogenic mutations and metabolic stress. Renal tubular senescence in response to ageing and injury is proposed as a driver of kidney fibrosis. Senescent cell depletion in mice improves outcomes in multiple organs including the kidney. There are currently no non-invasive biomarkers for quantifying renal senescence available. We are using a multi-omics approach and utilising human renal proximal tubular epithelial cells (hRPTECs) in culture, a murine model of renal senescence and human samples, to identify urinary biomarkers of renal tubular senescence and to determine if they can predict decline in kidney function.

**Method:** In vitro: We modelled a human senescent cell line (RPE-1) in hRPTECs. Senescence was induced in RPE-1 using the inhibitor of Akt N17429. Senescent cells were identified by CDKN1A and reduced LMNB1 and MKI67 in keeping with senescence induction. Other transcripts including CXCL8 and IL6 rose in irradiated cells.

**Results:** Irradiated and Nutlin 3A treated cells had increased mRNA levels of CDKN1A and reduced LMNB1 and MKI67 in keeping with senescence induction. Other transcripts including CXCL8 and IL6 rose in irradiated cells compared to controls. 1272 genes were differentially expressed in the same direction in Nutlin 3A treated cells compared to controls but fell in Nutlin 3A treated cells. The results of the 3D CT-FMT quantification for Cy7-BiPPB in kidneys are shown as bar at 24h (b) and 48h (c) post injection presented as percentage of the injected dose per gram (%ID/g). d) Example 2D FRI of one mouse per group are shown 48h p.i. for all organs (L = Liver; Lu = Lungs; S = Spleen; P = Pancreas; A = Aorta; H = Heart; K = Kidneys; SK = Skin; B = Bone; M = Muscle; I = Intestine; St = Stomach). e) Representative pictures from immunohistochemical stains of PDGFR-β, Collagen III and F4/80 in WT, Mutant, and Mutant Imatinib mice. Bar graph = 50 μm.
IONIZED MAGNESIUM LEVELS IN PATIENTS WITH MODERATE-TO-ADVANCED CHRONIC KIDNEY DISEASE: RELATIONSHIP WITH TOTAL MAGNESIUM AND ASSOCIATED FACTORS

Maxime Pluquet1, Solene Laville1,2, Céline Lange1,4, Aghiles Hamroun5, Maurice Laville1,2, Luc Frimat6,9, Edith Bigot-Corbel10, Natalia Alencar de Pinho4, Said Kamel1,11 and Sophie Liabeuf1,2

1University of Picardie Jules Verne, MP3CV Laboratory, Amiens, France, 2Amiens University Hospital, Division of Clinical Pharmacology, Amiens, France, 3Biomedicine Agency, Saint-Denis, France, 4Paris-Saclay University, Versailles Saint Quentin University, Centre for Research in Epidemiology and Population Health (CESP), INSERM UMRS 1018, Villejuif, France, 5Centre Hospitalier Régional Universitaire de Lille, Nephrology Department, Lille, France, 6Lyon University, CarMeN, INSERM U1060, Pierre-Bénite, France, 7Lyon Sud Hospital, Nephrology Department, Pierre-Bénite, France, 8Lorraine University, APEMAC, Vandœuvre-lès-Nancy, France, 9Centre Hospitalier Régional Universitaire de Nancy, Nephrology Department, Vandœuvre-lès-Nancy, France, 10Nantes University Hospital, Laboratoire de Biochimie HGRL, Saint-Herblain, France and 11Amiens University Hospital, Department of Biochemistry, Amiens, France

Background and Aims: Magnesium (Mg) is involved in a multitude of essential physiological processes. In chronic kidney disease (CKD), the mechanisms compensating for the decrease in glomerular filtration rate (eGFR) become insufficient and Mg excretion tends to decrease, potentially resulting in hypermagnesemia. On the other hand, hypomagnesemia seems also to be common in CKD, due to changes in Mg intake through diet, reduced absorption and drug-induced hypomagnesemia. To date, a few studies have shown an association between increased cardiovascular risk in CKD and either low or high total Mg levels. However, the physiologically active fraction of extracellular Mg is ionized Mg (iMg), which is not routinely measured. In critical ill patients, the correlation between iMg and total Mg has been shown to be poor. Similar data on patients with CKD would be important to future studies aiming at clarifying the link between Mg and outcomes, and ultimately to determine the interest of iMg assay in routine practice. The objectives of this study are i) to study the correlation between total Mg and iMg and ii) to evaluate the relation between serum ionized magnesium, estimated GFR (eGFR) and demographic and biologic parameters.

Method: CKD-REIN is a French, prospective, nationally representative cohort study of 3033 CKD patients under nephrology care not receiving maintenance dialysis (stage 3-5: eGFR<60 mL/min/1.73 m² based on 2009 CKD-EPI equation). Baseline iMg and total Mg serum concentrations were respectively centrally measured using the NOVA BIOMEDICAL Stat Profile PRIME ES analyser and with Atellica® CH SIEMENS analyser. Normal range of serum total Mg considered was 0.66 to 1.06 mmol/L (from Atellica®). Mean ± standard deviation (SD) ionized Mg level evaluated in a cohort of 457 healthy volunteers (age = 45 ± 17 years; eGFR = 72.3 ± 13 mL/min/1.73 m²) was 0.49 ± 0.05 mmol/L (median [tertile 1 – tertile 3] = 0.49 [0.45-0.52] mmol/L).

Correlation between iMg and total Mg was very high (r = 0.88; p<0.001). (Figure). Ionized Mg was weakly inversely correlated with eGFR (r = -0.22; p<0.001). Consequently, the mean iMg level differed according to CKD stages, being more elevated in the advanced stages (0.65 mmol/L in stages 2-3A; 0.47 mmol/L in stage 3B; 0.50 mmol/L in stages 4-5 (p<0.001)). In a fully adjusted linear regression model, iMg concentration was significantly associated with age, decline of eGFR, history of cardiovascular disease and the use of diuretics, and inversely associated with calcium and triglycerides levels, systolic blood pressure, diabetes, and the use of proton pump inhibitors and potassium chelators. The same factors were associated with total Mg.

Conclusion: Total Mg and iMg were strongly correlated. Decline of kidney function was associated to an increase of iMg in patients with moderate-to-advanced CKD. Additional studies need to compare the difference between total Mg and iMg as a biomarker to predict hard outcomes.
LONG-TERM LONGITUDINAL CHANGES OF PULSE WAVE VELOCITY AND THEIR ASSOCIATION TO CARDIOVASCULAR RISK FACTORS IN MAINTENANCE HEMODIALYSIS PATIENTS

Moritz Lattermann1, Julia Matschkal1, Matthias Braunisch1, Siegfried Wassertheurer2, Christopher Mayer2, Roman Guenthner1, Uwe Heemann1 and Christoph Schmaderer1

1Klinikum rechts der Isar der Technischen Universität München, Nephrology, München, Germany and 2AIT Austrian Institute of Technology GmbH, Wien, Austria

Background and Aims: The incidence of end-stage renal disease (ESRD) is increasing worldwide. The mortality rate in this patient cohort remains unacceptably high. The WHO estimates ESRD as one of the ten global causes of premature death. Approximately half of all death cases are due to cardiovascular complications. A main cardiovascular risk factor is enhanced arterial stiffness. The measurement of pulse wave velocity (PWV) for evaluation of progressive atherosclerosis is known to be an independent risk predictor for cardiovascular and all-cause mortality in chronic dialysis patients.

Method: The study cohort contains patients from the “Risk stratification in end-stage renal disease - the ISAR study”, a multicenter prospective longitudinal observational cohort study. A total of 105 patients on maintenance hemodialysis were examined and followed-up for up to 72 months. Pulse wave velocity was obtained by the Mobil-O-Graph 24h PWA Monitor device at baseline and follow-up. We assessed the PWV change over time and correlated PWV with known cardiovascular risk factors using Pearson correlation coefficient adjusting for age. Longitudinal changes were examined using t-tests for paired and independent samples.

Results: Patients had a median age of 61.2 years (IQR 23.2), 36 (34%) were female. Median baseline dialysis vintage was 105 months (IQR 71), and median adapted Charlson Comorbidity Index 2 (IQR 3). During a median follow-up of 74.1 months there was a significant increase in PWV from baseline (9.25 m/s) to 6YFU (10.18 m/s, \( p < 0.001 \)), a delta-PWV of 0.92 m/s, appropriate to a yearly change of 0.15 m/s. Patients with hypertension had a significant higher PWV (10.47 m/s) than those with normal blood pressure (8.91 m/s, \( p = 0.034 \)). The Pearson correlation coefficient analysis showed after adjustment for age a significant correlation between blood pressure and both 6YFU-PWV (systolic \( r = 0.89 \), diastolic \( r = 0.62 \), \( p < 0.001 \)) and delta-PWV (systolic \( r = 0.71 \), diastolic \( r = 0.48 \), \( p < 0.001 \)). Additionally, after adjustment for age delta-PWV correlated with LDL-cholesterol (\( r = 0.27 \), \( p = 0.023 \)). Neither 6YFU-PWV nor delta-PWV showed significant associations to other traditional cardiovascular risk factors such as diabetes, high cholesterol or obesity.

Conclusion: In this cohort, we found a longitudinal increase of pulse wave velocity over 6 years. However, the average change in PWV per year was significantly lower in our cohort compared to other studies with a shorter observation period. A main reason might be the long follow-up time, with the occurrence of several deaths in the primary cohort of the ISAR-Study before reaching the follow-up point and therefore including more younger and possibly healthier patients. Nevertheless, in this cohort blood pressure in contrast to diabetes, high cholesterol or obesity was a primary factor in the change of PWV. The reasons for the deceleration of cardiovascular and mortality risk after a long term in this sub cohort remains unclear and requires further investigation.
#5662
PRELIMINARY RESULTS FROM iBEAT ANCILLARY-STUDY: A NOVEL CLASSIFICATION OF RENAL DAMAGE IN DIABETES
Paola Pontrelli1, Michele Rossini1, Francesca Conserva1, Francesco Pescio2, Teodora Ardillo1, Marco Moschetta1, Francesco Giorgino1, Luigi Laviola1, Steven Sourbron2, Kim Gooding1, Maria Gomez4, Matthias Kretzler3 and Loreto Gusolali1
1University of Bari Aldo Moro, Italy, 2University of Sheffield, United Kingdom, 3University of Exeter Medical School, United Kingdom, 4Lund University Diabetes Centre, Sweden and 5University of Michigan, United States
Background and Aims: Renal damage in diabetes can manifest as real diabetic glomerulosclerosis (DN) or non-diabetic renal disease (NDRD). DN and NDRD differ in terms of prognosis and treatment thus kidney biopsies remains the gold standard. The iBEAT study conducted within the frame of IMI project BEAT-DKD (https://www.beat-dkd.eu/; GA No 115974) aims to determine whether renal imaging biomarkers capture by magnetic resonance (MRI) and ultrasound (US) can detect DKD heterogeneity. This ancillary sub-study in iBEAT aims to explore correlations between imaging biomarkers, clinical, molecular and renal histopathological data, in order to identify different DKD phenotypes.
Method: Up to January 2023 we enrolled 69 patients with: ages18-80; diagnosis of type 2 diabetes; eGFR ≥ 15 ml/min/1.73m2. Patients underwent kidney biopsy, US and MRI, along with biofluids and clinical data collection. For each patient, a total of three renal cores were collected, one was fixed in formalin, embedded in paraffin and used for routine diagnostics, the other was split and either included in OCT or used for electron microscopy, while the last was stored in RNA later for omics analysis.
Results: Among the 69 patients enrolled, 57 underwent kidney biopsy and US, with 47 also undergoing MRI. According to the KDIGO guidelines our cohort included: 12 A1 stage patients (1 G1, 1 G2, 2 G3a, 6 G3b, 2 G4); 27 in A2 stage (7 G1, 7 G2, 4 G3a, 7 G3b, 2 G4) and 21 in A3 (2 G1, 6 G3a, 6 G3b, 7 G4). According to the histological classification by Mazzucco et al (Am J Kidney Disease, 2002), 31% of DKD patients were categorized as Class I (diabetic glomerulosclerosis); 33% as Class 2 (vascular and ischemic glomerular changes); 4% as Class 3a (glomerular diseases superimposed on DN); 31% as Class 3b (other glomerulonephritis in the absence of DN).
Pathologists assessment evidenced the presence of heterogeneous lesions among patients included within the same Mazzucco class. We thus proposed a novel classification of DKD, based both on renal pathology and according to the pathogenetic drivers. We identified 7 different histological classes of DKD: i) Class I: pure DN; ii) Class II: DN and nephroangiosclerosis; iii) Class III: DN and acute tubular necrosis; iv) Class IV: DN and Focal Segmental Glomerulosclerosis (FSGS); v) Class V: Nephroangiosclerosis; vi) Class VI: FSGS and other GN; vii) Class VII: FSGS and nephroangiosclerosis. According to the pathogenic drivers of DKD, we then grouped these classes in: pure metabolic damage (class II), metabolic damage and other drivers (including classes II, III, IV), pure vascular damage (class V) and immunological damage (classes VI, VII). Applying the newly proposed classification, we observed a significantly different distribution of key clinical parameters, uACR (p = 0.02), eGFR (p = 0.012), serum creatinine (p = 0.002) and proteinuria (p = 0.004). PAS glomerular staining positivity confirmed the more severe immunological damage of patients with vascular from those with immunological damage (p = 0.002). Finally, the renal resistive index measured through US significantly discriminated pure DN from mixed forms (p = 0.02).
Conclusion: The classification of renal damage in diabetes could represent a key strategy in the stratification of patients for precision medicine. The integration of renal pathology, US, ongoing MRI and omics data from the same patient has the potential to unlock new diagnostic tools and criteria to more accurately define the variety of renal phenotypes in diabetes.

#3503
IMPACT OF ADOPTING THE NEW CKD-EPI 2021 EQUATION ON eGFR AND CKD DETECTION IN A MULTI-ETHNIC DUTCH POPULATION: THE HELIUS STUDY
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Background and Aims: The 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is the current standard method for estimating GFR. There has been debate whether or not to exclude the race/ethnicity coefficient from this equation. Recently, the National Kidney Foundation and American Society of Nephrology Task Force on Reassessing Race in Diagnosing Kidney Disease recommended a new 2021 CKD-EPI race-free creatinine-based equation. The impact of this equation has not thoroughly been evaluated in the European population. We explored the impact of adopting this formula on both eGFR and estimates of CKD prevalence in a multi-ethnic Dutch population.
Method: We cross-sectionally analysed baseline data of 21,617 participants (mean age 44yr, 42% male) of the multi-ethnic HELIUS cohort study (Amsterdam, the Netherlands). Three groups were distinguished: participants of African Surinamese (4,151), Ghanaian (2,339) and other, non-African (15,127) background. eGFR was calculated using the 2009 and 2021 CKD-EPI equation. Multiple regression analyses were performed to determine differences in eGFR with additional adjustments for age, sex and traditional cardiovascular and renal risk factors. CKD prevalence (i.e., eGFR < 60ml/min/1.73m2) and/or ACR (≥ 3mg/mmol) was calculated. In each ethnic group three approaches to improve CKD case detection for both equations were compared by targeting participants with traditional renal risk factors (i.e., diabetes mellitus, hypertension or cardiovascular disease), by subsequently adding an age criterion (>40, > 50, or > 60 yrs), and low socio-economic status (none or elementary schooling). For each approach, c-statistics for CKD probability were compared.

#6853
KIDNEY ELASTOMETRY, KIDNEY MISMATCH INDEX AND CHRONICITY INDEX: NEW METHODS TO INTERROGATE THE DISEASED KIDNEY
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Background and Aims: Standard ultrasound mainly offers information about structural kidney alterations which may provide dates regarding the mass of the filtrating kidney (e.g. the nephron number), or obstructive alterations. Furthermore, the parenchymal Doppler ultrasound offers the resistance index, which is highly correlated to the plasma creatinine levels. However, in isolated proteinuria with normal kidney function these two classical methods do not reveal any alteration. We have hypothesized that kidney stiffness and a mismatch between creatinine levels and parenchymal resistance indices may offer additional features which may help the nephrologist in the classification of kidney diseases.
Method: In this respect, we have performed a transversal study on 468 patients with available resistance index of both the kidney and the spleen, clinical variables (including hemoglobin, creatinine, cholesterol, proteinuria, hypertension, diabetes) and shearwave elastometry, which gives an estimate of parenchymal stiffness. In order to identify patients with a mismatch between creatinine and renal resistance index we have introduced the kidney mismatch index (KMI) derived from the ratio between the renal resistance index and the creatinine levels. In order to identify chronic patients, we argued that in acute settings the creatinine levels (and hence the resistance index) are altered whereas the kidney size is normal: therefore the ratio of resistance index over the kidney size was tested as a quantitative marker of chronicity.
Results: Results confirm a strong correlation between kidney resistance index and creatinine (Pearson coeff. 0.318, p < 0.01). Interestingly, this index is also significantly dependent on age and cholesterol levels using a multiple regression model, after adjusting for creatinine levels. On the contrary, the resistance index of the spleen does not correlate neither with creatinine nor eGFR, whereas it correlated with cholesterol levels. Overall, creatinine levels could be predicted by the kidney size (longitudinal diameter, LD) and by the kidney resistance index (RI) using the following formula: creatinine = 1.8 - 0.175 LD + 2.601 RI Conversely, shearwave stiffness is only correlated to proteinuria (Pearson coeff. 0.497, p = 0.008) but not with creatinine. Finally, the kidney mismatch index (resistance index dissociated from creatinine levels) does not correlate with proteinuria and seems to identify particular subsets of patients with abnormal microcircular dynamics despite normal filtration rate, and should be tested in future studies as a prognostic factor.
Conclusion: In conclusion, kidney elastometry and kidney mismatch indices may prove additional sources of valuable informations that can be gathered from ultrasound methods which allow the identification of a diseased kidneys even in presence of normal architecture and normal resistance index.
Results: Differences between groups varied according to the equation used. Compared with non-African backgrounds (mean eGFR 102 mL/min/1.73m²), age- and sex-adjusted differences (p < 0.001) in the mean eGFR (SE) were 4.6 ± 0.2 and -8.9 ± 0.2 mL/min/1.73m² in participants with African Surinamese, and 3.2 ± 0.3 and -10.4 ± 0.3 mL/min/1.73m² in participants with Ghanaian background for the 2009 and 2021 CKD-EPI equations, respectively. Further adjustments did not change this. However, CKD prevalences were similar for both equations: 10.6% vs 10.8% (p = 0.30) in the whole cohort, 10.9 vs. 11.6% (p = 0.33) among African Surinamese and 12.0 vs 12.6% (p = 0.21) among Ghanaians. CKD case detection did not differ between the screening approaches nor between both equations. Also, c-statistics for CKD probabilities were not influenced by either equation.

Conclusion: In our cohort, adoption of the 2021 CKD-EPI equation leads to lower eGFR in participants of African Surinamese and Ghanaian background. However, only small not statistically significant differences in CKD prevalences, overall and in high-risk groups, were found. Our study indicates that discontinuation of the race-coefficient may have little impact on CKD detection in a multi-ethnic Dutch population.

#6881 ELEVATED LEVELS OF THE C5B9 TERMINAL COMPLEMENT COMPLEX IN PATIENTS RECEIVING RENAL REPLACEMENT THERAPY

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Background and Aims: The complement cascade and its inhibitors play an important role in health and disease. Complement activation represents a key pathogenic mechanism underlying inflammatory diseases affecting the kidney. The study aimed to investigate the C5b9 system in renal biopsies, where we stained all obtained kidney biopsies from the year 2017 (n = 256).

Method: Antibody staining against terminal C5b9 was performed, and a C5b9 score for each glomerulus (n = 1942) was generated based on automated image analysis. Mean scores for the interstitium, tubules and blood vessels, and whole biopsy sections were also calculated.

Results: Globally and segmentally, sclerosed areas in glomeruli stained much stronger than their non-sclerosed glomerular counterparts. The results were linked with Renal Replacement Therapy (RRT) status and clinical data from the Norwegian Kidney Biopsy Registry. The study’s main findings were that elevated levels of C5b9 were present in patients on RRT in glomeruli, blood vessels and whole section staining. Fibrillar glomerulopathy and Membranous Glomerulonephritis had the highest C5b9 scores, while glomeruli from Hypertensive Nephrosclerosis were represented with a low score. C5b9 scores correlated weakly or non-significantly with clinical variables like age, blood pressure and eGFR. The degree of fibrosis showed an associated positive correlation to C5b-9 staining intensities. Additionally, patients with an elevated C5b9 score (from the 50th percentile and above) showed a significantly elevated risk of receiving RRT within 60 months of biopsy.

Conclusion: C5b9 levels were significantly elevated in sclerotic glomeruli as well as in patients receiving RRT. A weak correlation between C5b9 scores and clinical variables for renal function suggest that the C5b9 complement system may be an independent effect in CKD.

#2697 ASSOCIATION OF CARDIOMETABOLIC PROTEINS WITH EGFR DECLINE IN OLDER ADULTS WITH ADVANCED CHRONIC KIDNEY DISEASE

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Background and Aims: Cardiovascular disease and advanced chronic kidney disease often coexist and share risk factors in older individuals. We investigated the association of cardiometabolic and cardiovascular proteins and pathways with decline in estimated glomerular filtration rate (eGFR).

Method: Two plasma protein panels (Olink®, cardiometabolic T96 and cardiovascular II T96, Uppsala, Sweden) were analysed at the baseline visit of individuals enrolled in the prospective observational European QUALity (EQUAL) study of older people > 65 years with advanced CKD (incident eGFR < 20 ml/min/1.73m²). Generalised linear mixed effects models with a log link and random intercept and slope were used to determine annualised eGFR slope (CKD-EPI 2009 equation) using a complete case model. The model was executed in a "discovery" sample (Germany, United Kingdom and Poland) and positive results (< false discovery rate [FDR] of 5%) were tested in a Swedish "validation" sample using the same FDR criterion. The primary analysis was adjusted for baseline age, sex, country, diabetes mellitus status, primary renal disease, systolic blood pressure, albumin to creatinine ratio (ACR), and the use of renin-angiotensin aldosterone inhibitors and β-blockers. A sensitivity analysis was conducted to determine the effect of informative censoring on eGFR slope using a joint model.

Results: The discovery and validation samples had 254 subjects (median age 67 years, 41% female, median baseline eGFR 18 ml/min/1.73m²) and 247 (median age 75 years, 28% female and median baseline eGFR 18 ml/min/1.73m²) respectively with longer follow-up time for the validation sample (median 3.6 versus 2.6 years) primarily due to less kidney replacement therapy initiation (33% versus 37%) and fewer losses to follow up (5% versus 12%). Two of the 175 proteins showed more rapid eGFR annual decline per doubling in protein levels (Figure 1): Receptor-type tyrosine-protein phosphatase S [PTPRS] (−15%; 95% confidence interval [CI] −24 to −7%, pFDR = 0.01) and Insulin-like growth factor-binding protein 6 [IGFBP6] (−8%; 95% CI −12 to −3%, pFDR = 0.03) (Figure 2). Predicted slopes were similar across both samples and for the sensitivity analyses.

Conclusion: Receptor-type tyrosine-protein phosphatase S and Insulin-like growth factor-binding protein 6 were associated with more rapid CKD progression. Further research is needed to determine if these proteins are pathophysiologically linked to accelerated progression of CKD in older people or a secondary consequence of disturbances in protein sequestration or excretion.
ASSOCIATION BETWEEN THE SERUM CREATININE-TO-CYSTATIN-C RATIO AND RAPID PROGRESSION OF CHRONIC KIDNEY DISEASE

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Background and Aims: Chronic Kidney Disease (CKD) is a common and progressive condition that affects a significant portion of the global population. It is a leading cause of death and requires timely evaluation and monitoring to ensure proper management. Cystatin C has been shown to be an effective marker of kidney function and a predictive marker of CKD progression. However, there is limited research evaluating the relationship between the serum creatinine-to-cystatin-C (Cr/cysC) ratio and the rapid progression of CKD. This study aims to investigate the effectiveness of the Cr/cysC ratio in predicting rapid progression of CKD.

Method: A retrospective study was conducted on 1,104 patients with CKD who were treated at the Nephrology Outpatient Clinic of Hanyang University Guri Hospital between December 2020 and November 2022. Eligible patients had at least two simultaneous measurements of serum creatinine and cystatin C, with a minimum interval of 6 months. The definition of rapid progression of CKD was a decrease in creatinine-based estimated glomerular filtration rate (eGFR) of more than 4 mL/min/1.73 m² over a 1-year period or initiation of renal replacement therapy (RRT). In addition, considering the short duration of the study, initiation of RRT was considered as a secondary outcome only in CKD stages 3b, 4, and 5.

Results: The study population consisted of patients with CKD stages 1 to 5, with a mean age of 69.7 years and 57.7% of the population being male. The mean baseline body mass index was 25.8 kg/m², and the mean initial eGFR was 46.7 mL/min/1.73 m². 38.4% of the total patients showed rapid progression of CKD. The analysis showed that a lower Cr/cysC ratio was significantly associated with an increased risk of rapid progression of CKD (OR: 0.812, 95% CI: 0.761-0.867, p < 0.001). After adjusting for age, sex, body mass index, and initial eGFR, a lower Cr/cysC ratio remained a significant risk factor for rapid progression of CKD (OR: 0.760, 95% CI: 0.685-0.844, p < 0.001). The initiation of RRT increased with the advancement of CKD stage, with 11 patients with CKD stage 3b, 30 patients with CKD stage 4, and 41 patients with CKD stage 5 initiating dialysis treatment. After adjusting for all variables, the OR was 0.774 (95% CI: 0.667-0.898, p = 0.001), indicating that as the Cr/cysC ratio increased, the progression of dialysis significantly decreased by 22.6%.

Conclusion: In this study, a lower Cr/cysC ratio was significantly associated with an increased risk of rapid progression of CKD and initiation of RRT. The results of this study suggest that monitoring the Cr/cysC ratio may provide valuable information for the management of CKD patients.
OMEGA-3 FATTY ACID ACTIVATES MITOCHONDRIAL BIOGENESIS AND PINK1 DEPENDENT MITOPHagy IN KIDNEY AND HEART OF ADENINE INDUCED UREMIC RATS

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1Dong-A University Hospital, Internal medicine, Busan, Korea, Rep. of South
2CHA Gumi Medical Center, CHA University, Internal medicine, Korea, Rep. of South and 3Dong-A University, College of Medicine, Internal medicine, Busan, Korea, Rep. of South

Background and Aims: Mitochondrial homeostasis is controlled by biogenesis, dynamics, and mitophagy. Mitochondrial dysfunction plays a central role in cardiovascular and renal disease and omega-3 fatty acids (FA) are beneficial for cardiovascular disease. We aimed to investigate whether omega-3 FA regulates the expression of mediators of mitochondrial biogenesis, dynamics, and mitophagy in kidney and heart of adenine-induced uremic rats.

Method: Sprague-Dawley rats were divided into three groups: normal control, adenine control, and omega-3 FA. Uremia was induced by feeding diets containing 0.75% adenine and 2.5% protein for the first 3 weeks. During next 4 weeks, they were received 2.5% protein with or without omega-3 FA (300 mg/kg/day). The renal and cardiac expression of PGC-1α, SIRT1/3, Nrf2, DRP-1, OPA1, Mfn1/2, PINK1, BNIP3 and NIX were examined by western blot analysis. The qPCR was used to determine mitochondrial DNA (mtDNA).

Results: Compared to normal, serum creatinine and heart weight/body weight in adenine control was increased and improved in omega-3 FA group. Compared with normal, PGC-1α, SIRT1/3 and Nrf2 were down-regulated in kidney and heart of adenine control. PGC-1α expression of kidney and heart was recovered in omega-3 FA group. DRP-1 of kidney was up-regulated but DRP-1 of heart was down-regulated in adenine control. DRP-1 of heart was recovered in omega-3 FA group. PINK1, BNIP3 and NIX were down-regulated in heart of adenine control and recovered in omega-3 FA group. PINK1 was down-regulated but BNIP3 and NIX were up-regulated in kidney of adenine control and those were mitigated in omega-3 FA group. mtDNA was decreased in kidney and heart of adenine control group but mtDNA of heart was recovered in omega-3 FA group.

Conclusion: DRP-1 related with mitochondrial fission may oppositely work in uremic kidney and heart. Omega-3 FA is beneficial for mitochondrial homeostasis by activating mitochondrial biogenesis and PINK1 dependent mitophagy in kidney and heart of uremic rats.

ALBUMINURIA IS ASSOCIATED WITH DECREASED SEVR AND ANKLE-BRACHIAL INDEX IN PATIENTS WITHOUT CKD

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Background and Aims: Albuminuria signifies subclinical vascular damage in the kidneys and other organs and is associated with systemic endothelial dysfunction and increased future cardiovascular risk. Subendocardial viability ratio (SEVR) is defined as diastolic to systolic pressure-time integral ratio and is a marker of subendocardial perfusion. Reduced SEVR has been uncovered in patients with chronic kidney disease (CKD) and simultaneous albuminuria. Albuminuria is also considered a risk factor for peripheral artery disease, especially in patients with additional atherosclerosis risk factors or diabetes mellitus. The aim of our study was to determine the impact of albuminuria on SEVR and ankle-brachial index (ABI) in patients without known CKD.

Method: We included 111 patients (73% male, mean age 64.2±9.3 years) that were hospitalized at our Cardiology department between 2016-2020 due to elective cardiac catheterization. Albuminuria was determined by urine albumin to creatinine ratio (UACR) from a random urine specimen. SEVR was determined by using application tonometry on radial artery (Sphygmocor, Atcor Medical, Australia). Ankle-brachial index (ABI) was measured by using an automated, non-invasive waveform analysis device (MESIÒ, Slovenia). Reduced SEVR has been uncovered in patients with chronic kidney disease (CKD) and simultaneous albuminuria. Albuminuria is also considered a risk factor for peripheral artery disease, especially in patients with additional atherosclerosis risk factors or diabetes mellitus. The aim of our study was to determine the impact of albuminuria on SEVR and ankle-brachial index (ABI) in patients without known CKD.

Results: Basic descriptive statistics, comorbidities, and medications are presented in Tables 1 and 2. Spearman’s correlation test showed significant correlation between UACR and SEVR (r = -0.238; p = 0.017) and UACR and ABI (r = -0.304; p = 0.003). Multiple regression analysis with SEVR as the dependent variable and waist-to-hip ratio, body mass index (BMI), arterial hypertension, diabetes, dyslipidemia, eGFR and UACR as independent variables, showed a significant association between UACR and SEVR (b = -0.232; p = 0.029). The same model was used for ABI as the dependent variable, and a significant association was found only between UACR and ABI (b = -0.232; p = 0.029).

Conclusion: Albuminuria is independently associated with decreased SEVR and ABI even in the absence of CKD.

Figure 1: Expression of mitochondrial dynamics and mitophagy related molecules in uremic kidney and heart.
Table 1: Basic descriptive statistics of included patients (n = 111).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.2 ± 9.3</td>
<td>27 – 82</td>
</tr>
<tr>
<td>Body Mass Index – BMI (kg/m²)</td>
<td>28.3 ± 4.3</td>
<td>18.9 – 37.8</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>1.0 ± 0.1</td>
<td>0.8 – 1.1</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>140.8 ± 12.9</td>
<td>98 – 171</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>4.9 ± 7.0</td>
<td>3 – 55</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>77.6 ± 14.0</td>
<td>49 – 108</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate – eGFR (ml/min/1.73 m²)</td>
<td>81.3 ± 9.4</td>
<td>62 – 90</td>
</tr>
<tr>
<td>Urinary albumin-to-creatinine ratio – UACR (mcg/mg)</td>
<td>20.1 ± 22.4</td>
<td>0 – 154</td>
</tr>
<tr>
<td>Mean ankle-brachial index – ABI</td>
<td>1.1 ± 0.1</td>
<td>0.8 – 1.3</td>
</tr>
<tr>
<td>Subendocardial viability ratio – SEVR (%)</td>
<td>165.9 ± 36.1</td>
<td>92 – 299</td>
</tr>
</tbody>
</table>

Table 2: Most common comorbidities and prescribed medications of included patients (n = 111).

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypertension</td>
<td>86 (77.5)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>63 (56.8)</td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>23 (20.7)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>12 (10.8)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>5 (4.5)</td>
</tr>
</tbody>
</table>

**Prescribed medication**

<table>
<thead>
<tr>
<th>Prescribed medication</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylsalicylic acid</td>
<td>96 (86.5)</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>80 (72.1)</td>
</tr>
<tr>
<td>Angiotensin-convertase inhibitors</td>
<td>64 (57.7)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>35 (31.5)</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>25 (22.5)</td>
</tr>
<tr>
<td>Angiotensin-II receptor antagonists</td>
<td>19 (17.1)</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>6 (5.4)</td>
</tr>
</tbody>
</table>

Results: In both CSF and plasma, levels of all four uremic solutes were elevated in HD patients compared to healthy subjects (Table 1). The ratio of CSF-to-plasma levels was <100% for all solutes. Ratios for HD patients are altered compared to those reported in healthy subjects (Table 1). Longitudinal plasma and CSF solute levels are shown in Figure 1. Plasma RR for IS, pCS, TMAO and urea were 32%, 23%, 77%, and 67%, respectively. The respective CSF RR were 29%, 20%, 3%, and 25%.

**Conclusion:** To the best of our knowledge, this is the first report on CSF levels of IS, pCS, and TMAO in HD patients. Our results indicate that uremic solute levels are elevated in the CSF from HD patients compared to healthy subjects. Moreover, HD only moderately reduces uremic solute levels in CSF. Whether increased CNS levels of uremic solutes are related to cognitive impairment warrants further investigation.

#4580

ELEVATED LEVELS OF UREMIC SOLUTES IN THE CEREBROSPINAL FLUID OF HEMODIALYSIS PATIENTS

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**Background and Aims:** Uremic solutes are considered as contributing factors to impaired cognitive function in end stage kidney disease (ESKD) [1]. However, the distribution and accumulation of uremic solutes in the central nervous system (CNS) of ESKD patients are not well understood. We measured four uremic solutes in the cerebrospinal fluid (CSF) and plasma of two ESKD patients and investigated the role of routine hemodialysis (HD) in clearing these solutes from their CNS.

**Method:** We accessed CSF in HD patients with a ventriculo-peritoneal shunt. A review of about 160,000 electronic health records revealed 30 eligible patients, two of whom consented to participate in this IRB-approved one-week study (Western IRB #20172182). On dialysis days, CSF and plasma were collected 2 hours pre- and 2 hours post-HD. Non-dialysis day samples were collected 20 hours post-HD. Samples from healthy subjects were purchased from BioIVT (Westbury, NY). Urea was measured using Horiba C400 Chemical Analyzer. Indoxyl sulfate (IS), p-cresol sulfate (pCS) and trimethylamine N-oxide (TMAO) were analyzed using Agilent Ultivo triple quadrupole mass spectrometer. The dialytic reduction ratio (RR; in %) was calculated as 100 × (pre-HD level – post-HD level) / pre-HD level.

### Concentrations of uremic solutes in CSF and plasma of HD patients A and B, and healthy subjects.

<table>
<thead>
<tr>
<th>Uremic Solute</th>
<th>Patient A</th>
<th>Patient B</th>
<th>Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS (μg/mL)</td>
<td>4.89 ± 0.16</td>
<td>7.9 ± 0.72</td>
<td>0.14 ± 0.03</td>
</tr>
<tr>
<td>pCS</td>
<td>3.38 ± 0.19</td>
<td>28.0 ± 2.04</td>
<td>0.52 ± 0.13</td>
</tr>
<tr>
<td>TMAO</td>
<td>2.01 ± 0.15</td>
<td>2.19 ± 0.36</td>
<td>0.05 ± 0.01</td>
</tr>
<tr>
<td>Urea</td>
<td>1080 ± 98</td>
<td>1153 ± 186</td>
<td>277 ± 32</td>
</tr>
<tr>
<td>IS (μg/mL)</td>
<td>0.006 ± 0.001</td>
<td>0.046 ± 0.003</td>
<td>Not detected</td>
</tr>
<tr>
<td>pCS</td>
<td>Not detected</td>
<td>0.038 ± 0.006</td>
<td>Not detected</td>
</tr>
<tr>
<td>TMAO</td>
<td>0.204 ± 0.013</td>
<td>0.157 ± 0.032</td>
<td>0.007 ± 0.002</td>
</tr>
<tr>
<td>Urea</td>
<td>766 ± 71</td>
<td>779 ± 39</td>
<td>221 ± 36</td>
</tr>
<tr>
<td>CSF (in % of plasma levels)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td>0.12 ± 0.02</td>
<td>0.59 ± 0.04</td>
<td>0.42 ± 0.21</td>
</tr>
<tr>
<td>pCS</td>
<td>Not determined</td>
<td>0.13 ± 0.01</td>
<td>0.19 ± 0.27</td>
</tr>
<tr>
<td>TMAO</td>
<td>10.4 ± 1.1</td>
<td>8 ± 2</td>
<td>39 ± 29</td>
</tr>
<tr>
<td>Urea</td>
<td>70.9 ± 0.9</td>
<td>71.8 ± 9.3</td>
<td>89 ± 1.9</td>
</tr>
</tbody>
</table>

¹CSF (n = 9) and plasma (n = 9) samples in healthy subjects were not from the same subject. ²CSF-to-plasma ratios of IS, pCS and TMAO in healthy subjects (n = 9) were reported in Sankowski et al. 2020 [2] and the ratio of urea (n = 13) in Funder and Wieth 1967 [3]. In both references, CSF and plasma samples were from the same subject.
Background and Aims: Diabetic kidney disease (DKD) has an enormous disease burden globally. In the area of personalised medicine, biomarker is set to play an important role in the management of DKD. Prior studies have reported the possible association of Tumour Necrosis Factor Receptor 1 (TNFR1), Dickkopf-3 (DKK3) and B cell lymphoma 3 (BCL-3) with the pathogenesis of DKD. However, there had been no prior studies that investigate the association of these biomarkers as prognostic markers for DKD disease progression. Hence, we aim to investigate the correlation of these biomarkers with renal progression among the diabetic population with and without kidney disease.

Method: A total of 156 subjects were recruited, which consisted of 64 control vs 92 patients with DKD. The principal outcomes of this study were rapid renal decline (doubling of serum creatinine, renal decline > 5ml/min/year and > 10 ml/min/year) and their association with serum TNFR1, BCL-3 and urine DKK3. A bivariate analysis was used to test the association of rapid renal decline, and sensitivity and specificity were used to test the validity of the level of the biomarkers with outcomes.

Results: The baseline parameters for both case and control: age 50.19±9.22 vs 60.35±13.73, serum albumin 38.97±2.07 vs 33.01±8.98g/L (p< 0.001), eGFR 117.96±31.94 vs 38.00±22.04 ml/min/1.73 m² (p< 0.001), serum creatinine 77.34±14.15 vs 247.45±148.09 μmol/L (p < 0.00), uPCI g/day 0.001±0.0 vs 4.268±5.29 (p < 0.001), HbA1c 7.83±1.88 vs 7.86±1.78 mmol/L (p = 0.942), sTNFR1 11781.91±337.46 vs 4394.03±1960.06 pg/mL (p < 0.001), uDKK3/creatinine 132.84±37.61 and 1243.63±495.27 pg/mg (p < 0.001), and sBCL3 194.60±32.81 vs 490.17±259.02 pg/mL(p < 0.001). During the follow-up, there was a significant association of sTNFR1 with rapid renal decline > 5ml/min/year, > 10 ml/min/year and doubling of serum creatinine [p < 0.003 [IQR = 2891.50-4885.75], p < 0.009 [2891.50-4885.75], p < 0.001 [2891.50-4885.75]] but not with uDKK3 and sBCL-3 (Table 1). Specificity and sensitivity analyses on the performance of the biomarkers versus outcomes were highly significant (Figure 1).

Conclusion: Despite TNFR1, BCL-3 and urine DKK3 were all elevated in our DKD patients, there was a strong association between incident serum TNFR1 level and the subsequent deterioration of renal function which has not been reported in the literature before. In addition, TNFR1 level had consistently picked up cases of DKD that would experience rapid renal progression, be it > 5ml/min/year, > 10 ml/min/year or doubling of serum creatinine. The correlation studies have shown TNFR1 level high sensitivity, and specificity with renal progression among the diabetic population with and without kidney disease.

Table 1: The association of the renal outcome (doubling of serum creatinine, renal decline > 5ml/min/year and > 10 ml/min/year) with the level of biomarkers compared with the conventional markers. Results show there is a significant association of sTNFR1 with all renal outcomes but not with uDKK3 and sBCL3.

<table>
<thead>
<tr>
<th>Outcome/Biomarkers</th>
<th>&gt; 5 ml/min/year</th>
<th>&gt; 10 ml/min/year</th>
<th>Doubling of serum creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>p</td>
<td>IQR</td>
</tr>
<tr>
<td>sTNFR1 pg/mL</td>
<td>3783.50</td>
<td>0.003</td>
<td>2891.50-4885.75</td>
</tr>
<tr>
<td>uDKK3 pg/mg</td>
<td>1287.50</td>
<td>0.812</td>
<td>815.75-1702.00</td>
</tr>
<tr>
<td>sBCL3 pg/mL</td>
<td>451.80</td>
<td>0.790</td>
<td>306.32-630.62</td>
</tr>
<tr>
<td>Baseline UPCI g/day</td>
<td>1.90</td>
<td>0.073</td>
<td>0.50-7.0</td>
</tr>
<tr>
<td>Baseline Creatinine mmol/L</td>
<td>210.00</td>
<td>0.025</td>
<td>142.75-305.25</td>
</tr>
<tr>
<td>Baseline eGFR ml/min</td>
<td>34.55</td>
<td>0.000</td>
<td>24.42-47.14</td>
</tr>
<tr>
<td>Baseline Albumin g/L</td>
<td>35.50</td>
<td>0.000</td>
<td>29.00-39.00</td>
</tr>
</tbody>
</table>

*The Mann-Whitney U test
of TNFR1 on the rapid renal function decline. Thus, we believe in our DKD population, targeting TNFR1 pathway could be a promising tool in monitoring and treating our DKD population.

#2758

AMBIENT HEAT EXPOSURE AND ESTIMATED GLOMERULAR FILTRATION RATE Trajectory: A POST-HOC ANALYSIS OF THE DAPA-CKD TRIAL

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Background and Aims: Higher ambient temperatures have been associated with higher rates of admission for kidney stones and acute kidney injury. Occupational heat stress is also a risk factor for impaired kidney function in several rural resource-poor settings. It is unclear if higher ambient heat exposure is associated with a faster loss of kidney function in patients with established, all-cause, chronic kidney disease (CKD). We therefore undertook a post-hoc analysis of the DAPA-CKD trial linking participant data to publicly available climate measurements.

Method: The DAPA-CKD trial randomized 4304 patients with proteinuric CKD (estimated glomerular filtration rate, eGFR, 25-75 mL/min/1.73 m²; urinary albumin-to-creatinine ratio, ACR, 23-566 mg/mmol) to dapaglifozin or placebo in addition to standard of care. We examined the association between daily study centre-level ambient heat exposure (defined as a mean heat index, HI, >30; European Centre for Medium-Range Weather Forecasts ERA5 reanalysis dataset) and individual-level change in eGFR using both a linear-mixed effects model and a case-time series approach to address potential unmeasured individual- and centre-level confounding.

Results: Climate and eGFR data were available on 3915 (91%) participants across 361 centres in 21 countries. Over a median of 28 months, participants (mean age: 62 years; mean eGFR: 43mL/min/1.73 m²) were followed-up at centres where there was a median of 1 day (interquartile range: 0 to 64 days) with an HI>30. Each 30-day period of HI>30 over the study period was associated with a change in eGFR of ~0.7% (95% CI: -1.0% to -0.3%), equivalent to an additional eGFR loss of between 1.2 and 4.0mL/min/1.73 m² per year in a patient with an eGFR of 45mL/min/1.73 m² located in a very hot versus temperate environment. Similar estimates were obtained using the case time series approach. This association persisted after adjustment for potential haemoconcentration effects on the day of testing and further analyses provided no evidence that these findings varied with baseline eGFR, albuminuria or

Figure 1: Association between heat index and change in eGFR in subgroups. Linear mixed model of eGFR measures nested within individual-level random effects nested within centre-level random effects. Model adjusted for the following baseline variables: age; sex; ethnicity; smoking status; diagnosis of diabetes; history of cardiovascular disease; BMI; systolic blood pressure; urinary ACR; eGFR; ACE/ARB use; statin use; diuretic use; DAPA-CKD study arm; and time interactions (reflecting associations with eGFR slope) with age; BMI; systolic BP; eGFR; urinary ACR and DAPA-CKD study arm. Average marginal effects estimates presented for subgroups. Error bars show 95% confidence intervals. The DAPA-CKD trial was funded by AstraZeneca.

#4592

A HIGH PROTEIN DIET INDUCES DEPRESSION-LIKE BEHAVIOR IN CKD RODENT MODELS

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1KU Leuven, Department of Nephrology, University Hospitals Leuven, Leuven, Belgium and 2KU Leuven, Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium

Background and Aims: The prevalence of depression among patients with Chronic Kidney Disease (CKD) is higher than the general population. Around 21-27% of CKD patients is estimated to be affected by depression. Several studies hypothesized that mood disorders may be due to reduced family support, older age, low educational status and low quality of life. However, adults with CKD are also known to exhibit altered tryptophan metabolism

Figure 1: A high specificity and sensitivity analyses of the biomarkers versus outcome sTNFR1 74% p < 0.001, 68.2% p = 0.009 and 73.8% p < 0.001, uDKK3 39.7% p = 0.102, 51.4% p = 0.839 and 42.8% p = 0.26 and sBCL-3 60.5% p = 0.096, 46.0% p = 0.561 and 52.1% p 0.744.
causing reduced plasma levels of tryptophan and elevated kynurenine and kynurenic acid. Moreover, CKD patients showed increased levels of indoxyl sulfate and indole-3-acetic acid, two protein-bound uremic toxins deriving from the gut microbiome metabolism of tryptophan. We postulate that depression is not just due to reduced quality of life but also to a biological reason. In addition, we hypothesize that a high protein diet may influence tryptophan metabolism and therefore affect depression symptoms.

Method: Eighteen Sprague-Dawley male rats (Janvier, Le Genest - St Isle, France), 7-8 weeks old, were induced with CKD utilizing 5/6 nephrectomy and were randomly assigned to a low protein (n = 10) or a high protein (n = 8) diet. A sham-operated control group for each diet was used (n = 7 respectively). The splash test was adopted to assess depressive symptoms in rats. In short, the splash test is a behavioral test consisting in sprinkling a 10% sucrose solution on the dorsal coat of a rat. Latency (time before the initiation of grooming) and duration of grooming were recorded for 5 min and used as an indication of self-care behavior. Delayed and reduced grooming is considered as a depression-like behavior of rats. Blood and urine creatinine were determined with standard laboratory techniques. Total plasmatic concentrations of tryptophan, kynurenine, kynurenic acid and indoxyl sulfate were measured using LC-MS/MS.

Results: The latency before the starting of the grooming behavior was significantly higher (p = 0.049) in CKD rats on a high protein diet compared to sham rats on the same diet while no difference was seen between the low protein groups. CKD rats reported significantly higher plasma levels of indoxyl sulfate and kynurenic acid and reduced tryptophan. Interestingly, kynurenic acid plasma levels were significantly reduced when administering a low protein diet to CKD rats (p = 0.025). Among CKD rats, the latency of the grooming behavior was correlated with plasmatic levels of creatinine clearance (Spearman r = -0.57, p value = 0.19), indoxyl sulfate (Spearman r = -0.64, p value = 0.007), and kynurenic acid (Spearman r = -0.63, p value = 0.009). The total grooming time was shorter in both CKD groups compared to the sham rats, but not significantly (p = 0.4881 and p = 0.4312, respectively).

Conclusion: These results suggest that biological factors contribute to depression onset and that the decline of kidney function and the accumulation of uremic toxins are potential risk factors for depression. Dietary interventions such as a low protein diet, are potential strategies to lower the plasmatic levels of uremic toxins which may alleviate depressive-like symptoms.

### #5000

**DIFFERENCES IN CIRCULATING IMMUNE CELLS PROFILE BETWEEN MALES WITH CARDIORENAL SYNDROME TYPE II AND CKD PATIENTS WITHOUT CARDIOVASCULAR DISEASE**

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1University Hospital of Ioannina, Department of Nephrology, IOANNINA, Greece; 2University Hospital of Ioannina, Second Department of Cardiology, IOANNINA, Greece; 3University Hospital of Ioannina, Laboratory of Hematology - Unit of Molecular Biology, IOANNINA, Greece and 4Hatzikosta General Hospital of Ioannina, Internal Medicine Department, IOANNINA, Greece

**Background and Aims:** Maladaptive activation of the immune system plays an important role in the pathogenesis of cardiovascular disease (CVD) and chronic kidney disease (CKD). The immune system components can act as mediators of organ cross-talk and may be involved in the reciprocal dysfunction that occurs in cardiorenal syndromes (CRS). The aim of our study was to investigate potential differences in blood levels of specific immune cells subsets between a cohort of type II CRS patients and CKD patients without established CVD.

**Method:** 40 stable male patients with CRS type II and 30 male CKD patients with proteinuria were enrolled for eGFR (CKD-EPI) were enrolled in this cross-sectional study. Exclusion criteria were history of malignancy, autoimmune and active or chronic infections. The peripheral blood immune cell subsets CD14++CD16-, CD14++CD16+ and CD14+CD16+ absolute values and percentages out of total monocytes and NK cells (CD3+CD16+56+), CD3-CD19- B lymphocytes, CD3+ CD4+ T cells, CD3+CD8+ T cells and Tregs (CD4+CD25+FoxP3+) absolute values and percentages out of total lymphocytes were measured by flow cytometry. In a randomly selected subgroup of 40 patients, the correlation between the peripheral blood immune cell subsets and laboratory and echocardiographic data was assessed. Multiple regression analyses to assess independent relationships were performed by building separate models with each of the immune cells as the dependent variable and respective univariate correlates including patient group.

**Results:** Mean age of patients with CRS and CKD was 72±10 versus 66±10 years respectively (p = 0.01), mean eGFR was 37±14 and 33±16ml/min/1.73 m² respectively (p = 0.28) and median urinary protein to creatinine ratio (UPCR) was 0.19 (IQR: 0.10-0.52) versus 1.03 (IQR: 0.17-2.09) g protein/gr creatinine (p = 0.02) respectively. CRS patients displayed increased levels of pro-inflammatory, intermediary CD14++CD16+ monocyes [41 (IQR, 24-78)/μL compared to their CKD counterparts [35 (IQR, 18-43)]/μL (p = 0.04). A higher Tregs percentage was found in CRS patients [2.7% (IQR, 2.0%-3.9%)] compared to CKD patients [2.0% (IQR, 1.6%-2.6%)] (p = 0.03). Lower mean levels of lymphocytes were observed in CRS patients [153 (IQR, 80-245)]/μL compared to the CKD cohort [192 (IQR, 545-791)μL (p= 0.04). Finally, CRS patients displayed lower NK cell counts [148 (IQR, 103-258)]/μL compared to CKD patients [324 (IQR, 179-368)]/μL (p = 0.001). Age and UPCR did not correlate with immune cells subsets in the whole cohort, neither in the two groups separately. At multivariate regression analysis, the differences in immune cells between the two groups remained statistically significant. Specifically, in patients with CRS the intermediate CD14++ CD16+ monocyes counts correlated positively with CRP (p = 0.002) and ESR (p = 0.02). A positive correlation was found between eGFR and total lymphocytes (p = 0.009), T cells (p = 0.005) and CD4+ T cells (p = 0.005) counts. The number and percentage of nonclassical CD14+CD16+ macrophages were higher in CRS patients with left ventricular ejection fraction (LVEF) less than 30% compared to patients with LVEF above 30% [33 (IQR, 18-37)]/μL versus 13 (IQR, 10-29)/μL (p = 0.02) and 4.5% (IQR, 3.4%-7.2%) versus 2.7% (IQR, 1.9%-5.4%) (p = 0.03) respectively. With regard to etiology, patients with dilated cardiomyopathy compared to patients with ischemic CVD displayed increased counts of intermediate CD14++CD16+ monocytes [75 (IQR, 41-104)]/μL versus 36 (IQR, 22-61)]/μL (p = 0.01) and non-classical CD14+CD16+ macrophages [35 (IQR, 19-51)]/μL versus 21 (IQR, 12-32)]/μL (p = 0.02). Finally, NK cells and Tregs levels were lower in patients with atrial fibrillation compared to those without [133 (IQR, 79-173)]/μL versus 260 (IQR, 151-314)]/μL (p = 0.01) and [32 (IQR, 21-43)]/μL vs 47 (IQR, 34-85)]/μL (p = 0.006) respectively.

**Conclusion:** Patients with CRS type II exhibit alterations of the immune cells subsets profile in the peripheral blood compared to CKD patients of similar kidney function but without CVD. Our findings suggest that distinct immune mechanisms might be involved in the pathogenesis or the chronic course of CRS type II as compared to CKD. Future research is required to test their pathophysiological or prognostic significance.

### #3390

**ADPKD PREDICTOR: A CLOUD-BASED PROGNOSTIC TOOL FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE**

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**Background and Aims:** ADPKD is a progressively debilitating genetic disease characterized by the growth of numerous cysts in the kidneys, leading eventually to end-stage renal disease. Total Kidney Volume (TKV) is accepted by FDA and EMA as a prognostic biomarker and quantitative predictor of kidney function decline, and is currently used to select patients to receive Tolvaptan treatment. However, TKV calculation from manual tracing of medical images is labor-intensive; for better accuracy, current available methods involve the injection of an iodinated contrast medium for CT scan, with important limitations in patients with impaired renal function. We developed ADPKD Predictor, a user-friendly cloud-based tool for fast and accurate estimation of disease classification and progression, based on automated kidney and cysts segmentation from MRI data.

**Method:** An online tool was designed on Microsoft Azure Cloud to automate the set-up and running of a previously developed algorithm implemented in MATLAB to automatically detect kidneys and cysts contours from MRI data (T2-weighted turbo-spin-echo SPIR), based on advanced image processing techniques [1]. Through the web interface, the user is requested to upload the MRI data and select one point inside kidney’s parenchyma in the central slice (Figure 1). Then, TKV is automatically calculated and eGFR based on CKD-EPI equation, ADPKD Imaging Classification and future eGFR [2], estimated Tolvaptan treatment effect [3], and GFR Category based on KDIGO CKD staging system are also obtained (Figure 2). The MRI dataset is anonymized before upload to the cloud; data and results are stored in a secure and reliable environment controlled by the user.

**Results:** The proposed solution is very fast and precise compared to manual segmentation of medical images (absolute mean error 2.4% ± 2.7%) [1]. Moreover, it is faster and more accurate than the commonly used ellipsoid-based method, resulting in a manifold reduction of misclassification.
error (2.5%) [1] and therefore potential therapeutic consequences. Another advantage is its usability, with no specific computational expertise, numerical software or dedicated hardware required, since all computations are run remotely in the cloud.

**Conclusion:** ADPKD Predictor provides a fast and reproducible assessment of risk classification and disease progression, based on precise morphologic classification of the renal and cysts volume of patient. The proposed solution represents an extremely useful tool for researchers and clinicians to easily obtain an accurate estimation of risk classification potentially helping in a correct and effective stratification of patients, and monitor patient’s disease progression, hence supporting a correct and effective therapy administration. Also, it would represent a great benefit for the patient, since the tool analyzes medical images obtained without the use of contrast medium.

Figure 1: ADPKD Predictor web interface – Input page - User uploads MRI data, scrolls through images and selects one point inside kidney’s parenchyma in the central slice.
ADPKD Predictor web interface – Output page showing TKV and ADPKD Imaging Classification, eGFR history, future eGFR and estimated effect of Tolvaptan treatment, GFR Category.

REFERENCES


#4176

ROLE OF KIDNEY FUNCTION ON NRF2 MRNA LEVELS IN TYPE-2 DIABETES

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1CNR-Institute of Clinical Physiology, Italy, 2Nephrology, Dialysis, and Transplantation Unit (GOM-BMM), Italy, 3AMD-Associazione Medici Diabetologi, Italy, 4Endocrinology and Diabetes Unit (GOM-BMM), Italy, 5Renal Research Institute, United States of America, 6BIOGEM, Italy and 7IPNET, Italy

**Background and Aims:** Nuclear factor erythroid 2-related factor 2 (Nrf2) is a transcription factor that induces the expression of genes coding for antioxidant proteins and phase II detoxifying enzymes. Repressor molecule Kelch-like ECH-associated protein 1 (Keap1) and several microRNAs (miRNA) negatively regulate Nrf2 gene expression at post-transcriptional level. Oxidative stress is a major factor for kidney damage in diabetes but the role of Nrf2 in kidney dysfunction in diabetes is still unclear.

**Method:** To test whether the gene expression of Nrf-2 is downregulated in type-2 diabetes and whether kidney dysfunction per se further reduces Nrf2 in diabetic patients with diabetic nephropathy, we carried out a case-control study including 99 participants divided into three independent groups: 33 patients with diabetic nephropathy (DN), 33 patients with type 2 diabetes without nephropathy (D) and 33 control subjects (C), all accurately matched for age and sex. Standard ANOVA compared outcome measures in the three groups. Multiple linear regression analysis was used to test the expression levels of Keap1, miR-28-5p, miR-93-5p, miR-30e-5p, miR-125b-5p and miR-150-5p as potential mediators in the observed reduction of Nrf2 mRNA levels in patients with diabetic nephropathy.

**Results:** In patients with diabetic nephropathy, Nrf2 gene expression levels (0.82 arbitrary units, AU, IQR: 0.60-1.22 AU) were significantly lower than in diabetic patients without nephropathy (1.19 AU, 0.90-1.38 AU, *P* = 0.01) and control subjects (0.82 AU, 0.60-1.22 AU vs 1.04 AU, 0.87-1.66, *P* = 0.02) while there was no difference between diabetic patients without nephropathy and control subjects (*P* = 0.69). Keap1 gene expression levels were almost identical in patients with and without diabetic nephropathy (1.15 AU, 0.63-2.14 AU vs 1.13 AU, 0.79-1.73 AU, *P* = 0.91) and higher than in control subjects (1.15 AU, 0.63-2.14 AU vs 0.79 AU, 0.49-1.08 AU, *P* = 0.046). MiRNA expression levels were comparable in diabetic patients with and without nephropathy, but miRNA 30e-5p was lower in patients with diabetic nephropathy than in diabetic patients without nephropathy (0.91 AU, 0.76-1.10 AU vs 1.06 AU, 0.89-1.23 AU, *P* = 0.016). The expression levels of Nrf2 and miRNA 30e-5p were unrelated in patients with (*r* = 0.15, *P* = 0.44) and without (*r* = -0.02, *P* = 0.90)
diabetic nephropathy. In linear regression analyses, eGFR emerged as the first factor in rank for explaining the difference in Nrf2 mRNA levels (adjusted variance 76%) among patients with and without diabetic nephropathy.

**Conclusion:** This case-control study comparing the gene expression level of Nrf2 in diabetic patients with and without nephropathy shows that kidney dysfunction is the key factor that explains the variability in Nrf2 mRNA levels in diabetes. These data suggest a primary role of Nrf2 in redox homeostasis and kidney damage in diabetic nephropathy.

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**#4761**

**ESTIMATED GLOMERULAR FILTRATION RATE USING CYSTATIN C AND CREATININE IN CHILDREN WITH NEUROGENIC BLADDER – IMPACT OF DEMOGRAPHICS AND PROTEINURIA**

Bebiana Sousa 1, Luis Salazar 1, Sofia Poço Miranda 1, Sofia Ventura 1, Rosa Amorim 1, Maria Do Sameiro Faria 2, Teresa Costa 3 and Maria Conceição Mota 5

1 Centro Materno Infantil do Norte, Pediatrics, Portugal, 2 Unidade Local de Saúde do Alto Minho, Pediatrics, Portugal, 3 Hospital do Divino Espírito Santo, Nephrology, Portugal, 4 Centro Hospitalar e Universitário de Santo António, Physiatrics, Portugal and 5 Centro Materno Infantil do Norte, Pediatric Nephrology Unit, Portugal

**Background and Aims:** There is a high-risk of progressive chronic kidney disease (CKD) in patients with neurogenic bladder (NB) and early detection of estimated glomerular filtration rate (eGFR) reduction is essential, preventing delayed diagnosis. Creatinine-based formulas can overestimate eGFR in these patients due to decreased muscle mass. This study aims to compare eGFR calculated by different equations using serum creatinine (Cr) and/or cystatin C (CysC), in children with NB, and analyse the influence of demographic variables and proteinuria.

**Methods:** Data on pediatric patients with NB and CKD stage 1 and 2, based on eGFR calculated by the CKiD-Cr formula, were collected from January 2009 to December 2022, in a Pediatric Nephrology Unit from a tertiary hospital. The eGFR was calculated using CKiD CysC, Schwartz combined Cr/CysC, Zapitelli-CysC and Zapitelli combined Cr/CysC formulas. Proteinuria was defined by urine protein-to-creatinine ratio greater than 0.2 (mg/mg).

**Results:** Fifty patients were evaluated, with a median (25th-75th percentile) age of 14.2 (9.0-16.7) years, 48% (n = 24) female, with a median height of 142 (119.8-154.3) cm, mostly below 5th percentile (64%, n = 32) and a median body mass index of 20.5 (15.5-26.7) kg/m2, 58% (n = 29) of patients had lipo/myelomeningocele and 76% (n = 38) were classified as stage 1 CKD. The median eGFR (ml/min/1.73m2) calculated by different formulas was: CKiD-Cr 108.1 (89.2-129.6); CKiD-CysC 77.1 (59.7-87.7); CKID-Cr/CysC 86.6 (67.4-98.1); Zapitelli-CysC 83.3 (63.3-95.7) and Zapitelli combined- Cr/CysC 101.4 (75.5-121.2). When compared to CKiD-Cr, all the CysC-based formulas showed significantly lower values of eGFR (p < 0.01). No statistical differences were obtained in eGFR calculated by CKiD-Cr and CKID-CysC equations regarding age, sex, percentile of height or body mass index. In patients without independent gait (wheelchair or orthosis), with more muscle atrophy and underdeveloped lower limbs (54%, n = 27), the eGFR calculated by CKID-Cr was higher than in the patients who are ambulatory (119.0 (102.8-150.0) vs 91.6 (64.5-111.8); p = 0.01). On the other hand, there were no differences regarding eGFR obtained by CKiD-Cr and CKID-CysC equations in all those two groups of patients (p = 0.64). Proteinuria was detected in 39% (n = 15) of the patients with stage 1 CKD and of these 87% (n = 13) had CKD upstaging using CKID-CysC equation. In addition, the difference between the median Cr-eGFR and CysC-eGFR was significantly higher in the group of patients with proteinuria (53.1 (36.2-59.7) vs 32.6 (13.4-45.9); p = 0.007). Proteinuria was significantly higher in the group of children with more muscle atrophy, without independent gait (wheelchair or orthosis) compared to ambulatory (0.30 (0.12-0.43) vs 0.12 (0.06-0.20); p = 0.021).

**Conclusions:** In pediatric patients with NB and poor muscle mass Cr-based formulas can overestimate eGFR and delay the diagnosis and correct staging of CKD. In these patients CysC-based equations seem to be more reliable in assessing kidney function. In children with NB proteinuria appears to be a possible early and sensitive marker of CKD progression, mostly in those with more muscle depletion.

**#4879**

**PREDICTORS OF KIDNEY DISEASE PROGRESSION IN MALES WITH X-LINKED ALPORT SYNDROME**

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**Background and Aims:** Alport’s syndrome is the second most common monogenic cause of end-stage renal disease (ESRD). Males with X-linked Alport’s syndrome (XLAS) have a high risk of early ESRD development. The aim of study was to determine the predictors of unfavorable renal prognosis in boys with XLAS.

**Method:** The children with genetically confirmed XLAS (n = 84, age 8.7±4.3 yrs, eGFR 102±16.2 ml/min/1.73 m2, 59 pts with missense COL4A5 mutations) were included in observation single center study (FU 6.8±2.4 yrs). Seventy three pts (q = 0.87) were treated with ACEi (age of start 7.6±3.3 yrs, dose for Ramipril 2.7±0.8 mg/m2/day). Arterial blood pressure (BP), proteinuria (Pt, mg/m2/day), eGFR (Schwartz equation, ml/min/1.73 m2), gene mutation type and ACEi-treatment data (age of pts and disease stage at the therapy start, ACEi dosage, dynamics of Pr and eGFR) were obtained and updated for each patient. BP >90 perc for gender, age and height was defined as uncontrolled (uBP); Pr was categorised according to its level as a low (100<250 mg/m2/day), moderate (250-500 mg/m2/day), high (>500-1000 mg/m2/day) and nephrotic (>1000 mg/m2/day). Gene mutations were divided into severe (nonsense, deletion, splicing) and less severe (missense) mutations. The eGFR<60 ml/min/1.73 m2 was defined as primary outcome.

**Results:** Twenty seven pts (q = 0.24, age 13.5±2.96 yrs) reached the end point during observation period. Non-missense COL4A5 mutations (HR = 4.28, 95% CI 1.47-12.4, p = 0.007), uBP (HR = 20, 95% CI 4.68-29.6, p < 0.001), persistent Pr >250 mg/m2/day (HR = 20, 95% CI 3.36-21, p < 0.001), absence of ACEi treatment (HR = 10.7, 95% CI 2.45-147, p = 0.02) or start therapy at proteinuric stage of disease (HR = 20, 95% CI 2.2-138, p < 0.001) were the risk factors of disease progression. Multiple regression analysis adjusted for age, initial eGFR revealed that late start of ACEi treatment (β = 0.23, p = 0.036), persistence of uBP (β = 0.26, p = 0.008) and Pr > 250 mg/m2/day (β = 0.17, p = 0.04) had independent significance and predict unfavorable renal prognosis (R = 0.76, R2 = 0.57, p < 0.000).

**Conclusion:** Persistent proteinuria and uncontrolled blood pressure, initiation of ACEi treatment at the proteinuric stage of glomerulopathy are the factors of unfavorable prognosis in male with XLAS.
Conclusion: Our data indicate that PPARγ agonist pioglitazone not only attenuates the TGF-β induced miR-21 overexpression, but also the renal dysregulation of miR-130a and miR-199, supporting its anti-fibrotic effects.

REFERENCE

#5591
CIRCULATING ACTIVIN A REFLECTS THE SEVERITY OF RENAL FIBROSIS IN BIOPSY-PROVEN KIDNEY DISEASES—THE TAIPEI RENAL BIOPSY COHORT STUDY
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Taipei Veterans General Hospital, Division of Nephrology, Department of Medicine, Taipei, Taiwan, Rep. of China

Background and Aims: Despite considerable evidence indicating circulating activin A as a novel renal biomarker, its performance for predicting the severity of renal fibrosis and major adverse renal events (MARE) has not yet been extensively studied.

Method: We sought to assess the relationship between plasma activin A, renal fibrosis severity, and incidence of MARE in 339 patients undergoing clinically indicated native renal biopsies. To determine the primary source of circulating activin A, RNA-sequencing and histological analyses were performed on kidney biopsy specimens from patients with chronic kidney disease (CKD). We also conducted in vitro experiments to investigate whether inhibiting endogenous activin A could attenuate TGF-β-mediated activation of cultured fibroblasts.

Results: The median baseline eGFR and proteinuria were 36 mL/min/1.73 m² and 2.9 mg/mg creatinine, respectively. After multivariable adjustment, elevated plasma activin A was associated with the extent of renal fibrosis. Histological analysis showed increased activin A expression in kidney tissues from patients with CKD, mainly in interstitial myofibroblasts. RNA-sequencing of tubulointerstitial tissue from human biopsy samples also revealed a direct correlation between tissue activin A mRNA expression and plasma activin A levels. During a median follow-up of 22 months, 113 participants suffered MARE. Cox proportional hazards analysis revealed that plasma activin A was associated with higher risk of renal events; however, the association became insignificant after correcting for confounders. Results from in vitro studies demonstrated that knocking down activin A expression could prevent TGF-β-induced activation of NRK49F fibroblasts.

Conclusion: The findings of this study support activin A as a potential diagnostic and therapeutic target in fibrotic kidney disease.

Figure 1: Cumulative incidence of MARE associated with low vs high plasma activin A (ActA) group in patients undergoing clinically indicated kidney biopsies. The median follow-up time for each group was as follows: for the high ActA group 19.4 months (interquartile range 10.5–28.7) and the low ActA group 23.6 months (interquartile range 16.7–32.6).
Figure 2: Reduction of TGF-β-induced pro-fibrotic effects by interrupting activin A signaling in renal fibroblasts. (A and B) The qPCR-based analysis of mRNA levels of *Inhba* (A), *Acta2*, *Ccn2*, and *Col3a1* (B) in NRK49F cells transfected with negative control or si-*Inhba* following treatment with vehicle or 10 ng/ml TGF-β for 24 h. (C) Representative images of Western blotting showing the protein expression levels of activin A, collagen 3a1, and α-SMA in different groups of NRK49F cells. (D) Densitometric analysis of the western blot results presented in C.

#5879
PILOT MONITORING STUDY IN PATIENTS WITH DIABETIC KIDNEY DISEASE USING NORA APPLICATION

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¹Vall d’Hebron, Hospital, Nephrology, Spain and ²Vall d’Hebron, Hospital, Neurology, Spain

**Background and Aims:** Diabetic Kidney Disease (DKD) is the most common cause of end-stage chronic kidney disease (CKD), conditioning these patients to a worse renal prognosis and higher cardiovascular mortality and/or requirement for renal replacement therapy. The use of novel information and communication technologies (ICTs) focused on the field of health, may facilitates a better quality of life and disease control in these patients. Our objective is to evaluate the effect of monitoring DKD patients using NORA-app.

**Method:** Prospective feasibility/validation study of NORA-app in patients with DKD stage G3bA3 or higher, followed in outpatient clinics of a tertiary care hospital. NORA-app is an application for smartphones designed to control risk factors, share educational medical information, communicate via chat with health professionals, increase treatment compliance (Morisky-Green), and collect patient reported outcomes such as anxiety and depression using HADs scale. Clinical-laboratory variables were collected at 3 months and compared to control patients who declined using NORA-app.

**Results:** From 01/01/2021 to 03/03/2022 the use of NORA-app was offered to 118 patients, 82 accepted and 36 declined (controls). After a mean follow-up period of 6.04 months and at the time of data extraction 71 (86.6%) NORA-app patients remain active users, 2 have completed the follow-up at one year and 9 are inactive (3 due to death and 6 due to non-locatable). There were no differences in baseline characteristics including Creatinine [2.1 (1.6-2.4) vs. 1.9 (1.5-2.5)] mg/dL and alb/creat [962 (475-1784) vs. 1036 (560-2183)] mg/gr between Nora and control patients respectively. The therapeutic compliance rate in the NORA-app group was 77%, improving at 90 days to 91%. Patients in the NORA-group showed significantly lower levels of alb/creat than controls (768 (411-1971) mg/g Vs 2039 (974-3214) p = 0.047) at 90-day follow-up.

**Conclusions:** In patients with DKD the use of NORA-app was maintained in the long-term, leading to high levels of treatment compliance, and achieving a better disease control. Our study suggests that the generalized use of ICTs may help in the personalized monitoring of these patients to delay the progression of kidney disease.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Use of the app (n = 40)</th>
<th>I don’t use the app (n = 21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinina, mg/dL</td>
<td>2.3 (1.9-2.7)</td>
<td>2.1 (1.7-2.9)</td>
<td>0.763</td>
</tr>
<tr>
<td>FGe (CKD-EPI ml/min/1.73m²)</td>
<td>26.4±8.5</td>
<td>28.7±10.6</td>
<td>0.169</td>
</tr>
<tr>
<td>Albuminuria, mg/gr</td>
<td>768 (411-1971)</td>
<td>2039 (974-3214)</td>
<td>0.047</td>
</tr>
<tr>
<td>HbA1C, %</td>
<td>6.9 (6.3 - 7.5)</td>
<td>7.3 (6.3 - 7.9)</td>
<td>0.309</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>158±41</td>
<td>167±34</td>
<td>0.179</td>
</tr>
<tr>
<td>Cholesterol HDL, mg/dL</td>
<td>42±10</td>
<td>44±8</td>
<td>0.179</td>
</tr>
<tr>
<td>Cholesterol LDL, mg/dL</td>
<td>84±34</td>
<td>82±27</td>
<td>0.578</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>12.9±2.2</td>
<td>13.0±2.0</td>
<td>0.419</td>
</tr>
<tr>
<td>Ferritin, ng/mL</td>
<td>214 (57 - 313)</td>
<td>173 (63 - 251)</td>
<td>0.747</td>
</tr>
<tr>
<td>IST, %</td>
<td>30±11</td>
<td>25±5</td>
<td>0.957</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.6 (9.2-9.8)</td>
<td>9.7(9.3 - 9)</td>
<td>0.220</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>3.7 (3.4-4.1)</td>
<td>3.7 (3.3-4-3)</td>
<td>0.424</td>
</tr>
<tr>
<td>PTH, pg/mL</td>
<td>186 (119-286)</td>
<td>158 (120-244)</td>
<td>0.850</td>
</tr>
<tr>
<td>Calcidiol, ng/mL</td>
<td>16.3 (10.7-26.)</td>
<td>16.3(9.7-28.0)</td>
<td>0.348</td>
</tr>
<tr>
<td>Sodium mmol/L</td>
<td>139±2.0</td>
<td>140±1.9</td>
<td>0.428</td>
</tr>
<tr>
<td>Potassium mmol/L</td>
<td>4.6±0.6</td>
<td>4.6±0.5</td>
<td>0.471</td>
</tr>
</tbody>
</table>
RISK FACTORS AND TRANSITIONAL PROBABILITY OF CLINICAL EVENTS IN KOREAN CKD PATIENTS USING THE MULTI-STATE MODEL: RESULTS FROM THE KNOW-CKD STUDY

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Background and Aims: Compared to western countries, Korean CKD patients show distinctive differences in clinical outcomes including lower cardiovascular disease (CVD) and higher end-stage kidney disease (ESKD) events. This study analysed the risk factors, transition probability and cumulative hazards associated with clinical events using the multi-state model.

Method: This study included 1423 patients at CKD stages 1-4 from Korea NCohort Study for Outcome in Patients With Chronic Kidney Disease. Multivariate multi-state model analysis was performed to investigate the risk factors, 10-year transition rate and cumulative hazard estimates for five clinical event status including ESKD, CVD, death, death after ESKD and death after CVD events.

Results: Among 1423 patients (age 54 [44-63] years), the overall prevalence of clinical events were the following: ESKD (22.6%), CVD (7.5%), death (3.3%), death after ESKD (3.6%) and death after CVD (1.2%). Different risk factors were associated with different clinical outcomes and in particular the risk factors associated with higher ESKD event were underlying CVD, diabetes, polycystic kidney disease, fibroblast growth factor-23 while hypertension, increased age and estimated glomerular filtration rates were associated with lower risks. The 10-year progression probability for each event status include the following: 0.23 for ESKD, 0.08 for CVD, 0.04 for death, 0.09 for death after ESKD and 0.01 for death after CVD (Figure 1). The 10-year cumulative hazard estimates for each event status were the following: ESKD [0.43, 95% CI (0.37-0.49)], CVD [0.12, (0.10-0.15)], death [0.05, (0.03-0.06)], death after ESKD [0.52, (0.20-0.84)] and death after CVD [0.27, (0.15-0.40)] (Figure 2).

Conclusion: Different risk factors were associated with varying clinical outcomes in Korean CKD patients. The 10-year progression probability was the highest in ESKD followed by death after ESKD events. Also, the 10-year cumulative hazard estimate was the highest for death after ESKD followed by ESKD events. These findings correlate with the distinctive clinical outcome features of Korean CKD patients.

Figure 1: 10-year progression probability for each clinical event status.
INTERACTIONS BETWEEN FIBROBLAST GROWTH FACTOR 23 AND SYSTEMIC INFLAMMATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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1Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Department of Nephrology, Dialysis and Renal Transplantation, Milan, Italy, 2Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Renal Research Laboratory, Milan, Italy and 3University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Background and Aims: In patients with Chronic Kidney Disease (CKD), serum concentration of Fibroblast Growth Factor 23 (FGF23) is inversely correlated with Glomerular Filtration Rate (eGFR), as an adaptive mechanism to counterbalance the alterations of mineral metabolism. Transcription, secretion and cleavage from the intact form (iFGF23) to the c-terminal fraction (cFGF23) are regulated by several mechanisms among which inflammatory mediators seem to play a significant role. We investigated whether there was any correlation between FGF23 and several inflammatory mediators.

Method: In the present study we evaluated cross sectionally the correlation between FGF23 (iFGF23 and c-FGF23) and some pro-inflammatory (IL-6, TNFα) and anti-inflammatory (IL-10) cytokines in a cohort of 111 prevalent CKD patients stages III-V not yet on dialysis. We excluded patients with infections or chronic inflammatory diseases in the last 3 months, neoplasia or under immunosuppressive therapy. FGF23 and cytokines were dosed by ELISA.

Results: Descriptive characteristics of the cohort are reported in Table 1. We found an increase in inflammation as eGFR declines: IL6 (r = -0.315, p < 0.001), TNFα (r = -0.202, p = 0.033) and MCP1 (r = -0.278, p = 0.003). Furthermore, the ratio between C-terminal FGF23 to intact FGF23 (c/iFGF23) was directly correlated to eGFR, even if it did not reach statistical significance (r = 0.127, p = 0.113). The correlations between FGF23 and markers of osteo-mineral metabolism and inflammation are reported in Table 2. We found positive correlations of iFGF23 with: IL-6 (r = 0.465, p < 0.001), TNFα (r = 0.241, p = 0.009) and IL-10 (r = 0.197, p = 0.061). After the adjustment for eGFR, iFGF23 maintained its correlations only with IL-6 (r = 0.370, p < 0.001) and TNFα (r = 0.163, p = 0.044) while c/iFGF23 was negatively correlated with IL-6 (r = -0.251, p = 0.008) and positively with MCP-1 (r = 0.204, p = 0.032).

Conclusion: Our data confirm that in CKD patients, as the renal function declines, there is an important increase of inflammatory cytokines and a tendency to an impaired cleavage of FGF23 from the intact to the C-terminal form. Furthermore, we observed strong correlations of iFGF23 with several inflammatory cytokines (IL-6, TNFα, IL-10) that seem to be independent of the adjustment for eGFR, even if it did not reach statistical significance (r = 0.264, p = 0.061).
of eGFR. On the contrary we did not find any correlation of cFGF23 with inflammatory mediators, except for MCP-1. Therefore, we believe that overall our results suggest that inflammatory markers are differently associated with cFGF23 and iFGF23, as if inflammation may independently influence FGF23 turnover (i.e., c/iFGF23 ratio).

#4204
MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING BIOMARKERS OUTPERFORM LAB BIOMARKERS FOR PREDICTING PROGRESSION OF DIABETIC KIDNEY DISEASE
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1Antaros Medical, Molndal, Sweden and 2Sahlgrenska University Hospital, Gothenburg, Sweden

Background and Aims: We recently showed that comprehensive non-contrast multiparametric Magnetic Resonance Imaging (mpMRI) allowed functional and structural assessment of diabetic kidney disease (DKD) and that an imaging endpoint, R1 cortex, showed significant predictive property for progression of DKD. We further investigated the performance of other MRI and lab biomarkers for predicting disease progression.

Method: In this prospective study, 38 DKD subjects aged 18–79 years and 20 age- and gender-matched healthy volunteers (HV) were included at baseline. 31 DKD subjects (2 stage 2, 13 stage 3, 14 stage 4, and 2 stage 5) and 17 HV were re-examined at 2 years ± 6 months. Clinical and lab examination, iohexol clearance for measured glomerular filtration rate (mGFR), urine albumin:creatinine ratio (UACR) and mpMRI were performed at both visits. A wide range of MRI biomarkers associated with kidney hemodynamics, oxygenation and macro/microstructure were included for evaluation. Disease progression was defined by at least one of the following at 2 years: decrease in mGFR slope of >5 mL/year/1.73 m²; worsening UACR category; or any major adverse kidney event defined as sustained decrease in eGFR of >40%; doubling of serum creatinine from baseline; development of kidney failure with mGFR <15 ml/min/1.73 m²; or death from renal cause. Univariable logistic regression analyses were performed to discriminate between progressors and non-progressors using each relevant lab and imaging endpoint as a predictor variable.

Results: Mean 2-year mGFR decline (ml/min/1.73 m²) in DKD patients was -2.7± 5.4 and in HV -1.9 ± 10.7. 13/31 (42%) DKD subjects and 4/17 (24%) HV progressed. Key lab biomarkers are shown in Table 1 and MRI biomarkers in Table 2.

Conclusion: Of all analyzed biomarkers, only the imaging biomarker R1 cortex, which reflects molecular environment viscosity, fibrosis, and inflammation (interstitial oedema, cellular swelling) showed significant predictive property for progression of DKD. UACR trended towards significance but was not statistically significant. R1 cortex outperformed all other imaging and lab biomarkers, but further studies with R1 cortex as a pre-specified endpoint are required to confirm these results.

Table 1: Logistic regression to predict 2-year progression using lab biomarkers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Progressor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>p-value</th>
<th>ROC AUC</th>
</tr>
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<tr>
<td>mGFR (mL/min/1.73 m²)</td>
<td>N</td>
<td>36</td>
<td>49.4</td>
<td>25.3</td>
<td>0.95</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>12</td>
<td>50</td>
<td>33.6</td>
<td>.</td>
<td></td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>N</td>
<td>36</td>
<td>51.5</td>
<td>23.4</td>
<td>0.50</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
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<td>12</td>
<td>50</td>
<td>23.4</td>
<td>.</td>
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</tr>
<tr>
<td>eGFR creat+cystatin C (2012) (mL/min/1.73 m²)</td>
<td>N</td>
<td>36</td>
<td>48.3</td>
<td>23.9</td>
<td>0.85</td>
<td>0.54</td>
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<tr>
<td></td>
<td>Y</td>
<td>12</td>
<td>46.8</td>
<td>28.3</td>
<td>.</td>
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</tr>
<tr>
<td>UACR ratio (g/mol creatinine)</td>
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<td>36</td>
<td>25.5</td>
<td>39.7</td>
<td>0.05</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>12</td>
<td>77.8</td>
<td>117.9</td>
<td>.</td>
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<tr>
<td>C-reactive protein (CRP) (mg/L)</td>
<td>N</td>
<td>36</td>
<td>3.44</td>
<td>5.85</td>
<td>0.22</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>12</td>
<td>1.5</td>
<td>0.80</td>
<td>.</td>
<td></td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>N</td>
<td>36</td>
<td>50.9</td>
<td>16.1</td>
<td>0.79</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>12</td>
<td>49.6</td>
<td>12.4</td>
<td>.</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>N</td>
<td>36</td>
<td>39.3</td>
<td>2.8</td>
<td>0.72</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>12</td>
<td>39.7</td>
<td>2.7</td>
<td>.</td>
<td></td>
</tr>
</tbody>
</table>
**Background and Aims:** Progression of chronic kidney disease (CKD) is a compound process, where activation of immunocompetent cells and subclinical inflammation play a pivotal role. Enhanced atrophy of the tubular cells, and finally, gradual fibrosis of tubulointerstitial tissue, are responsible for irreversible character of the disease. Multiple molecules influence above-mentioned processes. Growth differentiation factor (GDF)15, a member of TGF-β cytokine superfamily, is a marker of inflammation and an integrative signal in both acute and chronic stress conditions. Elevated serum concentrations of GDF15 were associated with increased risk of development and progression of CKD in adults, as well as with mortality in this group of patients. Our previous investigation revealed increased serum GDF15 concentrations in children on chronic dialysis. Epidermal growth factor (EGF), a tubule-specific protein, promotes proliferation, differentiation and migration of epithelial cells, and therefore, modulates regeneration of injured renal tubules. Decreased concentrations of EGF in urine were observed in variety of kidney diseases, including diabetic nephropathy, lupus nephritis or CKD. Our previous analysis of EGF serum concentrations in CKD children confirmed their decreased values on chronic dialysis. Neopterin is a product of activated monocytes and macrophages and serves as a marker of cell-mediated immunity. Elevated serum concentrations of neopterin were observed in CKD adult patients, our previous investigation revealed increased serum GDF15 concentrations in children on chronic dialysis. Epidermal growth factor (EGF), a tubule-specific protein, promotes proliferation, differentiation and migration of epithelial cells, and therefore, modulates regeneration of injured renal tubules. Decreased concentrations of EGF in urine were observed in variety of kidney diseases, including diabetic nephropathy, lupus nephritis or CKD. Our previous analysis of EGF serum concentrations in CKD children confirmed their decreased values on chronic dialysis. Neopterin is a product of activated monocytes and macrophages and serves as a marker of cell-mediated immunity. Elevated serum concentrations of neopterin were observed in CKD adult patients, our previous investigation revealed increased serum GDF15 concentrations in children on chronic dialysis.

**Method:** The study group consisted of 153 children with pre-dialysis CKD stages 1-5 (stage 1 – 27 patients, stage 2 – 26 patients, stage 3 – 51 patients, stage 4 – 28 patients, stage 5 – 21 patients). EGF, GDF-15 and neopterin serum concentrations were assessed by ELISA. The patient database was implemented into the artificial neural network. In detail, the recursively selected subsets of input variables constituted the input layer of an artificial neural network built of perceptrons (multi-layer perceptron). Anthropometric data, biochemical parameters, EGF, GDF15 and neopterin were included into the model, serum creatinine and eGFR, as direct classifiers of CKD stage, were excluded. Various models were tested, regarding their accuracy, AUROC and Matthews correlation coefficient (MCC) values.

**Results:** EGF serum concentrations decreased gradually, whereas GDF15 and neopterin values rose systematically with CKD progression, keeping statistically significant inter-stage differences. Moreover, the most precise ANN model, among the tested artificial neural networks, contained EGF, GDF15 and neopterin as input parameters and classified patients into either CKD 1-3 or CKD 4-5 groups. This model has put new patients into appropriate classes with excellent Accuracy of 96.77%, AUROC 0.9169 and Matthews correlation coefficient (MCC) of 0.9157.

**Conclusion:** The presented model of an artificial neural network, with serum concentrations of EGF, GDF15 and neopterin as input parameters, may serve as a useful predictor of CKD progression in the pediatric population. It suggests the essential role of inflammatory processes, defined by newly discovered markers, in the renal function decline towards advanced stages of CKD in children.

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**Table 2: Logistic regression to predict 2-year progression using MRI biomarkers.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Progessor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>p-value</th>
<th>ROC AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial flow (ml/min/1.73 m²)</td>
<td>Y</td>
<td>12</td>
<td>690</td>
<td>301</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Y</td>
<td>12</td>
<td>51.9</td>
<td>11.9</td>
<td>0.63</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>End diastolic velocity (cm/s)</td>
<td>Y</td>
<td>12</td>
<td>11.5</td>
<td>5.3</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Y</td>
<td>12</td>
<td>0.76</td>
<td>0.08</td>
<td>0.45</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>ASL perfusion cortex (ml/100g/min)</td>
<td>Y</td>
<td>12</td>
<td>117</td>
<td>60</td>
<td>0.31</td>
<td>0.58</td>
</tr>
<tr>
<td>Global Perfusion (ml/100g/min)</td>
<td>Y</td>
<td>12</td>
<td>98</td>
<td>44</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>ADC cortex (10-3 mm²/s)</td>
<td>Y</td>
<td>12</td>
<td>2.39</td>
<td>0.21</td>
<td>0.50</td>
<td>0.55</td>
</tr>
<tr>
<td>R1 cortex (s-1)</td>
<td>N</td>
<td>36</td>
<td>0.67</td>
<td>0.04</td>
<td>0.03</td>
<td>0.69</td>
</tr>
<tr>
<td>R1 medulla (s-1)</td>
<td>Y</td>
<td>12</td>
<td>0.64</td>
<td>0.06</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>R2* cortex (s-1)</td>
<td>N</td>
<td>36</td>
<td>0.55</td>
<td>0.02</td>
<td>0.28</td>
<td>0.62</td>
</tr>
<tr>
<td>R2* medulla (s-1)</td>
<td>N</td>
<td>36</td>
<td>1.4</td>
<td>1.4</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Kidney parenchyma volume (ml/1.73 m³)</td>
<td>N</td>
<td>36</td>
<td>192</td>
<td>39</td>
<td>0.62</td>
<td>0.53</td>
</tr>
</tbody>
</table>

#4277

**EGF, GDF-15 AND NEOPTERIN AS PREDICTORS OF CHRONIC KIDNEY DISEASE PROGRESSION IN CHILDREN BY MEANS OF ARTIFICIAL NEURAL NETWORK MODELS**

Agieszka Bargenda-Lange¹, Jakub Stojanowski², Tomasz Gołębiewski² and Kinga Musial³

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#4640

**PREDICTION OF CHRONIC KIDNEY DISEASE PROGRESSION WITH ARTIFICIAL INTELLIGENCE: A CHALLENGE WITHIN OUR REACH**

Oscar Galles¹, Miriam Caravaca Rodriguez¹, Remo Suppi², Edwar Macias³, Antoni Morell³, Jordi Comas⁴, Elisenda Martinez⁶, Tomas Salas⁶ and Jose Ibeas⁷

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**Background and Aims:** Chronic Kidney Disease (CKD) is a common and debilitating condition that affects over 850 million people worldwide. The disease is associated with high mortality rates that can reach up to 10-15%...
per year, multiple complications, among which cardiovascular ones stand out. These complications can contribute to the progression of CKD, and this in turn to the appearance of complications, feeding each other. Despite the availability of clinical guidelines and predictive models, accurately predicting disease progression and identifying risk factors for progression in CKD patients remains a challenge. The limitations of current methodologies, including simplifying complex relationships and relying on linear assumptions, have hindered progress in this area. The advancement of Artificial Intelligence and Machine Learning has provided a new opportunity to address these challenges. The goal of this study was to evaluate the performance of gradient boosting algorithms in predicting the progression of renal disease in a large dataset of 1327 patients with a follow up of 10 years.

**Method:** Design: Retrospective analysis of a historical cohort from the Register of Renal Patients of Catalonia (RMRC) and the Data analytics program for health research and innovation (PADRIS) from Health Quality and Assessment Agency of Catalonia (AQuAS). Inclusion Criteria: > 18 y.o. CKD stages from 2 to Renal Replacement Therapy (RRT) and adequate data after pre-processing the sample, N = 1,327 patients with 27,572 records. Follow up of 10 years (January 2010 - December 2020). Variables: Age, gender, BMI, Diagnoses

**Method:** By using Light Gradient-Boosting Machine (LGBM) testing CKD progression prediction horizon in quarterly windows for multiple periods. Methodology: 1. Pre-processing of the sample and data. 2. Training and testing for variables exploration. 3. Dataset structuring in quarterly windows. 4. Samples randomization and data separation for a 5-fold cross-validation (20% test - 80% training). 5. Training and tuning of LGBM model for different prediction horizons.

**Results:** Age: 62 ± 13 years; Gender: 34% female, 66% male. Best prediction horizon was for 8 quarters (2 years), with a ROC curve of 0.967 and accuracy of 0.960. The 10 variables with major relevance in the model in order were estimated Glomerular Filtration Rate, Age, Microalbuminuria, BMI, HDL, Glucose, Urea, Platelets, Triglycerides and Sodium.

**Conclusion:** 1. The prediction of CKD progression can benefit from the use of Machine Learning with results that outperform methods based on classical statistics. 2. It can allow the individualization of the prognosis and thus be able to carry out early interventions to improve the prognosis.

**Table 1: Metrics list for LGBM Classifier.**

<table>
<thead>
<tr>
<th>Metric Stage</th>
<th>Accuracy</th>
<th>Precision</th>
<th>Recall</th>
<th>F1 Score</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>-</td>
<td>0.795</td>
<td>0.854</td>
<td>0.824</td>
<td>0.986</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>0.793</td>
<td>0.806</td>
<td>0.799</td>
<td>0.944</td>
</tr>
<tr>
<td>4 &amp; 5</td>
<td>-</td>
<td>0.920</td>
<td>0.896</td>
<td>0.908</td>
<td>0.970</td>
</tr>
<tr>
<td>Avg.</td>
<td>0.860</td>
<td>0.836</td>
<td>0.852</td>
<td>0.844</td>
<td>0.967</td>
</tr>
</tbody>
</table>

**Figure 1:** ROC Curve for stages 2, 3, 4, and 5 of CKD.

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**Background and Aims:** Chronic kidney disease (CKD) is widely linked to chronic inflammation, with a higher incidence in the advanced stages of the disease. Recognition of systemic inflammation may be useful for prompt diagnosis and management of various CKD related disorders and may open the door towards the development and application of anti-inflammatory strategy treatments. This case-control and cross-sectional study investigates the association of neutrophil to lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), total iron binding capacity (TIBC) and serum albumin with high serum interleukin-6 (IL-6) in children with chronic kidney disease (CKD).

**Method:** NLR and PLR were measured in 53 patients (median age: 12.9 years) and 25 healthy controls, stratified by age and sex. Lipid and iron profile, glucose tolerance parameters, serum albumin, uric acid and IL-6 were measured in the patient group.

**Results:** Compared to controls, NLR and PLR were higher in patients (p = 0.004 and p = 0.032 respectively), and particularly in those with CKD on dialysis (CKD 5D) (17 patients) (p < 0.001 and p = 0.001). LnIL-6 was correlated to NLR (rs = 0.344, p = 0.014), albumin (rs = -0.350, p = 0.011) and TIBC (rs = -0.345, p = 0.012) after adjustment for CKD stage, while the correlation between lnIL-6 and PLR was not significant (rs = 0.206, p = 0.151). Patients with NLR ≥1.7, TIBC ≤300 μg/dl and albumin ≤3.8 g/dl presented a higher risk for increased IL-6 (15 patients) regardless CKD stage (OR 5.499, 95% CI 1.272-22.017, p = 0.016, OR 9.818, 95% CI 2.311-41.766, p = 0.002 and OR 7.543, 95% CI 1.891-30.083, p = 0.004). NLR ≥1.7 and TIBC ≤ 300 μg/dl and serum albumin ≤ 3.8 g/dl with the highest sensitivity (73.3%), while NLR ≥ 1.7, TIBC ≤ 300 μg/dl and serum albumin ≥ 3.8 g/dl with the highest specificity (97.4%).
Conclusion: Both NLR and PLR increase in pediatric CKD, especially in CKD 3D. NLR rather than PLR may serve as a diagnostic marker of systemic inflammation in pediatric CKD, along with TIBC and serum albumin.

CORTICAL IRON DEPOSITION ASSESSED BY MAGNETIC RESONANCE IMAGE IS ASSOCIATED WITH KIDNEY FIBROSIS

Carlos Couceiro1, Sergi Codina1, Diego Sandova1, Laia Oliveras1, Isabel Puig1, Eugenia De Lama1, Anna Sola2, Anna Manonelles1, Edoardo Melilli1, Nuria Montero3, Ana Coloma1, Alexandre Fava1, Mate Maus3, Manuel Serrano1 and Josep Cruzado2

1Bellvitge University Hospital, L’Hospitalet de Llobregat, Spain, 2IDIBELL Institut d’Investigació Biomèdica de Bellvitge, L’Hospitalet de Llobregat, Spain and 3IRB Barcelona - Institute for Research in Biomedicine, Barcelona, Spain

Background and Aims: Fibrosis is responsible for the loss of kidney function as a result of several insults, such as ischemia-reperfusion injury or hyperfiltration. This process can continue even after cessation of the primary insult, as documented in acute kidney injury to chronic kidney disease. Recently, we discovered that iron accumulation is a hallmark of fibrotic diseases [1]. We found that in mouse models, iron deposition in the kidney accompanies the progression of the disease. Based on these results, we propose that chronic-low grade hemolysis produced in situation like ischemia-reperfusion injury may be one of the drivers of fibrosis through the damage in the filtrated hemolytic iron cause to the kidneys. Early detection of this iron could help the detection of ongoing fibrogenesis and improve the outcomes by prompt intervention. The challenge of this approach is the lack of non-invasive markers of fibrosis. We evaluated if magnetic resonance image (MRI)-based detection of iron levels in the kidney are correlated to fibrosis in biopsies from kidney transplant recipients.

Method: After approval from the Institutional Revision Board, we carried out a transversal study in our center between 2020 and 2021. We evaluated iron deposits through MRI in patients who underwent a kidney biopsy (per protocol or by clinical indication) and its association with histological parameters. MRI was performed at the same period the biopsy was done. Iron deposits were assessed by using the R2* sequence considering the Grasedonio protocol [2].

Results: We collected data from 15 kidney transplant recipients. Mean age was 58.3 years old. Mean time from kidney transplant to the biopsy was 4.3 years and mean eGFR was 44.4 ml/min/1.73 m². We analyzed by MRI the R2* signal in the kidney cortex, and their level of fibrosis measured on the biopsies (IFTA score, interstitial fibrosis and tubular atrophy). We found that patients with high IFTA score (2 and 3) presented with significantly higher R2* signal (p = 0.005), than patients with low IFTA score (0 and 1). We also found positive and significant correlation between IFTA (0-3) and iron deposits (Spearman correlation index: r = 0.7537, p = 0.0012).

Conclusion: Iron deposits in the kidney are higher in patients with more fibrosis, and its detection through MRI could be considered a non-invasive marker.
THE ERROR OF ESTIMATED GFR IN PREDIALYSIS CARE: IMPACT ON CLINICAL DECISION MAKING
Beatriz Escamilla Cabrera¹, Sergio Luis Lima⁴, Eduardo Gallego Valcarce², Federico González Rinne⁴, Nuria Victoria Sánchez Dorta⁴, Natalia Negrá-n Mena³, Coriolano Cruz Perera⁶, Laura Diaz Martin⁶, Armando Torres Ramírez⁶ and Esteban Porrini⁴

¹Hospital Universitario de Canarias, Nephrology Department, San Cristóbal de La Laguna, Spain, ²Hospital Universitario de Canarias, Laboratory Department, San Cristóbal de La Laguna, Spain, ³Hospital Universitario Fundación Alcorcón, Nephrology Department, Madrid, Spain, ⁴Hospital Universitario de Canarias, Laboratory of Renal Function, San Cristóbal de La Laguna, Spain, ⁵Hospital Universitario de Canarias, Nephrology Department, Spain and ⁶Hospital Universitario de Canarias, Laboratory of Renal Function, Spain

Background and Aims: The error of estimated glomerular filtration rate (eGFR) and its consequences in predialysis are unknown.

Method: We analysed 315 predialysis patients who underwent measured GFR (mGFR) by the clearance of iohexol and eGFR by 52 formulas. We evaluated the agreement between eGFR and mGFR by the concordance correlation coefficient (CCC), total deviation index (TDI) and coverage probability (CP). In a sub-analysis we investigated the impact of the error of eGFR in decisions like (i) starting dialysis, (ii) preparation for renal replacement therapy (RRT) and (iii) continuing with clinical follow-up. For this sub-analysis patients who started dialysis due to uremia or fluid overload were excluded (n = 18).

Results: Patients: 315 patients were included, 70% male and mean age was 66 ± 13 years. 38% had diabetic nephropathy. Mean mGFR was 22 ± 8 ml/min. Mean eGFR was 22 ± 8 ml/min (CKD-EPI), 22 ± 8 ml/min (MDRD) or 26 ± 10 ml/min (24-h creatinine clearance). Cystatin C measurement was available in 266 patients (84%) and averaged 2.8 ± 1.08 mg/L. Over 70% of the patients had proteinuria 1588 ± 2204 mg/24 h. Agreement between eGFR and mGFR had very low precision and accuracy in reflecting mGFR as reflected by average CCC, TDI and cp of 0.60, 70% and 22%, respectively. The error was comparable between creatinine- and cystatin-based formulas. Extreme variations -larger than 10 ml/min- between mGFR and eGFR were frequent. Differences in clinical decision making: Concerning clinical decisions, the error of formulas (mainly GFR overestimation) would have suggested (a) early unnecessary preparation for RRT in 14% of clinically stable patients evaluated by mGFR; (b) to continue with clinical follow-up in 59% of the subjects in whom RRT was indicated by low mGFR and (c) to delay the starting of dialysis in all patients (n = 6) in whom RRT was indicated based on very low mGFR without uremic symptoms or fluid overload.

Conclusion: The error of formulas in predialysis care was frequent and large and may have consequences in clinical care.
Background and Aims: Low sodium intake is associated with a lower blood pressure and less proteinuria, which are important therapeutic targets in chronic kidney disease. In contrast, a low potassium intake has been associated with higher blood pressure and a higher incidence of chronic kidney disease and cardiovascular events. Counselling of patients regarding their sodium and potassium intake requires accurate estimation of their intake, but 24-hour urinary sodium and potassium excretion can deviate substantially from actual intake. Urinary sodium-to-potassium (Na/K) ratio is a promising alternative as it is less affected by incomplete urine collections and additionally captures both the effect of sodium and potassium. Our study aimed to assess whether the Na/K ratio in 24-hour urine reflects dietary intake more accurately than separate measurement of sodium or potassium in 24-hour urine.

Method: We performed a post-hoc analysis on data from the long-term sodium balance studies Mars105 and Mars520. Ten healthy participants consumed a diet with a known sodium and potassium content and collected 24-hour urine samples for 105 or 205 days. We calculated the log fold difference between dietary intake and urinary excretion of sodium, potassium and Na/K ratio. A mixed-effects model with a random intercept per subject was used to compare these estimates of accuracy. Subsequently, we performed a subgroup analysis per salt intake level (i.e. 6, 9 or 12 grams per day) and assessed the effect of increasing the number of 24-hour urine collections.

Results: Overall, the urinary Na/K ratio underestimated dietary Na/K ratio with a median difference of -0.21 (IQR -0.47 to 0.09). Estimation of dietary Na/K ratio intake using the urinary Na/K ratio was significantly less accurate compared to using urinary sodium or potassium measurement for estimation of sodium or potassium intake (Figure 1A). Only during a salt intake of 6 grams per day, the urinary Na/K ratio did not perform significantly worse than sodium measurements. Although increasing the number of 24-hour urine measurements to three or seven improved the accuracy of the urinary Na/K ratio, it remained inferior to separate assessment of urinary sodium and potassium excretion (Figure 1B).

Conclusion: The 24-hour urinary Na/K ratio is less accurate than 24-hour urinary sodium or potassium excretion for estimation of dietary intake in a controlled setting in healthy volunteers.

#4412

URINARY SODIUM-TO-POTASSIUM RATIO DOES NOT ACCURATELY REFLECT DIETARY SODIUM-TO-POTASSIUM RATIO
Anne Myrthe van Vliet1,2, Charlotte Z wager1,2, Manfred Rauh3, Jens Titze4,5,6 and Rik Olde Engberink1,2

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Background and Aims: Low sodium intake is associated with a lower blood pressure and less proteinuria, which are important therapeutic targets in chronic kidney disease. In contrast, a low potassium intake has been associated with higher blood pressure and a higher incidence of chronic kidney disease and cardiovascular events. Counselling of patients regarding their sodium and potassium intake requires accurate estimation of their intake, but 24-hour urinary sodium and potassium excretion can deviate substantially from actual intake. Urinary sodium-to-potassium (Na/K) ratio is a promising alternative as it is less affected by incomplete urine collections and additionally captures both the effect of sodium and potassium. Our study aimed to assess whether the Na/K ratio in 24-hour urine reflects dietary intake more accurately than separate measurement of sodium or potassium in 24-hour urine.

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Results: Overall, the urinary Na/K ratio underestimated dietary Na/K ratio with a median difference of -0.21 (IQR -0.47 to 0.09). Estimation of dietary Na/K ratio intake using the urinary Na/K ratio was significantly less accurate compared to using urinary sodium or potassium measurement for estimation of sodium or potassium intake (Figure 1A). Only during a salt intake of 6 grams per day, the urinary Na/K ratio did not perform significantly worse than sodium measurements. Although increasing the number of 24-hour urine measurements to three or seven improved the accuracy of the urinary Na/K ratio, it remained inferior to separate assessment of urinary sodium and potassium excretion (Figure 1B).

Conclusion: The 24-hour urinary Na/K ratio is less accurate than 24-hour urinary sodium or potassium excretion for estimation of dietary intake in a controlled setting in healthy volunteers.

Figure 1: Differences in clinical decision based on mGFR or eGFR in patients with non-clinical indication of dialysis initiation.
CROSS-TALK BETWEEN FRAILTY AND IMMUNOSENSCENCE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Noemi Ceprian1, Paula Jara Caro Espada2, Gemma Valera Arévalo1, Claudia Yuste Lozano2, Ignacio González de Pablo2, Andrea Figuer Rubio4, Matilde Alique4, Manuel Ramírez Chamond4, Enrique Morales2 and Julia Carracedo1

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Background and Aims: Chronic kidney disease (CKD) has been proposed as a model of premature ageing. The immune system is an important factor in the ageing process and can modulate the rate of ageing. The uremic environment highly affects this system, deteriorating its functionality and increasing susceptibility to infections, cancer, and pathologies like cardiovascular disease. Also, CKD patients are highly predisposed to frailty, which increases the organism’s vulnerability to disease. This premature ageing, partially caused by the immune disorder and increased frailty, is responsible for these patients’ high morbidity and mortality. Understanding these processes and how they are affected by different treatments will help generate better nutritional, pharmacological and lifestyle strategies. For this, the aim of this study was to determine the immune and frailty status of patients with CKD and their therapies.

Method: We performed a cross-sectional study involving 18 healthy subjects (HS) and 156 patients from the Nephrology Department of the Hospital Universitario “12 de Octubre” (Madrid, Spain). The distribution of patients was as follows: 40 with end-stage renal disease (ESRD), 40 on haemodialysis (HD), 36 on peritoneal dialysis (PD) and 40 patients who had received initial kidney transplantation (KT). The frailty status of the patients was assessed by the Edmonton Frail Scale test. Lymphocyte populations (T lymphocytes, T-helper lymphocytes, T-cytotoxic lymphocytes, and B lymphocytes) and monocytes (classical, intermediate, non-classical, and the expression of the adhesion molecule ICAM-1 and co-stimulatory B7.2) were determined in peripheral blood samples.

Results: The patients were similar in age and sex. The number of frail individuals was higher in patients (ESRD p < 0.001, PD p < 0.001, KT p = 0.004) than in HS, particularly in HD (p < 0.001) (Figure 1). Regarding immune phenotype (Figure 2), HD patients showed a lower number of T-cells (p < 0.001), particularly T-helper cells (p < 0.001), than the other groups. Also, DP patients presented fewer T and T-cytotoxic cells than HS (p = 0.029, p = 0.05). Also, HD showed lower T-cytotoxic and helper/cytotoxic ratios than HS (p = 0.022; p = 0.011) and ESRD (p = 0.017; p = 0.008). The proportion of classical monocytes decreased, and the proportion of intermediate and non-classical monocytes increased in HD with respect to the other groups (p < 0.001). The expression of the costimulatory molecule B7.2 was increased in the patients with respect to HS in all monocyte subsets (Classical: ESRD p = 0.002, HD p < 0.001, PD p < 0.001, KT p < 0.001; Intermediate: ESRD p = 0.014, HD p < 0.001, PD p < 0.001, KT p = 0.002; Non-classical: ESRD p = 0.006, HD p < 0.001, PD p < 0.001, KT p = 0.013), while adhesion molecules were only elevated in HD with respect to HS in all subsets (classical p < 0.001, intermediate p < 0.001, non-classical p = 0.023).

Conclusion: The CKD patients, regardless of the treatment, showed, in general, an alteration in the lymphocyte subsets. These alterations were more significant in dialysis patients, particularly in HD patients. This group also presented the most significant alterations in monocyte subsets and higher frailty. This may explain why haemodialysis patients show major adverse outcomes compared to other treatments. Determining immune profiles can help us to relate these alterations to adverse events to carry out preventive and personalised medicine.
**Figure 2**: Description of leukocyte subpopulations. Count of T-helper cells (A), helper/cytotoxic (CD4/CD8) ratio (B), B cells (C), monocytes subsets distribution (D), and the amount of the co-stimulatory molecule B7.2 (E) and adhesion molecule ICAM-1 (F) in healthy subjects, patients with end-stage renal disease (ESRD), haemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation (KT). Statistical significance was denoted by *p \leq 0.05, **p \leq 0.01, ***p \leq 0.001 vs HS; #p \leq 0.05, ##p \leq 0.01, ###p \leq 0.001 vs ESRD; $$p \leq 0.01,$$$p \leq 0.001 vs HD; &&p \leq 0.01 vs DP.

#6600
ASSOCIATION BETWEEN ADVANCED GLYCATION END-PRODUCTS AND SARCOPENIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE
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Milan, Italy

**Background and Aims**: In patients with chronic kidney disease (CKD), there is an overproduction and accumulation of advanced glycation end-products (AGEs). Since AGEs may have detrimental effects on muscular trophism and performance, we evaluated whether they may contribute to the onset of sarcopenia in CKD patients.

**Method**: We enrolled 117 patients. The AGEs were quantified by fluorescence intensity using a fluorescence spectrophotometer and soluble receptor for AGE (sRAGE) isoforms by ELISA. As for the sarcopenia definition, we used the European Working Group on Sarcopenia in Older People (EWGSOP2) criteria.

**Results**: The average age was 80 ± 11 years, 70% were males, and the mean eGFR was 25 ± 11 mL/min/1.73 m². Sarcopenia was diagnosed in 26 patients (with a prevalence of 22%). The sarcopenic patients had higher levels of circulating AGEs (3405 ± 951 vs. 2912 ± 722 A.U., p = 0.005). AGEs were higher in subjects with a lower midarm muscle circumference (MAMC) (3322 ± 919 vs. 2883 ± 700 A.U., respectively; p = 0.005) and were directly correlated with the gait test time (r = 0.180, p = 0.049). The total sRAGE and its different isoforms (esRAGE and cRAGE) did not differ in patients with or without sarcopenia.

**Conclusion**: In older CKD patients, AGEs, but not sRAGE, are associated with the presence of sarcopenia. Therefore, AGEs may contribute to the complex pathophysiology leading to the development of sarcopenia in CKD patients.

**Table 1**: Concentration of AGEs and sRAGE isoforms in sarcopenic and non-sarcopenic CKD patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N Snc (n = 91)</th>
<th>Src (n = 26)</th>
<th>p</th>
<th>P (eGFR Weighted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGEs (arbitrary unit)</td>
<td>2912 ± 722</td>
<td>3405 ± 951</td>
<td>0.005</td>
<td>0.02</td>
</tr>
<tr>
<td>sRAGE (pg/mL)</td>
<td>2338 ± 1280</td>
<td>2411 ± 1268</td>
<td>0.86</td>
<td>0.63</td>
</tr>
<tr>
<td>esRAGE (pg/mL)</td>
<td>656 ± 503</td>
<td>713 ± 448</td>
<td>0.60</td>
<td>0.96</td>
</tr>
<tr>
<td>cRAGE (pg/mL)</td>
<td>1693 ± 937</td>
<td>1698 ± 902</td>
<td>0.93</td>
<td>0.51</td>
</tr>
<tr>
<td>AGEs/sRAGE (arbitrary unit)</td>
<td>1.59 ± 0.89</td>
<td>1.8 ± 1.2</td>
<td>0.23</td>
<td>0.19</td>
</tr>
</tbody>
</table>

AGEs, Advanced Glycation End-products; sRAGE, soluble receptor for AGE; esRAGE: endogenous secretory receptor for AGE; cRAGE: cleaved receptor for AGE; CKD, chronic kidney disease; N-Snc, non-sarcopenic patients; Src, sarcopenic patients.
### Table 2: Concentration of AGEs and sRAGE isoforms classified according to the presence (yes) or absence (not) of alterations in the sarcopenic domains.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Yes</th>
<th>Not</th>
<th>p</th>
<th>p (eGFR Weighted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced MAMC*, n (%)</td>
<td>37 (31)</td>
<td>80 (69)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AGEs (arbitrary unit)</td>
<td>3322 ± 919</td>
<td>2883 ± 700</td>
<td>0.005</td>
<td>0.049</td>
</tr>
<tr>
<td>sRAGE (pg/mL)</td>
<td>2426 ± 1292</td>
<td>2350 ± 1287</td>
<td>0.77</td>
<td>0.58</td>
</tr>
<tr>
<td>esRAGE (pg/mL)</td>
<td>536 (398–707)</td>
<td>552 (368–787)</td>
<td>0.66</td>
<td>0.75</td>
</tr>
<tr>
<td>cRAGE (pg/mL)</td>
<td>1727 ± 921</td>
<td>1707 ± 959</td>
<td>0.91</td>
<td>0.53</td>
</tr>
<tr>
<td>AGES/sRAGE (arbitrary unit)</td>
<td>1.8 ± 1.1</td>
<td>1.6 ± 0.9</td>
<td>0.25</td>
<td>0.19</td>
</tr>
<tr>
<td>Reduced Gait Speed Test, n (%)</td>
<td>76 (64)</td>
<td>41 (36)</td>
<td>&lt;0.0001</td>
<td>0.001</td>
</tr>
<tr>
<td>AGEs (arbitrary unit)</td>
<td>2977 ± 750</td>
<td>3101 ± 882</td>
<td>0.42</td>
<td>0.26</td>
</tr>
<tr>
<td>sRAGE (pg/mL)</td>
<td>2373 ± 1310</td>
<td>2376 ± 1249</td>
<td>0.99</td>
<td>0.90</td>
</tr>
<tr>
<td>esRAGE (pg/mL)</td>
<td>630 (368–776)</td>
<td>526 (390–720)</td>
<td>0.75</td>
<td>0.66</td>
</tr>
<tr>
<td>cRAGE (pg/mL)</td>
<td>1728 ± 972</td>
<td>1687 ± 902</td>
<td>0.82</td>
<td>0.89</td>
</tr>
<tr>
<td>AGES/sRAGE (arbitrary unit)</td>
<td>1.6 ± 0.9</td>
<td>1.6 ± 1</td>
<td>0.94</td>
<td>0.93</td>
</tr>
<tr>
<td>Reduced handgrip strength, n (%)</td>
<td>68 (58)</td>
<td>49 (42)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AGEs (arbitrary unit)</td>
<td>3054 ± 809</td>
<td>2976 ± 787</td>
<td>0.60</td>
<td>0.78</td>
</tr>
<tr>
<td>sRAGE (pg/mL)</td>
<td>2343 ± 1330</td>
<td>2416 ± 1230</td>
<td>0.76</td>
<td>0.39</td>
</tr>
<tr>
<td>esRAGE (pg/mL)</td>
<td>543 (367–718)</td>
<td>515 (384–787)</td>
<td>0.50</td>
<td>0.84</td>
</tr>
<tr>
<td>cRAGE (pg/mL)</td>
<td>1662 ± 937</td>
<td>1782 ± 938</td>
<td>0.50</td>
<td>0.23</td>
</tr>
<tr>
<td>AGES/sRAGE (arbitrary unit)</td>
<td>1.7 ± 1</td>
<td>1.5 ± 0.9</td>
<td>0.34</td>
<td>0.30</td>
</tr>
</tbody>
</table>

AGEs, Advanced Glycation End-products; sRAGE, soluble receptor for AGE; esRAGE, endogenous secretory receptor for AGE; cRAGE, cleaved receptor for AGE; CKD, chronic kidney disease; MAMC, mid-arm muscle circumference. p values less than 0.05 are indicated in bold.

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**Figure 1:** Linear regression model of comparison between AGEs, handgrip strength, and gait test time; AGEs, Advanced Glycation End-products.

### #5541

**EVALUATION OF PROTEIN MALNUTRITION IN CKD PATIENTS ON LOW-PROTEIN DIET**

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1IRCCS San Raffaele Scientific Institute, Division of Nephrology and Dialysis, Milan, Italy and 2Università Vita Salute San Raffaele, Milan, Italy

**Background and Aims:** Low-protein diet is considered crucial in patients with chronic kidney disease to slow down kidney function deterioration and control metabolic variables such as serum phosphate, urea and bicarbonate. However, low-protein diet may result in malnutrition if patients do not respect nutritional prescription. Thus, the present study examined the risk of protein malnutrition in CKD patients who started a low-protein diet.

**Method:** We analysed anthropometric variables, nutrient intake and body composition in 27 patients with CKD stage 4-5 (M/F 15/12; 69±15 years; 72±18 kg; BMI 27.3±7 kg/m²; serum creatinine 4.9±1.9 mg/dl; GFR 11±4 ml/min; 10 diabetic patients) before and after 3-months of low-protein diet (0.6 g/kg). We estimated nutrient intake with a food frequency questionnaire composed of 37 items and administered by a nutritionist who also prescribed the low-protein diet. We also measured body fat mass (FM) and free-fat mass (FFM) and appendicular skeletal muscle mass using bioimpedimetry analysis (Akern, Florence). Patients having a protein intake lower than 0.6 g/kg at the nutritional survey was defined as malnourished.

**Results:** In the whole sample, after a 3-month diet protein intake decreased from 0.87±0.23 to 0.69±0.18 g/kg (p<0.001; Wilcoxon test). Protein intake was positively correlated with 24-h urine excretion of phosphate at baseline (r = 0.69, p = 0.012) and after 3-months of diet (r = 0.62, p = 0.02). The diet induced a decrease in body weight (72±18 to 70±17 kg; p = 0.001), BMI (27.3±7 to 26.7±6.8 kg/m²; p = 0.001), FM (24±11 to 21±11 kg; p = 0.006), serum phosphate (1.68±0.33 to 1.52±0.32 mmol/l; p = 0.033) and urea (166±53 to 133±42 mg/dl; p<0.001), whereas FFM, expressed as percentage of body weight, significantly increased (69±9 to 73±8%; p = 0.011). Six patients (22%; 3 diabetic patients) had a protein intake lower than 0.6 g/kg after 3-months of diet. Their protein intake was significantly lower than that in the other 21 patients with protein intake above 0.6 g/kg (0.43±0.1 vs 0.77±0.12 g/kg; p<0.001). These patients had lower FM (4±2 vs 4±1 kg; p = 0.03) and protein intake before starting the low-protein diet than the other 21 patients (0.64±0.06 vs 0.94±0.21 g/kg; p = 0.003). Patients with protein intake lower than 0.6 g/kg slightly decreased FFM after 3 months of diet compared to the value at baseline (52±7 to 50±7 kg; p = 0.07); conversely the other 21 patients did not change FFM (51±10 to 53±11 kg; p = 0.17), but significantly decreased FM (26±11 to 23±12 kg; p<0.001).

**Conclusion:** In conclusion, protein malnutrition may occur during a low-protein diet in CKD patients with a low consumption of proteins before starting this diet. Nutritional analysis is necessary to identify CKD patients at risk of

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protein malnutrition and to adequately follow up CKD patients on low protein diet.

#3103
OMENTIN-1 AND SUBCLINICAL ATHEROSCLEROSIS IN ESKD PATIENTS UNDERGOING HEMODIALYSIS AND IN KIDNEY TRANSPLANT RECIPIENTS

Marie Teresa Zicarelli, Manco Greco, Valentina Arcidiacono, Pierangelo Presta, Alfredo Caglioni, Michele Andreucci, Francesco Dragone, Daniela Foti, Giuseppe Coppolino and Davide Bolignano

Magna Graecia University, Catanzaro-Italy, Italy

Background and Aims: In end-stage kidney disease (ESKD) patients, atherosclerosis is a key-player for cardiovascular risk, being influenced by endothelial dysfunction, inflammation and mineral dysmetabolism. Omentin-1 is an adipokine involved in various pathological conditions (diabetes, metabolic syndrome, obesity), and has recently been studied as a prognostic factor for atherosclerosis progression and mortality in the general population. In this study, we evaluated the possible relationships between Omentin-1 and incident carotid atherosclerosis in the clinical setting of ESKD.

Method: Circulating blood Omentin-1 levels were measured in a cohort of 77 asymptomatic ESKD patients (40 kidney transplant recipients, Ktx and 37 chronic hemodialysis patients, HD) and in 30 healthy controls. Carotid intima-media thickness (cIMT) was measured before a single HD session or before a Ktx outpatient visit.

Results: Omentin-1 levels were higher in the entire ESKD cohort than in healthy controls (324 [90.3-770] vs. 110 [35.4-240.9] pg/ml; p = 0.03). Ktx patients had lower levels than HD patients (p = 0.01) while higher Omentin-1 levels were found in HD patients (474.9 [197.2-1432.1] ng/ml) compared to both healthy subjects (p = 0.009) and Ktx (p = 0.01). Mean cIMT in all ESKD was 0.78 ± 0.32 mm. 36 patients (46.7%) with pathological cIMT values displayed lower Omentin-1 levels as compared with others (168.7 [51.1-457.8] vs 474.9 [197.2-1432.1] and p = 0.004). Multivariate correlations analyses indicated Omentin-1 as the stronger independent predictor of carotid atherosclerosis (β = -0.687; p = 0.03) in the whole cohort, even more than age, total cholesterol and diastolic BP.

Conclusion: In ESKD patients, Omentin-1 reflects the severity of carotid atherosclerosis independently from traditional confounders and may serve as an additive biomarker for risk prediction and risk stratification. Further studies are awaited to confirm these preliminary findings in larger cohorts.

#3949
NPY GENE POLYMORPHISMS ARE STRONGLY LINKED TO CKD PROGRESSION: A MENDELIAN RANDOMIZATION STUDY

Belinda Spoto1, Francesca Mallamaci2,3, Cristina Politi2, Rosa Parlongo4, Giovanni Luigi Tripepi1, Daniela Leonardi4, Giovambattista Capasso5 and Carmine Zoccali6,7

1CNR-Institute of Clinical Physiology, Italy, 2Nephrology, Dialysis, and Transplantation Unit (GOM-BMM), Italy, 3CNR-Institute of Clinical Physiology, Reggio Calabria, Italy, 4CNR-Institute of Clinical Physiology, Italy, 5BIOGEM, Italy, 6Renal Research Institute, United States of America and 7IPNET, Italy

Background and Aims: Neuropeptide Y (NPY) is a 36 amino-acid neuropeptide that regulates various physiological processes in both the central and peripheral nervous systems, including cardiovascular and metabolic control. We showed that high plasma NPY predicts CKD progression (NDT 2018;33:1805-1812) in a cohort of 735 patients with stage G2-5 CKD. Whether this association is causal is nature is undetermined.

Method: In the same cohort of the case study, we tested the relationship between NPY gene variability, as assessed by six single nucleotide polymorphisms (SNPs) representative of the gene haplomblock structure which explained about 80% of gene variability, and the incidence rate of renal events (diabetes/transplantation/eGFR reduction >30%) over a median follow up of 36 months (inter-quartile range 33-37 months).

Results: Three variants (rs161316 [TT, n = 563; CT+CC, n = 172], rs16140 (CC+GG, n = 413; CC, n = 322), rs16148 (CT+CC, n = 456; TT, n = 279) coherently associated to the incidence rate of renal events (HR ranging from 1.36 to 1.57, P < 0.029). A dose response relationship was found between the number of risk variants and renal events, the HR for this outcome being highest in patients with three risk genotypes (HR: 1.66, 95% CI 1.05-2.61). In a multivariate model adjusting for traditional risk factors (age, gender, smoking, diabetes, cholesterol, systolic BP and background cardiovascular comorbidities) and factors peculiar to CKD (haemoglobin, eGFR, albumin, phosphate, C-reactive protein), the association remained highly significant (P for trend = 0.001). In a separate analysis including the three variants simultaneously, only the rs161316 variant maintained an independent association with the risk for renal events (HR: 1.58, 95% CI 1.11-2.24, P = 0.01).

Conclusion: This Mendelian randomization study based on three gene variants is fully in line with findings indicating that high plasma NPY predicts a high risk for renal events and lends support to the hypothesis that NPY is causally involved in CKD progression. Establishing the functional significance of the rs161316 variant is a clinical research priority. Drugs antagonizing circulating NPY or its receptors, indeed, might favourably impact on CKD progression.

#6157
PREDICTORS OF 24 PULSE WAVE VELOCITY IN HYPERTENSIVE CHRONIC KIDNEY DISEASE PATIENTS: A CASE CONTROL STUDY

Josipa Radic1, Marijana Vučković1, Hana Dogaš1, Andrea Gelemanović1, Ela Kolak1, Dora Bučan Nenadice2 and Mislav Radic3

1University Hospital of Split, Internal Medicine Department, Nephrology and Hemodialysis Division, Split, Croatia, 2University Hospital of Split, Internal Medicine Department, Nephrology and Hemodialysis Division, Split, Croatia, 3Mediterranean Institute for Life Sciences, Croatia, 4University Hospital of Split, Nutrition and Dietetics Department, Croatia and 5University Hospital of Split, Internal Medicine Department, Rheumatology, Allergy and Clinical Immunology Division, Croatia

Background and Aims: Pulse wave velocity (PWV) is a significant predictor of chronic kidney disease (CKD) progression and death in people with impaired kidney function. It is known that patients with type 2 diabetes mellitus have higher values of PWV. Our study assessed the difference in arterial stiffness parameters (value of peripheral and central blood pressure parameters and PWV) according diabetic status and to evaluate predictors of PWV in hypertensive CKD patients.

Method: This case control, cross-sectional study included 252 hypertensive CKD patients 143 (56.7%) men and 109 (43.3%) women, aged 67 years (IQR = 15). For each participant data about sex, age, height, presence of CKD, AH and other comorbidities were collected. Laboratory parameters (urea, creatinine, estimated glomerular filtration rate (eGFR), glycated hemoglobin (HbA1c)) were obtained from peripheral blood and 24-hour urine samples were collected to analyze albuminuria. Each participant underwent 24-hour ambulatory blood pressure measurement using the IEM Mobil-O-Graph based on the oscillometry. Tanita MC780 Multi Frequency segmental body composition analyzer was used to measure body weight and level of visceral fat. Body mass index (BMI) was calculated.

Results: Out of 252 participants with AH and CKD, 107 (42.5%) also had DM. Participants with DM were older (p < 0.001), had higher pulse pressure (p < 0.001) and PWV (p < 0.001) while the levels of peripheral and central diastolic pressure (p < 0.001) were lower. Regarding body composition parameters, DM participants had higher BMI (p = 0.001) and visceral fat level (p < 0.001). Positive predictors of PWV adjusted for age, sex, presence of DM and eGFR were HbA1c (β = 0.216, p = 0.007), albuminuria (β = 0.000, p = 0.002), central and peripheral systolic and diastolic blood pressure (β = 0.035, p < 0.001; β = 0.035, p < 0.001; β = 0.033, p < 0.001; β = 0.035, p < 0.001), pulse pressure (β = 0.047, p < 0.001) and mean arterial pressure (β = 0.042, p < 0.001). Body composition parameters were not found to be significant predictors of PWV.

Conclusion: We found significant differences in 24-hour blood pressure parameters and body composition in relation to the presence of DM. One possible explanation for the lower peripheral and central diastolic blood pressure in diabetic patients is the older age of these participants. Accordingly, PWV as a parameter of arterial stiffness, which is higher in DM participants, could also be due to age difference. As for the predictors of PWV, the expected predictors were blood pressure level. HbA1c and albuminuria were also associated with PWV as parameter of arterial stiffness in CKD patients with AH.

#3383
ASSOCIATION BETWEEN MELAMINE AND PHTHALATES AND URINARY RENAL INJURY MARKERS AMONG CHILDREN AGED 4 YEARS

Hui-Ju Tsai1, Ming-Tsang Wu2 and Yi-Chun Tsai3

1Kaohsiung Municipal Ta-Tung Hospital, Family Medicine, Kaohsiung, Taiwan, Rep. of China, 2Kaohsiung Medical University, Research Center for
Background and Aims: Chronic kidney disease (CKD) is a global public health issue and the prevalence and incidence of CKD and end-stage renal disease (ESRD) in Taiwan are among the highest in the world. The pathophysiology of renal function downhill is complex and multifactorial, and previous studies suggest that we should be concerned about the effects of low-dose environmental exposure to melamine and phthalate in increasing the risk of renal injury in susceptible populations such as children. However, the sex difference in renal injury related to environmental exposure among children is unknown. The aim of this study is to investigate the relationship between early renal injury biomarkers and melamine and phthalate exposure among boys and girls aged 4 years in Taiwan.

Method: In total, 1,676 pregnant women were enrolled in the original Taiwan Maternal and Infant Cohort Study (TMICS), a multicenter birth cohort study of 9 hospitals in northern, central, southern, and eastern Taiwan from October 2012 to May 2015. Of those, 694 children aged 4 years participated in follow-up questionnaire interviews, received physical examinations and blood and urine tests from August 2016 to February 2020. After excluding 142 participants with missing data, the final statistical analysis of follow-up data included 552 children. One-spot overnight urine specimens were used to simultaneously measure melamine, 11 phthalate metabolites, and two markers of renal injury, microalbumin and N-acetyl-beta-D-glucosaminidase (NAG). Average daily intake (ADI) levels of melamine and six parental phthalates, including DEHP (di-2-ethylhexylphthalate), DiBP (Dibutyl phthalate), DnBP (Di-n-butyl phthalate), BBzP (Butyl benzyl phthalate), and DEP (Diethyl phthalate), were estimated using a creatinine excretion-based model from urine melamine and phthalate metabolites. We used a weighted quartile sum (WQS) regression model to select the most important exposure variables of ADI levels of phthalates and melamine associated with urine microalbumin to creatinine ratio (ACR) and NAG; Furthermore, to examine effects of those most important exposure variables on ACR and NAG in multivariable linear regression models. The significance was set as two-sided p < 0.05.

Results: Of them, 319 (57.8%) and 223 (42.2%) were boys and girls, respectively, with a median age of 4.0±0.8 years old. Median ADI levels (μg/kg bw/day) were 5.73 for DEHP, 1.75 for DEP, 3.23 for DnBP, 0.07 for BBzP, 1.37 for DiBP, and 1.18 for melamine and there is not significantly different between boys and girls. Using the WQS regression model to examine the association between ADI levels of melamine and phthalates and urine ACR and NAG, we found that a significant and positive association between the WQS score and ACR (β1 = 0.083, p = 0.023). ADI levels of melamine had the highest weight (0.650). Furthermore, we found that the highest (quartile 4) of ADI levels of melamine had the significantly higher ACR in all children (adjusted β = 0.131, p = 0.036), compared to other quartiles (quartile 1, 2 and 3). In subgroup analysis, the significant association between melamine intake and urine ACR was found in boys (adjusted β = 0.249, p = 0.003), not in girls.

Conclusion: Environmental exposure to melamine may be associated with urine ACR among children aged 4 years in Taiwan, and boys may be easily affected by melamine exposure.
regulate post-transcriptional gene expression) has previously been implied in pathological cardiac remodelling. Nevertheless, scarce evidence has accrued so far on a possible significance in CV morbidity and mortality in HD patients, in relationship with the presence of uremic cardiomyopathy.

**Method:** We run a pilot, prospective, multicentre cohort study involving 74 ESKD patients undergoing chronic HD from 3 different hospitals in Italy and Greece. HD patients underwent a thorough clinical, laboratory and echocardiography assessment and were then prospectively followed for 24 months or until the occurrence of a composite endpoint of (CV and all-cause) mortality or non-fatal CV events. Through a systematic review of the literature, we identified a small panel of miRNAs (30a-5p, 23a-3p, 451a and let7d-5p), which levels are known to be altered in either major CV disorders and kidney failure. miRNAs were then measured in the blood of HD patients and in a small group of matched healthy controls.

**Results:** miRNAs 23a-3p (p < 0.0001), 451a (p = 0.001), 30a-5p (p = 0.003) and let7d-5p (p < 0.0001) were all reduced in HD patients as compared with controls. Significant correlations were found between miRNAs and indexes of cardiac dysfunction such as Vmax, TAPSE and E/E', as well as with some other laboratory parameters such as uric acid, sodium, potassium, HDL and CRP. During follow-up, 30/74 patients (40.5%) reached the composite endpoint. In these individuals, all miRNAs but let7d-5p were significantly reduced at baseline (p < 0.0001). As showed by multivariate Cox-regression analyses, miRNAs 23a-3p, 451a, 30a-5p were all predictors of the composite endpoint and Kaplan-Meier analyses confirmed a faster progression to the endpoint in subjects with miRNAs levels below an optimal ROC-derived cut-off value (p ranging from 0.001 to < 0.0001; crude HRs 7.95 to 8.61; Figure 1).

**Conclusion:** Our study demonstrated that the evaluation of a very small panel of circulating miRNAs (30-5p, 23a-3p and 451a) may impart important prognostic information in chronic HD patients with respect to mortality and CV risk. Although the biological meaning of their deregulation remains unanswered, these preliminary findings may set the stage for larger investigation to generalize their usefulness as biomarkers, as well as possible therapeutic targets.

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**SECOND, THIRD, AND MORE HITS: IMPACT OF SUCCESSIVE AKI EPISODES ON CKD PROGRESSION AND AKI TO CKD TRANSITION**

Isabel Acosta-Ochoa, Armando Coca, Paula Ardura, María Martínez Manrique, Carlos Merizalde, Kenia Cobo and Alicia Mendiluce

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**Background and Aims:** The second hit theory refers to the link between two or more deleterious events that cause AKI simultaneously (e.g., triple whammy) or successively (e.g., cardiac surgery after coronary angiography). We investigated the effect of 3 or more consecutive AKI episodes on baseline serum creatinine (SCr) and if these changes led to AKI to CKD transition (Transition), CKD progression (Progression) or stable SCr.

**Method:** Retrospective study of patients with AKI attended by nephrology during a 3-year period. AKI severity was categorized by KDIGO criteria. We searched for patient’s successive admissions and if suffered a new AKI episode and included all patients with ≥3 AKI episodes during the study period. We analyzed the baseline SCr for every episode and investigated if serial AKI episodes leaded to incident CKD, Progression, or no changes in SCr.

**Results:** 144 individuals that suffered 525 AKI episodes were included. We observed 36 patients in the Transition, 70 in the Progression group, and 38 didn’t vary their SCr. We found no statistically significant differences in hypertension, DM, Charlson’s Index, admission to ICU, severity of AKI or length of stay between groups. See Table 1A. We found that progressors had shorter time to nephrology consultation, they were more prone to receive acute HD and to be dialysis dependent at discharge. With no differences in the mortality rate between groups. See Table 1B. Figure 1 plots baseline SCr of every episode that shows a trend to incremental cyphers.

**Conclusion:** In our study the clinical characteristics between Transition and Progression groups were similar. We observed more individuals in the Progression group and their time to nephrology consultation was significantly shorter, maybe because no nephrology specialists are afraid of managing CKD patients. Patients that progressed needed acute HD more frequently and were more dialysis dependent at discharge, this finding could be explained by their diminished renal reserve, with no differences in the rate of in-hospital mortality. Successive AKI episodes portend a higher risk of adverse clinical outcomes, with excessive burden for patients with previous CKD. New AKI therapies could change the course of these ominous outcomes? This issue is under intense investigation, but it is very difficult to translate bench to bedside. Therefore, now we can only count on prevention and timely nephrological attention.
Figure 1: Plot of Baseline Serum Creatinine in Successive AKI Episodes, Showing a Slight Trend to Increments.

Table 1: A and B. Comparison of Individuals that Transitioned to or Progressed CKD.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Transition 36 (25)</th>
<th>Progression 70 (49)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age - ys</td>
<td>73 (+10)</td>
<td>75 (+13)</td>
<td>0.36</td>
</tr>
<tr>
<td>Sex (Masc)</td>
<td>29 (81)</td>
<td>44 (63)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33 (92)</td>
<td>68 (97)</td>
<td>0.22</td>
</tr>
<tr>
<td>DM</td>
<td>17 (47)</td>
<td>39 (56)</td>
<td>0.27</td>
</tr>
<tr>
<td>Charlson’s Index</td>
<td>6.0 (+2.7)</td>
<td>6.3 (+2.5)</td>
<td>0.58</td>
</tr>
<tr>
<td>Surgical Ward</td>
<td>15 (42)</td>
<td>18 (26)</td>
<td>0.05</td>
</tr>
<tr>
<td>ICU</td>
<td>10 (28)</td>
<td>17 (24)</td>
<td>0.43</td>
</tr>
<tr>
<td>Comm Acq AKI</td>
<td>26 (72)</td>
<td>50 (71)</td>
<td>0.56</td>
</tr>
<tr>
<td><strong>B. Results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KDIGO Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>17 (47)</td>
<td>23 (33)</td>
<td>0.10</td>
</tr>
<tr>
<td>2</td>
<td>2 (6)</td>
<td>7 (10)</td>
<td>0.35</td>
</tr>
<tr>
<td>3</td>
<td>17 (47)</td>
<td>40 (57)</td>
<td>0.20</td>
</tr>
<tr>
<td>T Nephr Consult</td>
<td>7 (+8.1)</td>
<td>4 (+3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LoS</td>
<td>16 (+13)</td>
<td>16 (+12)</td>
<td>0.93</td>
</tr>
<tr>
<td>Acute HD</td>
<td>5 (14)</td>
<td>18 (26)</td>
<td>0.04</td>
</tr>
<tr>
<td>HD Dependence</td>
<td>1 (3)</td>
<td>9 (13)</td>
<td>0.03</td>
</tr>
<tr>
<td>Mortality</td>
<td>14 (39)</td>
<td>39 (56)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Background and Aims: Kidneys have an intrinsic reserve capacity to respond to a higher workload by increasing filtration in their nephrons, called renal functional reserve (RFR). Despite the high clinical relevance of RFR, the necessary dynamic measurements are rarely done in the clinical routine, due to time- and workload as well as lack of standardized protocols.

Method: We developed a novel RFR protocol using 99mTc-DTPA (DTPA-Cl) before and after an oral protein load performed in an outpatient clinical setting within one day. Following a weak of low protein diet and using standardized hydration baseline and post-stimulation GFR were measured. 50 MBq activity were given i.v. at 0 and 240 mins, the plasma clearance was calculated based on the activity course at 13 time-points over 480 mins. RFR was expressed as the difference of post-protein stimulation peak mGFR to baseline mGFR in fasting state.

Results: In the pilot study we measured RFR in 7 healthy participants. The results showed a high heterogeneity. Therefore, we modified the study protocol for the next 16 patients by (a) extending the time of measurements to 330 min post-stimulation and (b) increasing the frequency of activity measurements to every 30 mins. In addition, we used a protein load of 1.5 g/kg bw of beef protein. These standardized measurements showed inter-individual time differences in reaching the peak GFR values post-protein load, the peaks detectable between 150 to 270 mins after the protein meal. The mean RFR (+SD) was 14 (+13) ml/min/1.73 m² corresponding to 16 (+15)% [Fig. 1]. All participants demonstrated a significant fall in DTPA-Cl 60 mins post-stimulation.

Conclusion: RFR can be measured with a same day pre- and post-stimulation DTPA-clearance protocol. Using a high oral load of beef protein and a long, post-stimulation period of measurements demonstrates inter-individual differences in reaching the hyperfiltration peak and a significant, previously not appreciated, post-prandial drop in GFR.
Results: hyperoxaluria following small bowel resections. Other medications include: on Azathioprine for his Crohn’s and his initial decline in renal function (subsequent reversal), inguinal herniorrhaphy, hypertension and BPH. He was right hemicolectomy 26 years ago with revision 4 years ago, ileostomy (with obstruction). His AKI was initially thought to be pre-renal and there was some improvement in renal function with fluids during his first admission although renal function didn’t return to baseline. His renal function progressively worsened in a spate of a few months. He had a baseline creatinine of 130 prior to his laparotomy which worsened to 184 post surgery but the improved to 9 months postop. He eventually had a renal biopsy that showed chronic damage and glomerular sclerosis. Ultrasound ruled out any obstruction. Despite pausing Azathioprine, renal function continued to deteriorate with creatinine peaking at 561 over the next 2 months. He subsequently had a renal biopsy that showed chronic damage with oxalate casts. He was subsequently commenced on haemodialysis.

Conclusion: These two cases highlight the need to consider enteric hyperoxaluria in patients presenting with unexplained decline in renal function who have had bowel surgery or have risk factors for fat malabsorption. This is important due to the usual poor prognosis in this group of patients [1].

REFERENCES

#6180
OXALATE NEPHROPATHY SECONDARY TO ENTERIC HYPEROXALURIA: A RARE CAUSE OF END STAGE RENAL FAILURE – A REPORT OF 2 CASES
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Background and Aims: Oxalate nephropathy is a rare cause of renal failure which is usually due to primary or secondary hyperoxaluria. Secondary hyperoxaluria results from increased intake or increased intestinal oxalate availability (enteric hyperoxaluria), increased intestinal oxalate degradation, or increased colonic permeability to oxalate [1]. Little is known about the burden of end stage kidney disease in this group of patients as most of the initial literature was from case reports and case series. More recently, prevalence of 1-4.01% was reported from biopsy studies suggesting that this entity is indeed a cause of kidney failure that needs to be considered [2,3].

Method: We present two cases of oxalate nephropathy secondary to enteric hyperoxaluria following small bowel resections.

Results: CASE ONE 82 year old man with a solitary kidney who was admitted in the ED on account of a decline in renal function on a background of episodes of loose stools. This was his second admission in two months on account of decline in renal function. He had emergency laparotomy and adhesiolysis as a result small bowel obstruction from volvulus 12 months earlier. Other past medical history include left nephroureterectomy for renal cancer, transurethral resection of bladder tumour, hypertension, Barretts and appendectomy. His medications were Omeprazole (which was switched to Famotidine due to hypomagnesaemia 7 months postop), Atenolol and Adcal D3. Renal immunology and myeloma screen were negative. Urine was bland and ultrasound did not show any obstruction. His AKI was initially thought to be pre-renal and there was some improvement in renal function with fluids during his first admission although renal function didn’t return to baseline. His renal function progressively worsened in a spate of a few months. He had a baseline creatinine of 130 prior to his laparotomy which worsened to 184 post surgery but the improved to about 109 few days post op. However, his renal function was noticed to decline 9 months post op and eventually his creatinine peaked at 751, fourteen months post op. He eventually had a renal biopsy 13 months post op that showed oxalosis, acute tubular injury and patchy interstitial fibrosis. His renal function continued to deteriorate and he was eventually commenced on haemodialysis.

CASE TWO
A 75 year-old man who was referred to the renal clinic on account of a decline in renal function. He had a past medical history of Crohn’s disease, previous right hemicolectomy 26 years ago with revision 4 years ago, ileostomy(with subsequent reversal), inguinal herniorrhaphy, hypertension and BPH. He was on Azathioprine for his Crohn’s and his initial decline in renal function was thought to be attributable to Azathioprine. Other medications include:

Amlodipine 5 mg, Finasteride 5 mg, Loperamide 2 mg bd, Tamsulosin 400mcg od. At referral, his renal function had progressively deteriorated over the previous few months from a baseline creatinine of 145 to 303, 44 months after his last surgery. Urinalysis showed trace of protein and + of blood however, urine ACR was normal. Vasculitis and myeloma screen were also normal. Ultrasound ruled out any obstruction. Despite pausing Azathioprine, renal function continued to deteriorate with creatinine peaking at 561 over the next 2 months. He subsequently had a renal biopsy that showed chronic damage with oxalate casts. He was subsequently commenced on haemodialysis.
filtration rate from baseline measurement or initiation of kidney replacement therapy.

**Results:** During 10,550 person-years of follow-up (median, 5.2 years), the composite outcome occurred in 800 (38.5%) participants. In the multivariable cause-specific hazard model, higher SBP was associated with an increased risk of CKD progression. There was a significant interaction between SBP and u-AGT/Cr ratio on the risk of the primary outcome (P-for-interaction = 0.019). In patients with u-AGT/Cr < 3.65 μg/gCr, the hazard ratios (HRs) (95% confidence intervals [CIs]) for SBP 120–129, 130–139, and ≥ 140 mmHg were 1.47 (1.08-2.01), 1.74 (1.26-2.39), and 2.43 (1.76-3.37), respectively, compared with SBP < 120 mmHg. In addition, each 10 mmHg increase in SBP was associated with an 18% higher risk of CKD progression. Moreover, there was a greater decline in the estimated glomerular filtration rate among the higher SBP categories. However, these associations were not observed in patients with u-AGT/Cr ≥ 3.65 μg/gCr.

**Conclusion:** Urinary angiotensinogen levels may modify the association between SBP and adverse kidney outcomes.

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**#3252**

**PRESEPSIN AS A POTENTIAL BIOMARKER FOR RENAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background and Aims:** Presepsin is a soluble CD14 subtype known as a sepsis biomarker. Recently, it has been reported to correlate with kidney function decline in elderly patients with chronic kidney disease and to predict acute kidney injury in patients with sepsis. However, the potential role of presepsin in systemic lupus erythematosus (SLE) with kidney involvement is still unclear. This study aimed to evaluate the relationship between serum presepsin level and SLE disease activity and laboratory parameters and to validate presepsin as a biomarker for lupus nephritis (LN).

**Method:** This cross-sectional study included 78 SLE patients aged 38.9±12.8 years. Among them, there were 68 (87.2%) women, 36 (46.2%) patients with LN, and 42 (53.8%) patients without LN. LN was diagnosed by renal biopsy and/or according to the renal SLE disease activity index (SLEDAI) criteria. Patients with infections were not included in the study. Serum presepsin level was determined by ELISA. The diagnostic value of presepsin level for the detection of LN was assessed by receiver-operating characteristic curves (ROC), the area under the curve (AUC), and 95% confidence intervals (CI). Spearman and Pearson correlation tests were performed to evaluate the relationships between presepsin level and SLEDAI score, serum complement concentrations, anti-double-stranded DNA antibodies (anti-dsDNA), inflammatory markers, urinary protein, and estimated glomerular filtration rate (eGFR) with CKD-EPI.

**Results:** The median serum presepsin level was significantly higher in patients with LN than in those without kidney damage [145 (110-197) pg/ml vs 102 (82-146) pg/ml, p = 0.011]. The ROC analysis found that the most appropriate cut-off point for presepsin concentration as a biomarker for LN in LSE patients was 106 pg/ml with a sensitivity of 81.8% (95% CI 64.5-93.0), and specificity of 54.3% (95% CI 36.6-71.2). The AUC was 0.714 (95% CI 0.592-0.837) with a positive predictive value of 62.8% (95% CI 46.7-77.0), and a negative predictive value of 76.0% (95% CI 54.9-90.6) (Fig. 1). The mean value of eGFR was 83.8±27.0 ml/min/1.73 m² in the LN group and 94.1±18.0 ml/min/1.73 m² in the non-LN group (p = 0.112). A significant negative correlation was observed between presepsin levels and eGFR in LN patients (Fig. 2). Moreover, presepsin levels in the LN group significantly correlated with SLEDAI score (r = 0.372, p = 0.036), anti-dsDNA titer (r = 0.363, p = 0.04) and severity of proteinuria (r = 0.630, p<0.01). No such associations were found in SLE patients without kidney involvement. Presepsin concentration did not correlate with C3, C4, C-reactive protein, erythrocyte sedimentation rate, and procalcitonin levels in both groups.

**Conclusion:** Serum presepsin may be considered a potential biomarker for the detection of kidney damage in patients with SLE. Further studies focusing on the clinical and pathological associations of presepsin in LN would be of interest.

**Figure 1:** ROC-curve for the cut-off value of serum presepsin concentration to predict renal involvement in patients with SLE.

**Figure 2:** The correlation between serum presepsin levels and eGFR in patients with lupus nephritis.
**#4935**

**TYG INDEX CORRELATED WITH PROGRESSION OF CHRONIC KIDNEY DISEASE IN METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE**

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Yonsei University College of Medicine, Department of Internal Medicine, Seoul, Rep. of South Korea

**Background and Aims:** Chronic kidney disease (CKD) is an established major risk factor for cardiovascular disease. Moreover, progression of CKD results in end-stage kidney disease, and an increased risk of death. The recently proposed metabolic dysfunction-associated fatty liver disease (MAFLD) has been suggested to better reflect risk of developing CKD. This study aimed to evaluate the association between the triglyceride-glucose (TyG) index and CKD progression in patients with MAFLD.

**Method:** In the data from the medical records database in Gangnam Severance Hospital from 2006 through 2020, a longitudinal analysis included participants with CKD. MAFLD was diagnosed in patients with was diagnosed in individuals with hepatic steatosis and at least one of the conditions as follows: 1) overweight or obese (defined as body mass index [BMI] ≥ 23 kg/m²), 2) type 2 diabetes mellitus, or 3) two or more metabolic abnormalities. Progression of CKD was defined by a reduction in the GFR ≥30% of baseline. Logistic regression analysis was used to obtain the association between TyG index and progression of CKD by adjusting for the influence of confounders.

**Results:** The study included 4,286 patients, of whom 582 had MAFLD. Mean age was 51.49 ± 11.451 years. After adjusting for age, sex, systolic blood pressure, fasting plasma glucose, CRP, LDL-cholesterol and smoking status, TyG index was associated with progression of CKD (OR 1.760 [1.089-2.844], P = 0.021).

**Conclusion:** This study demonstrated that TyG index was significantly associated with progression of CKD in patients with MAFLD.

**#6009**

**MUSCLE OXYGENATION AND MICROVASCULAR REACTIVITY ACROSS DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE: A NEAR-INFRARED SPECTROSCOPY STUDY**

Marieta Theodorakopoulou1, Andreas Zafeiridis2, Konstantina Dima2, Danai Faitatzidou1, Ággelo Koutras2, Michael Doumas3, Aikaterini Papagianni4 and Panetelis Sarafidis1

1 Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece, 2 Aristotle University of Thessaloniki, Exercise Physiology & Biochemistry Laboratory, Department of Sport Sciences at Serres, Serres, Greece and 3 Aristotle University of Thessaloniki, Second Propedeutic Department of Internal Medicine, Hippokration Hospital, Thessaloniki, Greece.

**Background and Aims:** Previous studies in chronic kidney disease (CKD) showed that vascular dysfunction in different circulatory beds is progressively deteriorating with CKD severity. This study evaluated muscle oxygenation and microvascular reactivity at rest, during an occlusion-reperfusion maneuver, and during exercise in patients with pre-dialysis CKD versus controls, as well as between different CKD stages.

**Method:** Continuous measurement of muscle oxygenation (tissue saturation index (TSI%) via near-infrared-spectroscopy at rest, during occlusion-reperfusion, and during a 3-min handgrip exercise(at 35% of maximal voluntary contraction). Aortic pulse wave velocity (PWV) and carotid intima-media thickness (cIMT) were also recorded.

**Results:** Resting muscle oxygenation did not differ among the study groups (control: 64.3 ± 2.9 stage-2: 63.8 ± 4.2 stage-3a: 64.1 ± 4.1 stage-3b: 62.3 ± 3.3 stage-4: 62.7 ± 4.3%; p = 0.6). During occlusion, no significant differences among groups were detected in TSIocl magnitude- and occlusion-slope. However, during reperfusion, the TSImax and the hyperemic response were significantly lower in groups of patients with more advanced CKD stages (controls: 11.2 ± 3.7 stage-2: 8.3 ± 4.6 stage-3: 7.8 ± 5.5 stage-3b: 7.3 ± 4.4 stage-4: 7.2 ± 3.3; p = 0.04). During handgrip exercise, muscle oxygenation (TSIaverage-decline) was marginally lower in CKD patients than controls, but no significant differences were detected between CKD stages.

**Conclusion:** Although no differences were observed in muscle oxygenation at rest and during occlusion, the microvascular hyperemic response during reperfusion was significantly impaired in CKD and deteriorated in more advanced CKD stages. This impaired ability of microvasculature to respond to stimuli may be a crucial component of the adverse vascular profile of CKD patients and may contribute to exercise intolerance.

**REFERENCES**


**#6545**

**URINARY FETUIN-A FRAGMENT EXCRETION IN PATIENTS WITH TYPE 2 DIABETES AND ITS CORRELATION WITH RENAL FUNCTION**

Varun Kumar Bandi1, Naga Sai Sri Harsha Narilla1, Sindhu Chaganti1, Sirisha Yarlagadda1 and Suresh Eadala2

1 Dr. Pinnamneni Siddhartha Institute of Medical Sciences & RF, Nephrology, Gannavaram, India, 2 Dr. Pinnamneni Siddhartha Institute of Medical Sciences & RF, General Medicine, Gannavaram, India and 3 Dr. Pinnamneni Siddhartha Institute of Medical Sciences & RF, Biochemistry, Gannavaram, India.

**Background and Aims:** Fetuin-A is associated with production of pro-inflammatory cytokines, which can lead to progression of vascular complications in patients with diabetes. We planned a study to evaluate the correlation of urinary excretion of post translationally modified fetuin-A fragment (PTM Fetuin A) with albuminuria and chronic kidney disease.

**Method:** We conducted a cross-sectional study between July to August 2022 in patients with type 2 diabetes. The baseline characteristics such as Age, Gender, history of Diabetes Mellitus, Hypertension, Cardiac disease, and CKD were obtained. The subject's blood pressure, Haemoglobin, Random blood sugar, Creatinine, was obtained, and eGFR (Glomerular Filtration Rate) was calculated using the CKD-EPI equation. The spot urine was tested for urine inflammatory cytokines, which can lead to progression of vascular complications in patients with diabetes.
albumin to creatinine ratio (UACR) and PTM-Fetuin-A: Creatinine ratio (FCR). PTM-Fetuin A was measured by an ELISA using DNLite-IVD103 ELISA test kit, Bio Preventive Medicine Corp, Taiwan.

Results: A total of 68 subjects were included, with 37 being men (54.4%). The mean age, eGFR, UACR, and FCR were 55 ± 11.4 years, 61.9 ± 37.5 ml/min/1.73 m², 1060.7 ± 1550 mg/g, and 522.2 ± 915.1 ng/g respectively. There was significant positive correlation between FCR and UACR (p<0.005), serum creatinine (p<0.005), and eGFR (p<0.001). There was a trend noted of increasing PTM-Fetuin A levels and UACR with worsening eGFR. The AUROC for UACR and FCR for predicting patients with CKD stage 3 onwards were 0.703 and 0.789 respectively (Figure 1). In our study, the significance of predicting CKD stage 3 onwards with a UACR cut-off of 300 mg/g, UACR cut-off of 1150 mg/g and a FCR cut-off of 123 ng/g were p = 0.008, p = 0.003, and p<0.0001 respectively.

Conclusion: PTM-Fetuin A is significantly associated with worsening renal function. It has very significant correlation with the albuminuria, and at a FCR cut-off of 123 ng/g, it could significantly differentiate CKD stages, compared to UACR. Further prospective studies are needed to evaluate the correlation between PTM-Fetuin A levels and rate of progression of nephropathy.

Figure 1: ROC curve for UACR and FCR for predicting CKD stage 3-5.
ASSESSING THE 3-YEAR RISK OF 40% EGFR DECLINE OR KIDNEY FAILURE IN THE US POPULATION

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Background and Aims: Prognostication of CKD progression currently relies exclusively on eGFR and albuminuria and do not consider comorbid conditions. Recently, the Chronic Kidney Disease Prognosis Consortium (CKD-PC) equation was developed to predict the 3-year risk of 40% eGFR decline or kidney failure in the general population [1]. The goal of our study was to assess the distribution of this risk in the US population.

Method: We included US adults from the 1999-2020 United States National Health and Nutrition Examination Survey (NHANES; N = 51,699). We calculated eGFR using the CKD-EPI 2021 equation and the 3-year risk of 40% eGFR decline or kidney failure using the CKD-PC equation (3-year risk). We categorized the 3-year risk as <1%, 1% to <5%, 5% to <10%, ≥10% and compared this with the current KDIGO 2012 CKD staging (eGFR<60 mL/min/1.73 m² or albuminuria≥30 mg/g).

Results: Among 199.8 million US adults, mean age was 46±15 years, 51% were female, 11% were non-Hispanic Black persons, and mean BMI was 29±6 kg/m². 71 million (36%) had hypertension and 26 million (13%) had diabetes. Table 1 shows the distribution of 3-year risk across stages of eGFR and albuminuria. Among 26 million US adults with CKD, the 3-year risks were <1% in 4 million (15%), 1% to <5% in 15 million (56%), 5 to <10% in 4 million (17%), and ≥10% in 3 million (11%). Importantly, among persons without CKD by current criteria, 1 million persons (0.58%) had a ≥5% 3-year risk, whereas only 331,840 (6%) persons with CKD 3a A1 had a ≥5% 3-year risk of CKD progression or kidney failure.

Conclusion: Calculating the 3-year risk of a 40% decline in eGFR or kidney failure can identify at-risk persons beyond the current eGFR and albuminuria staging. Our findings highlight the importance of factors besides eGFR and albuminuria in considering the risk for CKD progression.

REFERENCE

Table 1: Distribution of 3-year risk of 40% decline in eGFR or kidney failure across stages of CKD.

<table>
<thead>
<tr>
<th>eGFR Categories</th>
<th>US Population</th>
<th>3-Year Risk Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;1%</td>
</tr>
<tr>
<td>No CKD</td>
<td>173.9 million</td>
<td>139.3 million (80%)</td>
</tr>
<tr>
<td>CKD G1 &amp; G2</td>
<td>15.5 million</td>
<td>3.8 million (25%)</td>
</tr>
<tr>
<td>CKD G3a A1</td>
<td>5.7 million</td>
<td>0.3 million (5%)</td>
</tr>
<tr>
<td>CKD G3a A2 &amp; A3</td>
<td>1.7 million</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>CKD G3b</td>
<td>2.3 million</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>CKD G4 G5</td>
<td>651,295</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Legends:
eGFR = calculated using the CKD Epidemiology Collaboration 2021 creatinine equation (mL/min/1.73 m²).
UACR = urine albumin-to-creatinine ratio (mg/g).
CKD Staging: No CKD = eGFR≥60 with UACR<30; CKD G1 & G2 = eGFR≥60 with UACR≥30; CKD G3a A1 = eGFR<45 and <60 with UACR<30; CKD G3a A2 & A3 = eGFR<45 and <60 with UACR≥30; CKD G3b = eGFR≥30 and <45; CKD G4 & G5 = eGFR<30.
3-Year Risk Categories = calculated using the CKD Prognosis Consortium equation quantifying the 3-year risk of 40% eGFR decline or kidney failure.
Percentages are row percents.

KIDNEY FUNCTION-SPECIFIC CUT-OFF VALUES OF HIGH-SENSITIVITY CARDIAC TROPONIN T FOR THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION
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Background and Aims: Acute myocardial infarction (AMI) is the leading cause of death worldwide. Patients with kidney dysfunction have high prevalence of AMI, thus early detection of AMI is necessary. However, in patients with decreased estimated glomerular filtration rate (eGFR), using the traditional cut-off value (14 ng/L) of high-sensitivity cardiac troponin T (hs-cTnT) resulted in lower specificity for diagnosing AMI. Our study aims to determine and validate kidney function-specific cut-off values of hs-cTnT for diagnosing AMI in patients with different degrees of kidney dysfunction.

Method: This large, multicenter, observational cohort study included 21,912 hospitalized patients who had undergone coronary angiography in 6 clinical centers from 2013 to 2021. The study outcome was the diagnosis of AMI. In the derivation cohort, kidney function-specific cut-off values of hs-cTnT for diagnosing AMI were determined to improve the specificity without the cost of sensitivity, as compared to that using 14 ng/L as the cut-off value in the normal kidney function group. The efficacy of the novel cut-off values was validated in an independent validation cohort enrolled from another clinical center.

Results: In the derivation cohort (n = 12,900), 3,247 patients (25.2%) had an eGFR <60 mL/min/1.73m². Even in the absence of AMI, 1,485 (50.2%) participants with eGFR <60 mL/min/1.73m² had a hs-cTnT concentration ≥14 ng/L. Using 14 ng/L as the threshold of hs-cTnT for diagnosing AMI led to a significantly reduced specificity (9.1–52.7% vs. 75.0%) and positive predictive value (15.5–21.1% vs. 28.7%) in patients with kidney dysfunction, as compared with patients with normal kidney function. The kidney function-specific cut-off values (eGFR ≥60 mL/min/1.73m²: 14 ng/L, 60>eGFR≥30 mL/min/1.73m²: 18 ng/L, and eGFR <30 mL/min/1.73m²: 48 ng/L) were determined and remarkably improved the diagnostic accuracy for AMI in participants with different levels of kidney dysfunction (specificity: reach to 52.8–63.0%; positive predictive value: 18.7–33.6%), without compromising sensitivity (96.6–97.9%). The kidney function-specific cut-off values increased the diagnostic accuracy of hs-cTnT for diagnosing AMI in every eGFR subgroup in the independent validation cohort (n = 8,012).

Conclusion: The kidney function-specific cut-off values of hs-cTnT significantly improved the diagnostic accuracy of AMI in patients with kidney dysfunction, and might be generally useful in clinical practice.

Table 1: The performance of hs-cTnT for diagnosing AMI using the traditional (14 ng/L) or kidney function-specific cut-off values in the validation cohort stratified by eGFR.

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73m²)</th>
<th>No. AMI/Total</th>
<th>hs-cTnT cut-off</th>
<th>Sensitivity % (95%CI)</th>
<th>Specificity % (95%CI)</th>
<th>NPV % (95%CI)</th>
<th>PPV % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR≥60</td>
<td>1955/7683</td>
<td>14 ng/L</td>
<td>91.8 (90.6, 92.9)</td>
<td>71.5 (70.3, 72.7)</td>
<td>96.2 (95.7, 96.8)</td>
<td>52.4 (51.2, 53.5)</td>
</tr>
<tr>
<td>60&gt;eGFR≥30</td>
<td>132/314</td>
<td>14 ng/L</td>
<td>97.7 (94.7, 100)</td>
<td>22.5 (16.5, 28.6)</td>
<td>93.6 (85, 100)</td>
<td>47.8 (45.9, 50)</td>
</tr>
<tr>
<td>eGFR &lt; 30</td>
<td>7/15</td>
<td>14 ng/L</td>
<td>97 (93.9, 99.2)</td>
<td>35.2 (28, 42.3)</td>
<td>94.2 (88.3, 98.6)</td>
<td>52 (49.4, 55)</td>
</tr>
</tbody>
</table>

hs-cTnT, high sensitivity cardiac troponin T; AMI, acute myocardial infarction; eGFR, estimated glomerular filtration rate; NPV, negative predictive value; PPV, positive predictive value.

* N = 8,012.
INCIDENT CHRONIC KIDNEY DISEASE IN NEWLY DIAGNOSED DIABETES MELLITUS

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1Singapore General Hospital, Renal Medicine, Singapore, 2Singapore General Hospital, Health Services Research Unit, Singapore, 3Changi General Hospital, Department of Medicine, Singapore, 4Sengkang General Hospital, Department of Renal Medicine, Singapore, 5Singhealth Polyclinics, Singapore and 6Singapore General Hospital, Department of Endocrinology, Singapore

Background and Aims: Singapore has the world's 3rd highest rate of incident end-stage kidney disease (ESKD) on dialysis. Diabetes mellitus (DM) was the cause of ESKD in 68% of patients initiating dialysis in 2020. We explored the rate of incident CKD in newly diagnosed DM, and risk factors associated with the development of incident CKD.

Method: This is a retrospective cohort of patients newly diagnosed with DM in 2014-2020, in primary care and specialist clinics across Singapore's largest health system. Patients were excluded if they had known CKD, were not screened for CKD, or were diagnosed with CKD at the first screening (which may reflect pre-existing CKD). CKD was defined as a CKD-EPI glomerular filtration rate (GFR) <60 ml/min/1.73 m², and/or urine albumin-creatinine ratio (UACR) >3 mg/mmol. Two readings ≥3 months apart were required for diagnosis. Demographic and laboratory data was retrieved from electronic records, and analysed using Pearson's Chi-square, Wilcoxon rank-sum test, and Cox regression evaluating time to onset of incident CKD.

Results: Of 25714 patients with newly-diagnosed DM and no known CKD, 3963 (15.4%) were not screened for CKD, and 2019 (7.9%) were diagnosed with CKD at the first screening; both groups were excluded. The remainder 19732 patients (76.7%) formed the study cohort. This included 14175 Chinese (71.8%), 3085 Malay (15.6%), 1658 Indian (8.4%), and 814 patients of other ethnicities (4.1%). Baseline mean (SD) GFR was 90.7 (17.6) ml/min/1.73 m². Over a mean follow up of 2.28 (1.98) years, 5929 patients (30.0%) developed incident CKD after a mean of 1.35 (1.09) years. Of patients who developed CKD, 869 (14.7%) met the GFR criteria, 4847 (81.8%) developed albuminuria, and 213 (3.6%) met both criteria. GFR decline began in the first year. Baseline characteristics associated with incident CKD on bivariate analysis (Table 1) included older age (61(11) vs 59(12) years, p<0.001), female gender (p<0.001), lower GFR (89 (19) vs 91 (17) ml/min/1.73 m², p<0.001), higher systolic blood pressure (136 (17) vs 135 (17) mmHg, p<0.001), and ischemic heart disease (p<0.001). On multivariate Cox regression exploring characteristics associated with time to incident CKD, independent risk factors include female gender (HR 1.30, 95%CI 1.23-1.39), lower GFR (per 10ml/min/1.73 m² lower GFR, HR 1.10, 95%CI 1.08-1.11), higher systolic blood pressure (per 10mmHg rise, HR 1.06, 95%CI 1.04-1.08), higher HbA1c (per 1% rise, HR 1.06, 95%CI 1.05-1.08), cerebrovascular accident (HR 1.16, 95%CI 1.02-1.31) and gout (HR 1.16, 95%CI 1.01-1.32). Despite a prevalence of hypertension of 85%, only 5440 (28%) of the cohort with incident CKD received an angiotensin converting enzyme inhibitor (ACE) or angiotensin receptor blocker (ARB) (as at 6 months after diagnosis of DM). 498 patients (2.5%) received a sodium-glucose cotransporter-2 inhibitor, which was not widely available during the period of this study.

Conclusion: Incident CKD was frequent in early DM; the risk factors above may identify higher-risk patients who benefit from enhanced screening. The relatively low rate of ACE/ARB prescription may require further review.
#5476

SEX DIFFERENCES IN INCIDENT KIDNEY FAILURE AND THE IMPACT OF RISK FACTORS IN A POPULATION STUDY

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¹University of Glasgow, School of Cardiovascular and Metabolic Health, Glasgow, United Kingdom, ²University of Sydney, Sydney School of Public Health, Sydney, Australia and ³University of Sydney, Sydney Medical School, Sydney, Australia

Background and Aims: Chronic kidney disease (CKD) has different effects on women and men. Women are more likely to have CKD, but men are more likely to develop kidney failure requiring treatment (KFRT: dialysis or transplantation). Recent studies have highlighted sex differences in CKD progression and there is a need to determine if this relates to differential effects of risk factors.

Method: We used primary care data stored within the electronic health records repository Secure Anonymised Information Linkage Databank (SAIL) for adults with CKD stages G3/4 (estimated glomerular filtration rate (eGFR) 15-59 mL/min/1.73 m²) living in Wales, UK. We studied the relationship between sex and the development of kidney failure (KFRT or incident eGFR<15 mL/min/1.73 m² for ≥3 months). Sex-specific rates of kidney failure were compared using an event plot with patients censored on the date of death. Cox proportional hazards models tested associations between sex and kidney failure, before and after adjustment for other known risk factors (age, baseline eGFR, smoking, social deprivation, diabetes mellitus and hypertension). Interactions between sex and risk factors were sought and interaction terms were retained if these were statistically significant (p-value<0.05). Models were then stratified by sex to compare the impact of risk factors in men and women.

Results: 135,635 patients (median age 78 years, 57% female, median baseline eGFR 50 mL/min/1.73 m²) were followed up for a median of 6.8 years, representing a total of 782,237 patient years. 1.1% of women and 2.3% of men developed kidney failure. An unadjusted Cox model including both sexes showed a hazard ratio of 2.06 (95% confidence interval 1.89-2.24) for men. After adjustment for all risk factors and inclusion of interaction terms (between sex and baseline eGFR and sex and age), men were not more likely to develop kidney failure (aHR 0.91, 0.60-1.38) (Figure 1A). In sex-stratified models, kidney failure was most likely to develop in those with low baseline eGFR, younger age, current and ex-smokers, patients with diabetes mellitus and patients with hypertension (Figure 1B). Diabetes was a more important risk factor for kidney failure in women (aHR in women 1.73 (1.51-1.98) compared with men (aHR 1.56, 1.39-1.74). Hazard ratios for other risk factors were similar in men and women.

Conclusion: We found that sex differences in rates of kidney failure are related to a differential impact of risk factors – in particular diabetes – on CKD progression. These results warrant further investigation with a need to determine whether risk reduction strategies should be different in men and women with CKD, or whether current diagnosis, monitoring and treatment strategies are either applied differentially or have different benefit and harms by sex.

Table 1: Baseline characteristics by development of incident CKD.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Developed incident CKD (n = 5929)</th>
<th>Did not develop CKD (n = 13803)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>61 (11)</td>
<td>59 (12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender, %</td>
<td>3144, 53%</td>
<td>6334, 46%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Chinese, %</td>
<td>4474, 75%</td>
<td>9701, 70%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- Malay, %</td>
<td>903, 15%</td>
<td>2182, 16%</td>
<td></td>
</tr>
<tr>
<td>- Indian, %</td>
<td>344, 6%</td>
<td>1314, 10%</td>
<td></td>
</tr>
<tr>
<td>- Other, %</td>
<td>208, 4%</td>
<td>606, 4%</td>
<td></td>
</tr>
<tr>
<td>GFR, mean (SD)</td>
<td>89 (19)</td>
<td>91 (17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, mean (SD)</td>
<td>27.7 (5.4)</td>
<td>27.7 (5.5)</td>
<td>0.8</td>
</tr>
<tr>
<td>Systolic blood pressure, mean (SD)</td>
<td>136 (17)</td>
<td>135 (17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c, mean (SD)</td>
<td>7.38 (1.90)</td>
<td>7.31 (1.80)</td>
<td>0.3</td>
</tr>
<tr>
<td>LDL cholesterol, mean (SD)</td>
<td>2.70 (0.89)</td>
<td>2.69 (0.94)</td>
<td>0.5</td>
</tr>
<tr>
<td>HDL cholesterol, mean (SD)</td>
<td>1.30 (0.33)</td>
<td>1.27 (0.33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retinopathy, %</td>
<td>178, 3%</td>
<td>398, 3%</td>
<td>0.6</td>
</tr>
<tr>
<td>Ischemic heart disease, %</td>
<td>534, 9%</td>
<td>1470, 11%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cerebrovascular accident, %</td>
<td>320, 5.4%</td>
<td>664, 4.8%</td>
<td>0.083</td>
</tr>
<tr>
<td>Peripheral vascular disease, %</td>
<td>32, 0.5%</td>
<td>56, 0.4%</td>
<td>0.2</td>
</tr>
</tbody>
</table>
BURDEN OF NONCOMMUNICABLE DISEASES ATTRIBUTABLE TO KIDNEY DYSFUNCTION: RESULTS FROM THE GLOBAL BURDEN OF DISEASE STUDY 2019

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Background and Aims: Non-communicable diseases (NCD) represent a major public health and disability burden worldwide. The UN Sustainable Development Goal (SDG) target 3.4 called for reducing premature mortality from NCD by one third through prevention and treatment by 2030. To lessen the impact of the burden of NCD, evidence-based and precise data are needed for making policy and allocating resources. However, the burden of NCD attributable to kidney dysfunction has not been systematically estimated. We aimed to estimate the global latest trend of kidney dysfunction-related NCD quantified by death and disability-adjusted life-years (DALY) at global, regional, and national levels using data extracted from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019.

Method: In GBD study 2019, kidney dysfunction is classified as level 2 risk factor for disease in metabolic risk factors hierarchy, which refers to glomerular filtration rate (GFR) < 60 mL/min/1.73 m² or albumin-to-creatinine ratio (ACR) > 30 mg/g. The GBD study 2019 provides a systematic assessment of published, publicly available, and contributed data on mortality and disability-adjusted life-years (DALY), which were estimated with Bayesian geospatial regression using data at global, regional and country level. Further analyses were performed by year, age, sex, and regions in 204 countries. To assess the change trend, we calculated the estimated annual percentage change (EAPC) of age-standardized rate with the linear regression model. The Socio-demographic Index (SDI) was used as an comprehensive indicator of national socioeconomic status. we explored the relationship between age-standardized mortality or DALY rate and SDI using Pearson’s correlation analysis. Additionally, burdens in main types of NCD (including cardiovascular disease and chronic kidney disease) attributable to impaired kidney function were analyzed.

Results: From 1990 to 2019, the absolute numbers of death and DALYs increased, while the age-standardized rates of deaths and DALYs of NCD attributable to kidney dysfunction deceased worldwide. The age-standardized mortality decreased by an average of −0.35% (95% UI −0.41 to −0.29) per year, from 45.17 (95% UI 37.62 to 52.33) per 100,000 population in 1990 to 40.64 (95% UI 34.81 to 46.71) per 100,000 population in 2019. Over the same interval, the age-standardized DALYs rate declined from 1024.13 (95% UI 898.38 to 1154.8) per 100,000 population to 945.31 (95% UI 836.33 to 1066.77) per 100,000 population, with an EAPC of −0.25% (95% UI −0.31 to −0.19). Globally, gender imbalance existed over the past 29 years, the burden in males were higher than those in females. Besides, the burden of NCDs as a result of kidney dysfunction increased with age growth, and the elder had higher rate of death and DALYs. Geographically, the age-standardized DALYs rate attributed to kidney dysfunction increased in Central Latin America, Southern Sub-Saharan Africa, Caribbean, Central Asia, Andean Latin America, Oceania, Southeast Asia. Age-standardized death and DALY rates demonstrated a higher burden in low, low-middle and middle SDI countries than those in high-middle and high SDI countries.

Conclusion: The result of the present work implied that the NCD as a result of kidney dysfunction has been an important contribution to the increasing burden of NCD over the past several decades, particularly in developing countries. Therefore, greater efforts are needed to carry out early screening and detection, primary care, and reasonable resource allocation to reduce mortality and the long-term burden, especially in low-to-middle Socio-demographic Index regions. Our data would provide the necessary information for priority setting and precision planning of health services to prevent and control NCD.

HIGHER MORTALITY RISK WITH CHRONIC KIDNEY DISEASE IN TYPE 2 DIABETES IN YOUNGER AGES: A DANISH NATIONWIDE COHORT STUDY 2014-2018

Martin Nyeland1, Rasmus Rørth 1, Bendix Carstensen 1, Frederik Persson1, Peter Rossing1,2, and Dorte Vistisen 1,3

1Copenhagen University Hospital – Steno Diabetes Center Copenhagen, Clinical Research Unit, Herlev, Denmark, 2University of Copenhagen, Department of Clinical Medicine, Copenhagen N, Denmark and 3University of Copenhagen, Department of Public Health, Copenhagen K, Denmark

Background and Aims: Chronic kidney disease (CKD) is a frequent complication to diabetes. CKD is associated with significantly increased risk of morbidity and mortality among people with diabetes. It is well known that the incidence and progression of CKD differ between men and women. Women
are more likely to get CKD, while men have a more rapid progression of the disease. However, previous studies were based on small populations. We aimed to investigate the mortality with and without CKD in men and women with type 2 diabetes (T2D).

**Method:** Secular and age trends in mortality rates and sex differences were investigated in a dynamic, nationwide cohort of people with T2D. CKD was defined based on hospital diagnosis, procedure codes and laboratory measurements. Mortality rates were modelled as an age-period-cohort model using Poisson models with log person time, smooth effects of current age, and calendar time (date of follow-up), separate for each sex and CKD status.

**Results:** The study included 304,956 persons (55.9% men) and 1.2 million person-years. 87,696 persons were recorded with CKD, of which 34,967 people with and without CKD. The overall mortality rate was 37.8 [37.4; 38.2] versus 31.1 [30.4; 31.7] per 1000 person-years for people with T2D, without and with CKD, respectively. The mortality rate for people with T2D and CKD is larger and more pronounced in the younger ages. For elderly people the mortality rate is larger for people with T2D and without CKD. In general, mortality for men is higher than mortality for women at all ages, observed for both people with and without CKD. The overall secular trend per year was increasing for persons without CKD 2.0 [1.8; 2.2] %/year. For those with CKD, a decrease −2.4 [−2.1; −2.6] %/year was observed, decreasing until start 2017 followed by an increase. The overall M/F mortality ratios were 1.23 [1.20; 1.25] and 1.91 [1.83; 2.00], respectively.

**Conclusion:** The observed larger and more pronounced mortality rate for people with T2D and CKD in the younger ages, suggests a potential for early preventive intervention among young adults. Supported by an unrestricted grant from Bayer.

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**Background and Aims:** Incidence of cancer is increased in patients with chronic kidney disease (CKD), with a number of large population cohorts suggesting that lower estimated glomerular filtration rate (eGFR) increases overall risk of cancer death after adjustment for overlapping risk factors. In the general population, advanced cancer stage at presentation is associated with poorer outcomes. We sought to determine whether patients with CKD were more likely to present with advanced stage cancer, whether this impacted on their survival, and whether these factors varied by sex.

**Method:** Data were from Secure Anonymised Information Linkage Databank (SAIL), a Welsh primary care cohort with linkage to cancer and death registries. We included patients with a new cancer diagnosis between 2009 and 2020, and at least two kidney function tests before and within two years of diagnosis. eGFR based on serum creatinine (eGFRcr) was calculated using the CKD-EPI 2009 equation and measured in mL/min/1.73 m². Albuminuria was not routinely available. Logistic regression models determined odds of presenting with advanced cancer (stage 3 or 4 at diagnosis). Cox proportional hazards models tested associations between eGFRcr and all-cause mortality (reference group: eGFR 75 to <90). Comparisons were made both between- and within-sex.

**Results:** There were 95,689 patients: 43,720 (45.7%) were female, mean age was 70.3 (SD 13.8) years in women and 71.4 (SD 11.4) years in men; median eGFR at baseline was 77 (IQR 63 – 89) mL/min/1.73 m² in both women and men. Over a median follow-up time of 3.4 (IQR 0.9 – 5.7) years in women and 3.4 (IQR 0.9-5.5 years in men), there were 22,355 deaths in women and 27,681 in men. Adjusted for age, baseline eGFR, smoking status, number of comorbidities, deprivation and cancer site, men were slightly more likely to present with advanced cancer (aOR 1.02, 95% CI 1.01-1.04) and had higher hazards of death after cancer diagnosis than women (aHR 1.10 95% CI 1.08-1.13). In sex-stratified analyses, lower eGFRcr was weakly associated with higher odds of presenting with advanced cancer in men (eGFRcr 45–<60: OR 1.02, 95% CI 1.01-1.04; 30–<45: OR 1.02 95% CI 1.00-1.05; <30 OR 1.07 95% CI 1.03-1.11), but only in women with eGFRcr 45–<60 (OR 1.04 95% CI 1.02-1.06); Figure 1). Lower (and higher) eGFRcr was associated with higher hazards of death after cancer diagnosis in both men and women; however, the relative increase in hazards of death with eGFRcr <75 was stronger in women than in men, with a widening discrepancy as baseline eGFR decreased (Figure 1).

**Conclusion:** Men were more likely than women to be diagnosed with advanced cancer and more likely to die after cancer diagnosis than women. Lower eGFR was associated with higher hazards of death after cancer diagnosis in both men and women. Despite an initial survival advantage compared to men, women with lower eGFR had disproportionately higher hazards of death. Though potential explanations are manifold, scrutiny of efficacy and safety of cancer treatments in people with CKD – particularly women with CKD – are warranted.

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**Figure 1:** a. Mortality (2016) per 1000 person-years by age. b. Mortality (65 years) per 1000 person-years by calendar time in the period 2014-2018. Persons with T2D, with CKD (full line) and without CKD (dotted line). Men (blue) and women (red). Mortality rates are shown on a log scale. The shaded areas indicate 95% confidence intervals.
Figure 1: Forest plots of odds of presenting with advanced cancer (left; adjusted for age, smoking status, number of comorbidities, deprivation and cancer site) and hazards of death after cancer diagnosis (right; adjusted for age, smoking status, number of comorbidities, deprivation, cancer site and cancer stage).

#4506
ACCURACY OF NOVEL GFR ESTIMATING EQUATIONS BASED ON CREATININE, CYSTATIN C OR BOTH IN ROUTINE CARE
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Background and Aims: New equations to estimate GFR (eGFR) based on creatinine, cystatin C or both have been developed in the last two years. A comprehensive comparison of their accuracy is currently lacking, particularly in cohorts not involved in their development or validation and among people with comorbid conditions.

Method: We included 6174 adults from the Stockholm Creatinine Measurements (SCREAM) project referred for plasma clearance of iohexol during 2011-2021, in whom we observed 9579 concurrent measurements of creatinine, cystatin C and iohexol clearance. We assessed the performance against measured GFR (mGFR) of eGFR equations proposed by the CKD-EPI collaboration (CKD-EPI 2009, 2012 and 2021), European Kidney Function Consortium (EKFC 2021 and 2023), and the revised Lund-Malmö (2011) and CAPA (2014) equations, which are used in Sweden. Bias was expressed as the median difference in eGFR minus mGFR, with negative biases indicating underestimation of mGFR. P30 described the percentage of individuals with eGFR within 30% of mGFR. Correct classification was defined as agreement of eGFR and mGFR categories using the KDIGO GFR categories. Subgroup analyses were conducted according to age, sex, BMI, eGFR, cancer, cardiovascular disease, diabetes, heart failure and liver disease.

Results: Mean age was 57 years, 46% of participants were female, mean mGFR was 62 mL/min/1.73 m² and mean BMI was 26 kg/m². Cardiovascular disease was the most common comorbid condition (30%), followed by liver disease (28%), diabetes (26%) and cancer (26%). Equations that used both creatinine and cystatin C had better performance than eGFR using each marker alone, regardless of the equation used; all such equations had small bias and P30 close to 90%. Among creatinine-based equations, CKD-EPI 2009 and CKD-EPI 2021 showed larger overestimates of mGFR than EKFC 2021 and revised Lund-Malmö, with median biases of 5.6, 9.1, 2.7 and 0.2 mL/min/1.73 m², respectively (Table 1). There were no meaningful differences in performance across eGFR equations based on cystatin C. Findings were consistent across subgroup analyses stratifying for comorbid conditions (Figure 1).

Conclusion: eGFR equations that combined information on creatinine and cystatin C performed better than equations based on creatinine or cystatin C alone in this Swedish cohort of routine referrals for plasma clearance of iohexol. There was larger variation in the performance of equations based on creatinine than cystatin C.

Table 1: Bias, precision, accuracy and correct classification of different GFR estimating equations.

<table>
<thead>
<tr>
<th></th>
<th>Median Bias, mL/min/1.73 m² (95% CI)</th>
<th>P30, % (95% CI)</th>
<th>Correct classification, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Creatinine-based equations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD-EPI 2009</td>
<td>5.6 (5.3-6.0)</td>
<td>74.1 (73.2-75.0)</td>
<td>56.4 (55.4-57.4)</td>
</tr>
<tr>
<td>CKD-EPI 2021</td>
<td>9.1 (8.8-9.5)</td>
<td>68.1 (67.2-69.1)</td>
<td>51.8 (50.9-52.8)</td>
</tr>
<tr>
<td>EKFC 2021</td>
<td>2.7 (2.5-3.0)</td>
<td>79.5 (78.7-80.3)</td>
<td>58.9 (57.9-59.9)</td>
</tr>
<tr>
<td>RLM 2011</td>
<td>0.2 (-0.2-0.4)</td>
<td>82.2 (81.4-82.9)</td>
<td>58.6 (57.6-59.5)</td>
</tr>
<tr>
<td><strong>Cystatin C-based equations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD-EPI 2012</td>
<td>−2.6 (−2.9–2.3)</td>
<td>82.5 (81.7-83.3)</td>
<td>58.3 (57.4-59.3)</td>
</tr>
<tr>
<td>EKFC 2023 without sex</td>
<td>−3.7 (−4.0–3.4)</td>
<td>83.2 (82.5-84.0)</td>
<td>58.1 (57.2-59.1)</td>
</tr>
<tr>
<td>CAPA 2014</td>
<td>−1.1 (−1.4–0.9)</td>
<td>84.5 (83.8-85.2)</td>
<td>60.8 (59.8-61.7)</td>
</tr>
<tr>
<td><strong>Creatinine-cystatin C-based equations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD-EPI 2012</td>
<td>0.8 (0.6-1.0)</td>
<td>89.1 (88.4-89.7)</td>
<td>66.7 (65.7-67.6)</td>
</tr>
<tr>
<td>CKD-EPI 2021</td>
<td>2.5 (2.3-2.8)</td>
<td>87.6 (86.9-88.2)</td>
<td>66.3 (65.3-67.2)</td>
</tr>
<tr>
<td>Mean of EKFC 2021 and 2023</td>
<td>−1.5 (−1.7–1.3)</td>
<td>90.8 (90.2-91.4)</td>
<td>65.8 (64.8-66.7)</td>
</tr>
<tr>
<td>Mean of RLM 2011 and CAPA 2014</td>
<td>1.0 (0.8-1.3)</td>
<td>88.5 (87.9-89.2)</td>
<td>66.8 (65.8-67.7)</td>
</tr>
</tbody>
</table>

CAPA = Caucasian, Asian, Pediatric and Adult; CKD-EPI = CKD Epidemiology Collaboration; EKFC = European Kidney Function Consortium; RLM = Revised Lund-Malmö
Figure 1: Median bias for GFR estimating equations across subgroups of age, sex, BMI, eGFR, cancer, cardiovascular disease, diabetes, heart failure and liver disease. CAPA = Caucasian, Asian, Pediatric and Adult; CKD-EPI = CKD Epidemiology Collaboration; CVD = cardiovascular disease; DM = diabetes mellitus; EKFC = European Kidney Function Consortium; HF = heart failure; RLM = revised Lund-Malmö.

#4494

DRUG UTILIZATION FOLLOWING INCIDENT CHRONIC KIDNEY DISEASE: AN OBSERVATIONAL STUDY IN THE UNITED STATES AND JAPAN

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Background and Aims: Chronic kidney disease (CKD) affects >840 million individuals worldwide and is a leading cause of morbidity and mortality. Complications include cardiorenal outcomes (e.g. end stage kidney disease and heart failure (HF)) and premature death, which may be preventable with early identification and appropriate treatment of CKD. Treatment of CKD with renin-angiotensin-system inhibitors (RASI) has been the main recommendation of guidelines in the past 20 years, but prescribing rates remain low and discontinuation rates remain high, particularly after adverse events like
hyperkalaemia episodes. This study aims to describe RASi utilization following incident CKD.

**Method:** Adult patients with incident CKD in the United States (US; OPTUM Market Clarity until 31 March 2022) and Japan (Medical Data Vision until 28 February 2022) from 1 January 2016 onwards were included. CKD was defined as any of the following: a UACR measure of $\geq 30$ mg/g, two estimated glomerular filtration rate (eGFR) $\geq 90$ days apart of which the second was $\leq 75$ ml/min/1.73 m$^2$, or a CKD diagnosis code. Patients were included if they had an eGFR $\leq 60$ ml/min/1.73 m$^2$. Patients with ongoing RASi treatment at index, a history of diabetes, heart failure or dialysis were excluded.

**Results:** A total of 66,375 incident CKD patients were identified in the US ($n = 32,158$) and Japan ($n = 34,217$). Mean age was 66 and 78 years in the US and Japan, respectively, and about half of the patients were female. Mean eGFR was 48 and 40 ml/min/1.73 m$^2$ in the US and Japan, respectively. Approximately 30% of patients had cardiovascular disease, but only 13% (US) and less than 5% (Japan) were prescribed cardiovascular preventive drugs (e.g. statins and low dose aspirin). During a 1-year follow-up after the incident CKD index date, only 15% and 5% had been initiated on RASi in the US and Japan, respectively (Figure 1). Time to RASi initiation was shorter among those with a CKD diagnosis vs those without a diagnosis (US: 15 vs 19 months, Japan: 6 vs 11 months). Of those who initiated treatment, approximately 50% discontinued within one year (Figure 1). Results for initiation and discontinuation were similar across CKD stages in both countries.

**Conclusion:** In the US and Japan, initiation of RASi was remarkably low among newly identified CKD patients, and discontinuation of initiated treatment was substantial. Given that most patients with CKD benefit from multi-drug therapy (RASi + SGLT2i) for slowing CKD progression and reduction of adverse events, efforts to increase prescribing and adherence are needed.

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**EXTERNAL VALIDATION OF A NOVEL MULTIMARKER GFR ESTIMATING EQUATION**

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**Background and Aims:** The use of multiple markers may improve the accuracy in glomerular filtration rate (GFR) estimation especially when the interpretation of creatinine and cystatin C is limited. We sought to externally validate a recently developed multi-marker nuclear magnetic resonance (NMR)-based estimated GFR equation (eGFR-NMR) using the biracial Genetic Epidemiology Network of Arteriopathy cohort.

**Method:** We included 224 sex, race/ethnicity, and mGFR-category-matched participants. GFR was measured using urinary clearance of iothalamate (mGFR). We calculated eGFR-NMR using serum creatinine, valine, myo-inositol, and cystatin C, age, and sex. We compared the reliability of eGFR-NMR with current eGFR equations (2021 Chronic Kidney Disease Epidemiology Collaboration equations for creatinine [eGFR-Cr] and creatinine with cystatin C [eGFR-Cr-CysC]) using median bias, precision, and accuracy metrics. In particular, we evaluated its performance in age, sex, and race subgroups.

**Results:** In the overall cohort, mean age was 63 (±8) years, 54% were females, 49% were Black individuals, and mean mGFR was 78.7 (±24.3) ml/min/1.73 m$^2$. eGFR-NMR overestimated mGFR by 2 mL/min/1.73 m$^2$ (95% CI, 4 to 0.7) while eGFR-Cr-CysC underestimated mGFR by $-5$ ml/min/1.73 m$^2$ (95% CI, $-2$ to $-7$). All equations had acceptable accuracy metrics. When stratified by age, sex, and race, eGFR-NMR performed the best among Black males age <65 years compared to current equations (Figure 1). In this subgroup, eGFR-NMR was unbiased (bias, $2$ ml/min/1.73 m$^2$ [95% CI, $-3$ to $10$]) compared to substantial biases of eGFR-Cr (bias, 17 ml/min/1.73 m$^2$ [95% CI, 9 to 24]) and eGFR-Cr-CysC (bias, $15$ ml/min/1.73 m$^2$ [95% CI, 6 to 20]). In other subgroups, measures of accuracy for eGFR-NMR, eGFR-Cr, eGFR-Cr-CysC were generally similar.

**Conclusion:** eGFR-NMR can be used to estimate mGFR and was more accurate than CKD-EPI equations among Black males age <65 years.
Figure 1: Performance of eGFR-NMR compared to eGFR-Cr and eGFR-Cr-Cys in the GENOA cohort stratified by age, sex, and race. (1-A) Median bias is defined as the median of the differences between mGFR and eGFR, units in mL/min/1.73 m². A positive bias denotes that eGFR underestimates mGFR while a negative bias denotes that eGFR overestimates mGFR; (1-B) MAE is defined as the average of the absolute differences between each eGFR and corresponding mGFR, units in mL/min/1.73 m². GENOA = Genetic Epidemiology Network of Arteriopathy cohort; eGFR-NMR = estimated glomerular filtration rate calculated from the multi-metabolite nuclear magnetic resonance multiplex assay measuring serum creatinine, valine, and myo-inositol, with the addition of age, sex, and serum cystatin C; eGFR-Cr = GFR estimated using the race-free CKD-EPI 2021 creatinine equation; eGFR-Cr-CysC = GFR estimated using the race-free CKD-EPI 2021 creatinine and cystatin-C equation; mGFR = measured glomerular filtration rate; MAE = mean absolute error.
CANCER RELATIVE SURVIVAL IN DIALYSIS AND KIDNEY TRANSPLANT RECIPIENTS: A POPULATION-BASED STUDY IN AUSTRALIA AND NEW ZEALAND 1980-2019
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Background and Aims: Cancer survival in the general population has improved over time. Kidney failure population have a higher incidence of cancer with increased mortality. Relative survival following cancer diagnosis can provide more insight into the excess mortality directly or indirectly attributed to cancer in the kidney failure population.

Method: We estimated and compared the relative survival for dialysis patients, kidney transplant recipients and general population with cancer in Australia and New Zealand from 1980 to 2019. The general population was reference group for background mortality, matching on sex, age, calendar year and country. We used Poisson regression to quantify the excess mortality between these three groups with cancer.

Results: We included 4,089 dialysis patients and 3,253 kidney transplant recipients with an incident cancer. Dialysis patients were older, had a higher proportion of indigenous people and had more comorbidities than kidney transplant recipients. The kidney failure population had lower 5-year relative survival: 0.25 (95%CI: 0.23-0.26) for dialysis, 0.55 (95%CI: 0.53-0.57) for kidney transplant and 0.670 (95%CI: 0.669-0.670) in the general population with cancer (Figure 1). At any given time, dialysis patients had a 2.10 times higher adjusted excess mortality compared to the general population with cancer (2.10, 95%CI: 2.02-2.18), whereas kidney transplant recipients had no excess mortality (1.02, 95%CI: 0.97-1.08). Relative survival and excess mortality varied by cancer site: lung had the lowest relative survival rates, while kidney failure population with melanoma, breast and prostate cancers had the highest excess mortality. There were also sex differences: women had greater relative survival.

Conclusion: Relative survival was lower among the kidney failure population with incident cancer compared to the general population with cancer, for all-site and particularly for melanoma, breast and prostate cancer. Decreased survival may be due to poorer access to, more harm or less efficacy of treatments.

Figure 1: All-site cancer and cancer-type relative survival ratios.
THE ENVIRONMENTAL IMPACT OF CHRONIC KIDNEY DISEASE INTERNATIONALLY: RESULTS OF A LIFE CYCLE ASSESSMENT

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Background and Aims: The environmental impact of healthcare is high, and kidney care for chronic kidney disease (CKD) contributes significantly to this. Haemodialysis represents the only viable kidney replacement option for certain patients with CKD, in whom the clinical benefits are lifesaving. Haemodialysis is also resource-intensive, requiring frequent sessions, and energy- and water-intensive equipment. In recognition of this, the ERA has implemented a green nephrology initiative aiming to minimize the environmental impact of kidney care. However, there is a paucity of up-to-date analysis on the environmental impact of different dialysis techniques and CKD overall. This study presents an international, holistic life cycle assessment (LCA) of the environmental impact of CKD in adults at all CKD stages.

Method: LCA methodology was used, conducted according to ISO 14040/14044 international standards, to estimate the annual environmental impacts of each stage (1–5) of CKD per patient. At CKD Stage 5, supportive care, haemodialysis, peritoneal dialysis, and transplantation pathways were considered. A literature review was performed to identify all studies reporting healthcare resource use in CKD, stratified by CKD stage. The study boundary is summarised in Figure 1. GaBi software was used to model the pathway based on ecoinvent Life Cycle Inventory database version 3.8. Environmental impact categories were reported according to the impact assessment methods, ReCiPE 2016 v1.1 and TRACI 2.1 (US only). Here, we describe the preliminary analysis of the international study, presenting results on the annual environmental impact of in-centre haemodialysis in the UK, based on one patient receiving haemodialysis three times weekly for four hours per session. The inputs for in-centre haemodialysis comprised dialysis consumables and their transport, energy/water used by the haemodialysis machine (including reverse osmosis), heating/cooling/lighting of the healthcare area, waste disposal, and patient transport.

Results: A total of 93,600 litres of water and 3,058 kWh electricity was estimated per patient for in-centre haemodialysis annually in the UK. The carbon footprint of in-centre haemodialysis in the UK per patient was estimated to be 3,900 kg CO2 equivalents, comparable to the average UK persons annual greenhouse gas footprint, effectively doubling their yearly greenhouse gas impact. Several other environmental impact categories were measured beyond the carbon footprint, including photochemical oxidation potential (ground-level ozone formation) and fine particulate matter, measured as PM2.5. Across each impact category, the parameters that drove each environmental impact differed (Figure 2). For example, dialysis consumables, haemodialysis machine, and patient transport were the main environmental contributors of fine particulate matter, while patient transport was the main driver of terrestrial ecotoxicity.

Conclusion: The results of this LCA build upon previous published research and demonstrate a high carbon footprint for in-centre haemodialysis, in line with other studies. The results also show that the environmental impact of in-centre haemodialysis goes beyond that of its carbon footprint, to other important environmental aspects such as PM2.5 emissions, in which long-term exposure is associated with health problems, such as cardiovascular...
and respiratory diseases, and an increased risk of CKD. This study hopes to highlight the need for evidence-based policy interventions around the implementation of green nephrology initiatives such as use of renewable energy to power haemodialysis, utilisation of water conserving reverse osmosis systems, and reduction in waste. Furthermore, healthcare policy initiatives that could help detect patients in the early stages of CKD and thereby enable them to be managed proactively could eventually reduce the need for resource-intensive dialysis therapy.

**#3184**

**CHRONIC KIDNEY DISEASE IN NON-RENAL SOLID ORGAN TRANSPLANTATION: WHAT IS THE ROLE OF THE NEPHROLOGIST?**

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²University General Hospital of Valencia, Nephrology, Valencia, Spain and
³Cardenal Herrera-CEU University, Alfara del Patriarca, Valencia, Spain

**Background and Aims:** Chronic kidney disease (CKD) is a frequent complication of non-kidney solid organ transplant (NKSOT) and is related to increased morbidity and mortality. Identifying predisposing factors is crucial for an early approach and correct referral to Nephrology, a specialty with an important role in managing these patients.

**Method:** This is a single-center retrospective observational study of a cohort of CKD patients under follow-up in the department of nephrology during the period between January 2010 to December 2020. A total of 212 patients were analyzed. Patients transplanted before 2010 (101 patients), with combined transplantation with renal transplantation (9 patients), and those with no follow-up in external consultations (28 patients) were removed from the sample. A final population sample was obtained with 74 patients. Statistical analysis was performed between all the risk above factors (Figure 1) and the four dependent variables: advanced chronic kidney disease (ACKD), increased serum creatinine ≥50%, renal replacement therapy (RRT), and death in three different periods: pre-transplant period, peri-transplant period and post-transplant period.

**Results:** 74 patients were analyzed (7 heart transplant recipients, 34 liver transplant recipients, and 33 lung transplant recipients).

- 45 patients presented an increase in Creatinine ≥50%. Receiving a lung transplant confers more risk versus a liver (HR 0.048 [95% CI 0.012 to 0.192) or heart (HR 0.075 [95% CI] 0.01 to 0.5) transplant. It was significantly associated with pre-transplant obesity (p 0.003), peri-transplant mechanical ventilation (p < 0.001), peri-transplant (p 0.009) and post-transplant (p 0.005) anticalcineurin overdose, peri-transplant (p 0.046) and post-transplant nephrotoxics (0.03) and the number of hospital admissions (p. 0.002). Not having follow-up by Nephrology in the pre-transplant (p 0.027), peri-transplant (p 0.045), and the longest time until external consultations (HR 1.032 [95% CI] 1.011 to 1.054) conferred more risk.

- 24 patients developed ACKD. Receiving a lung transplant confers more risk versus a liver (HR 0.14 [95% CI] 0.045 to 0.463) or heart (HR 0.13 [95% CI] 0.015 to 1.28) transplant. Per-transplant mechanical ventilation (p 0.03), peri-transplant (p 0.024) and post-transplant (p 0.038) anticalcineurin overdose, peri-transplant (p 0.045) and post-transplant nephrotoxic antimicrobials (p. 0.04) and the number of hospital admissions (p 0.015) were significantly associated. The time to nephrology consultations after the transplant (p 0.035) conferred more risk. Mean ACKD-free survival was 93.29 months (95% CI of 79.04-107.5), 121.5 months in heart transplantation recipients (95% CI of 86.70-155.29), 104 months in liver transplantation recipients (95% CI of 86.67-122.134) and 66.86 months in lung transplantation recipients (CI at 95% of 55.93 – 80.79) (Figure 2).

- 8 patients required RRT. It was significantly associated with the active smoking habit in the pre-transplant period (p 0.02) and the overdose of calcineurin inhibitors in the peri-transplant period (p 0.045).

- 21 patients died. It was significantly associated with the active smoking habit in the pre-transplant (p 0.03) and the number of hospital admissions in the post-transplant (p 0.006).

**Conclusion:** Early follow-up by Nephrology is associated with a decrease in the deterioration of renal function and the development of advanced chronic kidney disease, by being able to act on the risk factors for each transplant recipient, such as an overdose of calcineurin inhibitors and nephrotoxicity, and allowing the identification of patients at higher risk, such as those requiring mechanical ventilation during peri-transplantation, patients with the highest number of hospital admissions, and lung transplant patients.
Background and Aims: The tissue pathology of both aging and chronic kidney disease (CKD) is nephrosclerosis defined by globally sclerotic glomeruli (GSG) and interstitial fibrosis and tubular atrophy (IFTA). We sought to determine if risk of CKD outcomes is better predicted by age-based or young adult-based thresholds for nephrosclerosis.

Method: Using the Aging Kidney Anatomy study, living kidney donors, kidney tumor patients, and native kidney disease patients had kidney biopsy images analyzed morphometric to quantify %GSG, %IFTA, and IFTA foci density (Figure 1). Using normotensive donors, young (18-29 y) thresholds and age-based (18-29 y, 30-39 y, 30-39 y, 50-59 y, 60-69 y, 70+ y) 95th percentile thresholds were defined. Progressive CKD was defined as a 40% decline in serum creatinine based estimated GFR or kidney failure (dialysis or transplantation) from a 4-month post-biopsy baseline (due to the nephrectomy event in tumor patients and due to the common occurrence of acute kidney injury in the native kidney disease patients at the time of biopsy). The age-adjusted risk of progressive CKD in tumor patients and native kidney disease patients was compared between those with nephrosclerosis that was "normal compared to young", "normal for age but abnormal compared to young", and "abnormal for age" (Figure 2).
Figure 1: An example of the TRI-stained biopsy image for kidney donors (A) were used to trace cortex (traced in green), non-sclerosed glomerulus (NSG) (traced in blue), each globally sclerosed glomerulus (GSG) (traced in red), and each distinct IFTA focus (traced in black). Example of PAS-stained biopsy section (B) for tumor patients. Example of TRI-stained section (C) for native kidney disease patients.

Figure 2: Conceptual model of young-threshold and age-based thresholds for nephrosclerosis measures defined using 2583 normotensive kidney donors. The 95th percentile for 18-29 years defined the abnormal compared to young threshold. The 95th percentile for 70-77 years defined the abnormal for age threshold for all persons 70 years and older.
Results: There were 2583 normotensive living kidney donors, 1363 tumor patients, and 314 native kidney disease patients studied. The 95th percentiles for 18-29y to 70 +y age groups among normotensive donors were 1.7% to 16% for %GSG, 0.18% to 6.5% for %IFTA, and 8.2 to 59.3 per cm2 for IFTA foci density. The risk of CKD outcomes did not differ between tumor patients and native kidney disease patients with nephrosclerosis “normal compared to young” versus “abnormal compared to young but normal for age” in both cohorts. Thus, these two categories were combined into “normal for age”. The risk of progressive CKD over a median 5.5 years follow-up for tumor patients was higher with %GSG, %IFTA, and IFTA foci density that was abnormal for age vs normal for age (HRs 2.28, 2.41, and 3.11, respectively, p<.0001 for all). The risk of progressive CKD over a median 7.2 years follow-up for native kidney disease patients was higher with %GSG, %IFTA, and IFTA density that was abnormal for age vs normal for age (HRs 1.87, 2.65, and 3.11, respectively, p<.0001 for all).

Conclusion: There is a substantial increase in nephrosclerosis from aging alone in healthy adults that is not prognostic for CKD outcomes. Age-based thresholds better identify clinically relevant CKD.

#3901
PROGRESSION OF INCIDENT CHRONIC KIDNEY DISEASE: A DANISH NATIONWIDE POPULATION-BASED COHORT STUDY
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Background and Aims: The increasing global burden of kidney failure calls for targeted interventions to slow progression of chronic kidney disease (CKD). However, the understanding of progression from CKD stage G3 is limited. We aimed to characterise individuals with incident CKD stage G3 in Denmark and to examine CKD progression defined by three different measures.

Method: We conducted a nationwide, population-based cohort study using routinely collected individual-level data from national health and administrative databases in Denmark (population ~5-9 million). Using creatinine tests performed in general practice and the outpatient hospital setting from 1 January 2017 to 31 December 2020, we included all adults in Denmark with incident CKD stage G3, based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria (≥2 creatinine measurements corresponding to an estimated glomerular filtration rate (eGFR) between 30-59 ml/min/1.73 m² separated by ≥90 days). We used the 2009 CKD Epidemiology Collaboration Creatinine Equation for calculating eGFR. The three years leading up to the study period constituted a washout period to minimize inclusion of patients with prevalent CKD. We explored CKD progression based on three outcome measures of different sensitivity, including 1) rapid CKD progression (decline in eGFR of ≥5 ml/min/1.73 m²/year, that is, for each eGFR measurement taken during follow-up, we considered this and the measurements taken in the prior year (requiring ≥2 eGFR measurements separated by ≥90 days)); 2) drop in GFR category (drop between GFR categories, 45–59 [G3a], 30–44 [G3b], 15–29 [G4], <15 [G5] ml/min/1.73 m², accompanied by ≥25% drop in eGFR from baseline); and 3) kidney failure (≥2 eGFR measurements <15 ml/min/1.73 m² separated by 90 days and/or kidney replacement therapy). The 1- and 3-year risks of CKD progression according to the three definitions and all-cause mortality were examined as cumulative incidences using the Aalen-Johansen method.

Results: We included 133,443 individuals with incident CKD stage G3. The median age at inclusion was 75 years (interquartile range (IQR): 69-82) and 55% were females with 59% having hypertension, 18% having diabetes and 10% having heart failure. The median eGFR at inclusion was 56 ml/min/1.73 m² (IQR: 51-58) and the median number of eGFR measurements was 3 (IQR: 2-5) in the prior year. Among the 133,443 individuals with incident CKD stage G3, 48,997 (37%) fulfilled the criteria for rapid CKD progression at inclusion. Among the 84,446 individuals without rapid progression on the day of inclusion, the 1- and 3-year risks of rapid CKD progression were 25.0% (95% confidence interval (CI): 24.7-25.3) and 46.0% (95% CI: 45.6-46.4), respectively. The risk of a drop in GFR category was 6.9% (95% CI: 6.8-7.1) after 1 year and 16.6% (95% CI: 16.4-16.8) after 3 years. The risks of kidney failure/renal replacement therapy were 0.1% (95% CI: 0.1-0.1) and 0.3% (95% CI: 0.3-0.4) after 1 and 3 years, respectively. All-cause mortality was 6.8% (95% CI: 6.7-6.9) in the first year and the 3-year mortality was 18.1% (95% CI: 17.9-18.4) (Table 1).

Table 1: Risks of CKD progression and mortality in individuals with incident CKD stage G3.

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<tr>
<th>Risk Category</th>
<th>1-year Risk</th>
<th>3-year Risk</th>
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<td>Rapid CKD progressiona</td>
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<td>46.0 (45.6-46.4)</td>
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<tr>
<td>Drop in GFR category</td>
<td>6.9 (6.8-7.1)</td>
<td>16.6 (16.4-16.8)</td>
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<tr>
<td>Kidney failure</td>
<td>0.1 (0.1-0.1)</td>
<td>0.3 (0.3-0.4)</td>
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<tr>
<td>All-cause mortality</td>
<td>6.8 (6.7-6.9)</td>
<td>18.1 (17.9-18.4)</td>
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#3953
TOXIC MICROBIOME AND CHRONIC KIDNEY DISEASE: INSIGHTS FROM THE CKD-REIN COHORT STUDY
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Background and Aims: Many uremic toxins (UTs) originate from gut microbiome, and contribute to chronic kidney disease (CKD) progression and cardiovascular morbidity. In order to reduce uremic symptoms and CKD progression, patients have several dietary restrictions, which may influence gut microbiome composition, and impact UTs production. An altered microbiome may contribute to UTs increase in those patients. However, the role of key bacterial taxa in producing UTs and the impact of diet on UTs variance in non-dialysis patients are not well known. The objectives of this study were, first, to compare microbial features between CKD patients and healthy controls, and, second, to investigate the relation of gut microbiome with uremic toxicity, as well as the potential impact of diet on such relationship.

Method: Characterization of gut metagenomes, 10 UTs and 3 precursors’ serum concentrations by LC-MS/MS, host characteristics and diet were obtained from 240 non-dialysis CKD patients from the CKD-REIN cohort (mean ± SD): age: 68 ± 11 years, 71% male, estimated glomerular filtration rate (eGFR): 33.2 ± 12.7 ml/min/1.73m². First, to identify microbial biomarkers characterizing the gut microbiome-related toxicity in CKD, we compared microbiome features between 78 CKD patients and 78 age-, sex-, and BMI-matched healthy controls from the Milieu Interieur (MI) cohort: age: 58 ± 13 years, 71% male, eGFR: 89 ± 13. Second, we performed a multomics’ data integration analysis via a supervised modelling to investigate cross-sectionally the association between host characteristics, gut microbiome, UTs, and diet-related features according to CKD severity (eGFR <30, n = 110 vs eGFR ≥30 ml/min/1.73m², n = 130).
Results: Compared to healthy controls, CKD patients had a significant reduced gut microbiome health index. Several Metagenomic Species Pan-genomes (MSPs) were significantly contrasted between M1 and CKD cohorts: 43 species were enriched in CKD patients vs 24 in controls. Species most enriched in CKD patients included several UTs producers such as Lachnospiraceae spp., Dysosmobacter – Oscillibacter spp, Butyricimonas fecalisomibins, Viciafilavis vadensis and Hungatella spp, some of which were positively correlated with the following UTs: 3-Carboxy-4-methyl-5-propyl-2-furanpropionate (CMPP), trimethylamine-N-oxide (TMAO), and indole-3-acetic acid (3-IAA). Moreover, species belonging to Enterocloster and Hungatella genera (both members of Lachnospiraceae family) were found to be negatively correlated with eGFR. Among species associated with CKD severity, species carrying genes for UTs production were observed such as Desulfovibrio faecalisomibins, Bacteroides clarus and Blautia obeum along with increasing alcohol and hot drinks consumption, CRP and several UTs (kynurenic acid, indoxyl sulfate and Phenylacetylglutamine) levels. In contrast, some taxa like Faecalibacterium prausnitzii and Dysosmobacter wellbi was associated with ileum intake but not with UTs.

Conclusion: Our study highlights an alteration of gut microbiome in CKD patients compared to healthy controls, with increased abundance of UTs producer species. The results of the multidimensional data integration modelling suggest a strong interplay between food intake, gut microbiome modifications, UTs accumulation and clinical features. These findings might open to promising therapeutic strategies to reduce microbiome-related toxicity.

#4420

EARLY DAPAGLIFLOZIN UTILIZATION FOR CHRONIC KIDNEY DISEASE TREATMENT IN JAPAN

Tadashi Sofue1, Masayoshi Takeda2, Yo Koto3, Jason Wright4, Lai San DISEASETREATMENTINJAPAN

Results:
- Among species associated with CKD severity, species carrying genes for UTs producer species. The results of the multidimensional data integration
- Metagenomic Species Pan-genomes (MSPs) were significantly contrasted between M1 and CKD cohorts: 43 species were enriched in CKD patients vs 24 in controls. Species most enriched in CKD patients included several UTs producers such as Lachnospiraceae spp., Dysosmobacter – Oscillibacter spp, Butyricimonas fecalisomibins, Viciafilavis vadensis and Hungatella spp, some of which were positively correlated with the following UTs: 3-Carboxy-4-methyl-5-propyl-2-furanpropionate (CMPP), trimethylamine-N-oxide (TMAO), and indole-3-acetic acid (3-IAA). Moreover, species belonging to Enterocloster and Hungatella genera (both members of Lachnospiraceae family) were found to be negatively correlated with eGFR. Among species associated with CKD severity, species carrying genes for UTs production were observed such as Desulfovibrio faecalisomibins, Bacteroides clarus and Blautia obeum along with increasing alcohol and hot drinks consumption, CRP and several UTs (kynurenic acid, indoxyl sulfate and Phenylacetylglutamine) levels. In contrast, some taxa like Faecalibacterium prausnitzii and Dysosmobacter wellbi was associated with ileum intake but not with UTs.

Conclusion: Our study highlights an alteration of gut microbiome in CKD patients compared to healthy controls, with increased abundance of UTs producer species. The results of the multidimensional data integration modelling suggest a strong interplay between food intake, gut microbiome modifications, UTs accumulation and clinical features. These findings might open to promising therapeutic strategies to reduce microbiome-related toxicity.
METABOLIC BLOOD BIOMARKER PROFILING FOR CHRONIC KIDNEY DISEASE PREDICTION – EVIDENCE FROM 275,000 INDIVIDUALS IN THE UK BIOBANK

Heli Julkunen
Nightingale Health Plc, Finland

Background and Aims: Early identification of individuals at high risk of developing chronic kidney disease and other chronic conditions is essential for targeted prevention. Here, we assess the utility of metabolic blood biomarkers in predicting the onset of chronic kidney disease in over 250,000 individuals from UK Biobank, beyond established risk factors and polygenic risk scores.

Method: Circulating blood biomarkers, including lipids, fatty acids, amino acids, glycolysis metabolites and inflammation markers were measured by a low-cost nuclear magnetic resonance (NMR) metabolomics assay in around 275,000 plasma samples from the UK Biobank. During a prospective 10-year follow-up, over 6000 incident chronic kidney disease events were obtained from national health registries. Using multivariable regression modelling, we derived a 10-year risk score for chronic kidney disease onset. We assessed the predictive performance of the biomarker risk score in comparison to standard risk factors (age, sex, prevalent diabetes, body mass index, systolic and diastolic blood pressure, smoking status and use of cholesterol lowering medication), clinical chemistry measurements (HbA1c, LDL and HDL cholesterol, total cholesterol and eGFR) and polygenic risk scores. We evaluated the performance of the risk score in two practical scenarios: in a general population screening setting and in a clinical use case of stratifying kidney disease risk among prevalent type 2 diabetics. Among diabetics with mildly to moderately decreased kidney function at the time of blood sampling (eGFR 60-90), adding the metabolic biomarkers in a comprehensive model including standard risk factors, clinical chemistry measurements and polygenic risk scores increased the AUC from 0.60 to 0.70.

Conclusion: Circulating metabolic biomarkers enhanced the prediction of chronic kidney disease onset beyond standard risk factors and polygenic risk scores. From a translational perspective, this may complement the identification of high-risk individuals in both general population and clinical settings beyond current risk factor assessment, while simultaneously informing on the risk of other chronic diseases.

CARDIOVASCULAR AND MORTALITY RISKS IN YOUNG HEALTH SCREENING EXAMINEES WITH MARGINAL ESTIMATED GLOMERULAR FILTRATION RATE

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1Seoul National University Hospital, Rep. of South Korea, 2Seoul National University Hospital, Rep. of South Korea and 3PaiChai University, Rep. of South Korea

Background and Aims: Additional evidence is necessary to interpret the kidney function parameters in young adults, particularly in those with marginal eGFR values. We aimed to study the clinical significance of marginal eGFR values in large-scale general health screening examinees of young age (20-39 years).
Method: We performed a nationwide retrospective cohort study using the health screening database of South Korea. We included young adults aged 20-39 years without a history of major cardiovascular events (MACE) or end-stage kidney disease who underwent a nationwide health screening in 2012. The study exposure was eGFR categorized into 15 mL/min/1.73 m² intervals, with a reference group and a main group of interest: < 30, 30-45, 45-60, 60-75, 75-90 (reference), 90-105, 105-120, and ≥ 120 mL/min/1.73 m². The risks of all-cause mortality and MACE were calculated using Cox regression analysis adjusted for various clinicodemographic characteristics.

Results: In total, 3,132,409 young adults were included in this study. During a median follow-up of 7.3 years, marginal eGFR (60-75 mL/min/1.73 m²) was not significantly associated with a higher risk of all-cause mortality [adjusted HR 0.92 (0.86-0.99)]. The results were similarly identified for the MACE outcome [adjusted HR 1.01 (0.94-1.07)]. On the other hand, those with presence of albuminuria, even the marginal eGFR range was significantly associated with higher risks of all-cause mortality [adjusted HR 1.52 (1.01-1.29)] and ischemic stroke [adjusted HR 1.73 (1.10-2.74)].

Conclusion: Marginal eGFR alone was not associated with higher risks of all-cause mortality and MACE in general young adults. However, in those with albuminuria, the mortality risk was higher even in eGFR of 60-75 mL/min/1.73 m².

#3437
THE ASSOCIATION OF INTERLEUKIN-6 TO ALBUMIN RATIO WITH MORTALITY IN PATIENTS WITH KIDNEY FAILURE
Xiejia Li1,2, Abdul Rashid Tony Qureshi1, Mohamed Suliman1, Olof Heimbürger1, Franz Peter Barany1, Peter Stenvinkel1 and Bengt Lindholm1

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Background and Aims: Systemic inflammation - characterized by high interleukin-6 (IL-6) and low albumin circulating concentrations - associates with worse outcomes in patients with kidney failure (KF). We examined the value of IL-6 to albumin ratio (IAR) to stratify risk of death in KF patients.

Method: In 435 incident dialysis patients (median age 56 years, 61.8% male, 31% diabetes mellitus (DM), 38.4% cardiovascular (CV) disease (CVD)), plasma IL-6 and albumin were measured at baseline to calculate IAR. We performed receiver operating characteristic curve (ROC) to compare the discriminatory performance of albumin, IL-6 and IAR for predicting all-cause and CV mortality. We divided patients into IAR tertiles and analysed: 1) cumulative incidence of all-cause mortality and CV mortality censored for renal transplantation during follow up of up to 60 months; 2) the association of IAR and all-cause and CV mortality risk according to Fine-Gray analysis taking renal transplantation as competing risk; and 3) the restricted mean survival time (RMST) and differences of RMST (ΔRMST) between IAR tertiles to describe quantitative differences of survival time.

Results: Among 435 patients, 146 patients (33.6%) died, and 175 (40.2%) patients underwent renal transplantation during median 24.9 months of follow-up; 83 (56.8%) of the 146 deaths were due to CVD. The area under the ROC curve (AUC) of IAR (0.696 for all-cause mortality; 0.657 for CV mortality) was higher than that of both albumin and IL-6. As shown in Fig. 1 A and B: 1) the cumulative incidence of all-cause and CV mortality of patients in middle and high IAR tertiles was significantly higher than in low IAR tertile; 2) higher IAR associated with higher risk of all-cause (sub-hazard ratio (shR) 1.93, 95% confidence interval (CI) 1.22-3.06 for high IAR tertile) and CV mortality (shR 1.99, 95% CI 1.03-3.87 for middle IAR tertile) risk after adjusting for age, sex, DM, CVD, and smoking; and 3) ΔRMST at 59 months showed shorter survival time in middle and high IAR tertiles compared with low IAR tertile for all-cause (ΔRMST -6.21 months for middle vs low tertile; ΔRMST -11.4 months for high vs low tertile) and CV mortality (ΔRMST -4.73 months for middle vs low tertile; ΔRMST -7.49 months for high vs low tertile).

Conclusion: Higher IAR was independently associated with significantly higher all-cause and CV mortality risk in KF patients. These results suggest that IAR may provide useful prognostic information in patients with KF.
**Figure 1:** Cumulative incidence of all-cause mortality (A) and CV mortality (B) censored for renal transplantation in IAR tertiles. Taking LT as reference, sHR of HT and MT, $\Delta$RMST at 59 months for HT and MT after adjusting for age, sex, DM, CVD and smoking are shown. Abbreviations: IAR, interleukin-6 to albumin ratio; LT, low tertile; MT, middle tertile; HT, high tertile; CV, cardiovascular; DM, diabetes mellitus; CVD, cardiovascular disease; $\Delta$RMST, difference in restricted mean survival time.

#3667

**REVEAL-CKD: PREVALENCE OF UNDIAGNOSED STAGE 3 CHRONIC KIDNEY DISEASE IN AUSTRALIA, BRAZIL, CANADA AND SPAIN**

Roberto Pecoits-Filho¹, Maria Cristina Ribeiro de Castro¹, Ana Cebrian³, Rafael Santamaría³, Kean-Seng Lim⁵, Eric Wittbrodt⁶, Salvatore Barone⁷, Matthew Arnold⁸ and Navdeep Tangri⁹

¹Pontifical Catholic University of Paraná, Curitiba Campus, Brazil, ²Hospital das Clínicas of the University of São Paulo, Brazil, ³Cartagena Casco Health Center, Servicio Murciano de Salud, Murcia, Spain, ⁴Hospital Universitario Reina Sofia, Córdoba, Spain, ⁵Mount Druitt Medical Centre, Mount Druitt, Australia, ⁶AstraZeneca, Wilmington, United States of America, ⁷AstraZeneca, Gaithersburg, United States of America, ⁸AstraZeneca, Cambridge, United Kingdom and ⁹University of Manitoba, Winnipeg, Canada

**Background and Aims:** Chronic kidney disease (CKD) is a progressive condition that affects >850 million people globally. Global clinical guidelines from KDIGO recommend early CKD identification and management to mitigate disease progression. The REVEAL-CKD study aims to assess the prevalence of, and factors associated with, undiagnosed stage 3 CKD across 11 countries. Here we report data from 4 countries in 4 continents.

**Method:** REVEAL-CKD is a multi-national, observational study, using secondary data from electronic medical records (EMR) and claims data. For this analysis, data were extracted from Australian General Practices through Pen CS (Australia), University of Sao Paulo (Brazil), the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) (Canada), and BIGPAC (Spain). The study cohort included patients aged ≥18 years with two consecutive estimated glomerular filtration rate (eGFR) values ≥30 and <60 mL/min/1.73 m² recorded 91-730 days apart. The date of the second qualifying eGFR was the index date. Patients with no CKD diagnosis code before and up to 6 months after their index date were considered undiagnosed. The prevalence of undiagnosed CKD was calculated as the ratio of undiagnosed patients to all patients meeting the study inclusion criteria.

**Results:** The prevalence and baseline characteristics of undiagnosed Stage 3 CKD appear in Table 1. In all 4 countries, the undiagnosed prevalence was >80% and predominantly was more commonly observed in female patients, in patients aged >65y, and remained high in patients with baseline comorbidities, particularly for those at highest risk of CKD (DM, CVD, HTN). Underreporting of CKD diagnosis in Brazil may be due to the inability to code for >1 condition in a patient.

**Conclusion:** These results indicate that a large proportion of patients across four world regions and who have biochemical evidence of early CKD lack a recorded diagnosis. An opportunity exists to identify, diagnose, and implement guideline-directed management for early CKD in order to delay its complications and improve clinical outcomes.
<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>AUSTRALIAN GENERAL PRACTICES THROUGH PEN CS, AUSTRALIA</th>
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<th>CPCSSN, CANADA</th>
<th>BIGPAC, SPAIN</th>
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<tr>
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<td>11101/11438</td>
<td>42226/45915</td>
<td>27481/32383</td>
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<td>(90.1%)</td>
<td>(97.1%)</td>
<td>(92.0%)</td>
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<td>MEAN AGE AT INDEX (YEARS +/- SD)</td>
<td>76.4 +/- 9.5</td>
<td>70.5 +/- 13.2</td>
<td>75.9 +/- 10.7</td>
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<td>109/118</td>
<td>3359/3542</td>
<td>5837/6486</td>
<td>5381/6036</td>
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<td></td>
<td>(92.4%)</td>
<td>(94.8%)</td>
<td>(90%)</td>
<td>(89.2%)</td>
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<tr>
<td>AGE &gt;65 YEARS</td>
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<td>7742/7896</td>
<td>36389/39428</td>
<td>22090/26337</td>
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<tr>
<td></td>
<td>(89.8%)</td>
<td>(98.0%)</td>
<td>(92.3%)</td>
<td>(83.9%)</td>
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<td>SEX</td>
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<td>FEMALE</td>
<td>589/649</td>
<td>5918/6036</td>
<td>24379/26317</td>
<td>13428/16166</td>
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<td></td>
<td>(90.8%)</td>
<td>(98%)</td>
<td>(92.6%)</td>
<td>(83.1%)</td>
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<td>17847/19597</td>
<td>13607/15700</td>
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<td></td>
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<td>(86.7%)</td>
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<tr>
<td>MEAN EGFR (ML/MIN/1.73 M² +/- SD)</td>
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<td>47.3 +/- 8.0</td>
<td>49.4 +/- 7.6</td>
<td>46.0 +/- 8.6</td>
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<td>HYPERTENSION</td>
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<td>442/466</td>
<td>29539/32192</td>
<td>17886/21255</td>
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<td></td>
<td>(83.0%)</td>
<td>(94.8%)</td>
<td>(91.8%)</td>
<td>(84.1%)</td>
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<tr>
<td>HEART FAILURE</td>
<td>35/46</td>
<td>642/682</td>
<td>4122/4556</td>
<td>6028/7348</td>
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<td>(94.1%)</td>
<td>(90.5%)</td>
<td>(82.0%)</td>
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<tr>
<td>AF</td>
<td>84/101</td>
<td>53/57</td>
<td>3550/4348</td>
<td>ND</td>
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<td>(83.2%)</td>
<td>(93.0%)</td>
<td>(88.5%)</td>
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<tr>
<td>CVD</td>
<td>130/148</td>
<td>631/655</td>
<td>5125/5794</td>
<td>9131/10950</td>
</tr>
<tr>
<td></td>
<td>(87.8%)</td>
<td>(96.3%)</td>
<td>(88.5%)</td>
<td>(83.4%)</td>
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<tr>
<td>DM</td>
<td>195/224</td>
<td>133/138</td>
<td>11255/12260</td>
<td>12250/14642</td>
</tr>
<tr>
<td></td>
<td>(87.1%)</td>
<td>(96.4%)</td>
<td>(91.8%)</td>
<td>(83.7%)</td>
</tr>
</tbody>
</table>

Notes: ¹(undiagnosed CKD/overall population)*100; ²in undiagnosed; CKD, chronic kidney disease; AF, atrial fibrillation; CVD, cardiovascular disease; DM, diabetes mellitus; ND, not done; SD, standard deviation.

Table 1: Prevalence of undiagnosed stage 3 CKD and by baseline characteristics.
GENETIC SUSCEPTIBILITY AS AN EFFECT MODIFIER FOR THE ASSOCIATION BETWEEN CHRONIC KIDNEY DISEASE AND RISK OF VENOUS THROMBOEMBOLISM

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Background and Aims: The association between chronic kidney disease (CKD) and the risk of developing venous thromboembolism (VTE) is still controversial. Further, it is unknown if genetic predisposition modifies this relationship. This study was conducted to investigate plausible effect modification of genetic factors on the association between CKD and incident VTE.

Method: Population-based cohort study of the UK Biobank, including 397,658 participants of European ancestry that were free of VTE at recruitment. We used cystatin C combining creatinine estimated glomerular filtration rate (eGFR) and albuminuria to classify participants with CKD stages 1-5 according to the low, intermediate, and high/very high-risk groups suggested by KDIGO (Kidney Disease: Improving Global Outcomes). Cox proportional hazards model was applied to evaluate the associations of CKD with incident VTE. In addition, we used externally validated polygenic risk score (PRS) for VTE to evaluate whether the genetic predisposition modified the associations of interest.

Results: During median follow-up of 12.7 years, 11,372 participants developed VTE. As compared with low KDIGO risk category, covariate-adjusted hazard ratios (HR) and 95% confidence intervals (CI) for future VTE risk with intermediate and high/very high KDIGO risk categories at baseline were 1.278 (1.191-1.372) and 1.892 (1.658-2.159), respectively. Participants at high/very high risk of CKD prognosis and in the highest tertile of PRS had the highest risk of developing VTE (HR, 4.397; 95% CI, 3.639-5.313), and this group had shown the most conspicuous additive interactions between CKD and the genetic predisposition, which responsible for 1.389-fold relative excess risk and accounted for 31.6% of incident VTE. Also, when either eGFR or urine albumin-creatinine ratio (ACR) was treated as the exposure, similar associations and supra-additive interactions were yielded.

Conclusion: CKD is associated with future VTE, especially in those with high genetic risk.
Additive interaction between the KDIGO risk category and genetic susceptibility on venous thromboembolism risk. Abbreviations: AP, attributable proportion; CKD, chronic kidney disease; PRS, polygenic risk score; RERI, relative excess risk due to interaction; VTE, venous thromboembolism. Reference was the group of low polygenic risk score and low risk of chronic kidney disease prognosis. All models were adjusted for age, sex, highest attained education, Townsend deprivation index, smoking, alcohol consumption, metabolic equivalents of physical activity, body mass index, hypertension, diabetes, cardiovascular diseases other than hypertension, cancer, cholesterol-lowering medications, anticoagulants, antiplatelet agents, top 20 principal components of ancestry, and genotyping batch.

THE GROWING BURDEN OF CHRONIC KIDNEY DISEASE IN THE UK: AN IMPACT CKD ANALYSIS
Juan Jose Garcia Sanchez1, David C. Wheeler2, Stephen Brown1, Stacey Priest3, Hannah Guiang3, Charlotte Johnston Webber4, George Wharton4, Salvatore Barone1 and Daniel Grima3
1BioPharmaceuticals, AstraZeneca, Cambridge, United Kingdom, 2University College London, Department of Renal Medicine, London, United Kingdom, 3EVERSANA, Value & Evidence, Burlington, Canada and 4London School of Economics and Political Sciences, London, United Kingdom

Background and Aims: Chronic kidney disease (CKD) is a major source of morbidity and mortality, with an increasing incidence and prevalence worldwide. Patients with CKD experience diminished quality of life associated with increased risk of cardiovascular (CV) events, acute kidney injury (AKI), and reduced renal function. Late-stage CKD (stage 5) is also associated with significant economic burden related to renal replacement therapy (RRT). Public health and policy planning should consider the broader burden of CKD, including its societal and environmental burden, in addition to its clinical impacts and direct costs. Hence, IMPACT CKD aims to quantify the clinical, economic, humanistic, societal, and environmental burden of CKD in the United Kingdom (UK).

Method: A patient-level simulation model was developed to simulate the UK population using parameter data from published literature, national statistics, and health surveys. Individuals were assigned key characteristics associated with CKD, such as estimated glomerular filtration rate (eGFR), albuminuria, co-morbidities (e.g., diabetes, hypertension, heart failure), and prior CV events (e.g., myocardial infarction and stroke). Individuals were categorized as not having CKD (i.e., non-CKD) or CKD stage 1, 2, 3a, 3b, 4 or 5, based on their eGFR and albuminuria levels. Among those with CKD, patients were either classified as diagnosed or undiagnosed. Progression through the CKD stages was predicted by the simulated patient’s annual eGFR rate of decline. Risk of CV and AKI events, as well as co-morbidity development were also considered in the model. Clinical progression and outcomes for the CKD population were simulated over 10 years. CKD prevalence was projected by stage and diagnosis status, as well as associated CKD and RRT costs, productivity losses from patients and caregivers, and environmental impacts as determined by CO2 emissions. Extensive validation and calibration was conducted.

Results: From 2022 to 2032, the prevalence of CKD is expected to increase by 4% from 8.27 million to 8.61 million people in the UK. Growth in the CKD population is driven by eGFR decline and increases in albuminuria, related to kidney function decline and AKI as the model population ages. In 2032, the prevalence of CKD by stage is projected to be 30.36%, 21.07%, 29.78%, 11.86%, 4.15%, and 2.78% in stage 1, 2, 3a, 3b, 4, and 5 patients, respectively. The diagnosed CKD population is projected to be 32.43% of the total CKD population and is primarily composed of CKD stage 3a/b, 4, and 5 patients in 2032. Patients with CKD receiving RRT are projected to increase by 4% from 73,365 in 2022 to 105,860 in 2032. The increase in late-stage CKD population is associated with an increase in RRT costs from £1.09 billion in 2022 to £1.85 billion in 2032. Over the 10-year time horizon, CKD is projected to result in 81.60 million missed workdays in diagnosed patients with CKD, and 11.89 million missed workdays by caregivers of patients with CKD. Environmental impacts equivalent to 1.35 million tonnes of CO2 emissions for patients receiving in-centre hemodialysis are predicted; however, the total environmental impact would likely be larger if the total CKD care pathway was included.

Conclusion: The IMPACT CKD model forecasts the prevalence and burden of CKD to remain high in the UK over the next ten years. In addition to the significant clinical burden and direct costs, CKD was also associated with extensive productivity loss and detrimental environmental impact. The model provides a validated framework for testing the sensitivity of the projections to data uncertainty, thereby identifying areas for further research.
THE ASSOCIATION BETWEEN POTASSIUM INTAKE AND RISK OF
CHRONIC KIDNEY DISEASE
Seung Hyeok Han, Hae-Ryong Yun and Hyo Jeong Kim
Yonsei University College of Medicine, Department of Internal Medicine, Seoul, Rep. of South Korea

Background and Aims: High potassium intake is closely related to lower risk of cardiovascular disease. However, the association between potassium intake and chronic kidney disease (CKD) development in the general population is uncertain.

Method: From UK biobank cohort, we included 317,162 participants without CKD between 2006 and 2010. The main predictor was spot urine potassium-to-creatinine ratio (KCR) as a surrogate of potassium intake. The primary outcome was incident CKD, defined based on ICD-10 and OPCS-4 codes. For secondary analysis, we included 141,180 participants who completed 24-h dietary recall questionnaire and dietary potassium intake was an additional predictor.

Results: At baseline, individuals with higher KCR had lower levels of blood pressure, BMI, and inflammation, and were less likely to have diabetes and hypertension than those with lower KCR. During a median follow-up of 11.9 years, the primary outcome events occurred in 15,255 (4.8%) participants. In competing risk model, adjusted hazard ratio (aHR) per 1-SD increase in KCR for incident CKD was 0.90 (95% confidence interval [CI], 0.89-0.92). In addition, compared with quartile 1 of KCR, the aHRs (95% CIs) for second, third, and fourth quartile were 0.98 (0.94–1.02), 0.90 (0.86–0.95), and 0.80 (0.76–0.84), respectively. In secondary analysis, higher potassium consumption was also inversely associated with risk of CKD. Compared with quartile 1 of dietary potassium intake, the corresponding aHRs (95% CIs) for each quartile were 0.85 (0.78–0.92), 0.73 (0.67–0.81), and 0.67 (0.60–0.75), respectively.

Conclusion: Higher urinary potassium excretion and potassium intake were associated with lower risk of incident CKD.

| Table 1: HRs for the incident CKD outcomes based on the spot urinary potassium-to-creatinine ratio. |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| per SD                          | Spot Urinary Potassium-to-Creatinine Ratio |
|                                 | Quartile 1                      | Quartile 2                      | Quartile 3                      | Quartile 4                      |
|                                 | HR (95% CI)                     | HR (95% CI)                     | HR (95% CI)                     | HR (95% CI)                     |
|                                 | P                               | P                               | P                               | P                               |
| Model 1                         | 0.86 (0.85 – 0.88)              | <0.001                          | Reference                       | 0.99 (0.94 – 1.03)              | 0.530                           | 0.88 (0.85 – 0.92)              | <0.001                          | 0.72 (0.68 – 0.75)              | <0.001                          |
| Model 2                         | 0.86 (0.84 – 0.88)              | <0.001                          | Reference                       | 0.93 (0.89 – 0.97)              | <0.001                          | 0.83 (0.79 – 0.86)              | <0.001                          | 0.71 (0.67 – 0.74)              | <0.001                          |
| Model 3                         | 0.90 (0.89 – 0.92)              | <0.001                          | Reference                       | 0.98 (0.94 – 1.02)              | 0.320                           | 0.90 (0.86 – 0.95)              | <0.001                          | 0.80 (0.76 – 0.84)              | <0.001                          |

Model 1: unadjusted.
Model 2: age, sex, race, town deprivation index, BMI, alcohol, smoking, handgrip strength, systolic blood pressure, medical history of cardiovascular disease, and diabetes, medications including RAAS blockers, diuretics, and statin.
Model 3: Model 2 plus laboratory parameters including hemoglobin, albumin, total cholesterol, log transformed hs-CRP, log transformed urine sodium creatinine ratio.

| Table 2: HRs for the incident CKD outcomes according to quartiles of potassium intake-to-weight ratio. |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| per SD                          | Dietary potassium intake-to-weight ratio |
|                                 | Quartile 1                      | Quartile 2                      | Quartile 3                      | Quartile 4                      |
|                                 | HR (95% CI)                     | HR (95% CI)                     | HR (95% CI)                     | HR (95% CI)                     |
|                                 | P                               | P                               | P                               | P                               |
| Model 1                         | 0.84 (0.81 – 0.87)              | <0.001                          | Reference                       | 0.85 (0.79 – 0.92)              | <0.001                          | 0.72 (0.66 – 0.78)              | <0.001                          | 0.65 (0.60 – 0.70)              | <0.001                          |
| Model 2                         | 0.84 (0.82 – 0.87)              | <0.001                          | Reference                       | 0.84 (0.78 – 0.91)              | <0.001                          | 0.72 (0.66 – 0.78)              | <0.001                          | 0.66 (0.60 – 0.71)              | <0.001                          |
| Model 3                         | 0.88 (0.86 – 0.91)              | <0.001                          | Reference                       | 0.89 (0.82 – 0.96)              | 0.002                           | 0.78 (0.72 – 0.85)              | <0.001                          | 0.74 (0.68 – 0.81)              | <0.001                          |
| Model 4                         | 0.83 (0.79 – 0.87)              | <0.001                          | Reference                       | 0.85 (0.78 – 0.92)              | <0.001                          | 0.73 (0.67 – 0.81)              | <0.001                          | 0.67 (0.60 – 0.75)              | <0.001                          |

Model 1: unadjusted.
Model 2: age, sex, race, town deprivation index, alcohol, smoking, handgrip strength, systolic blood pressure, medical history of cardiovascular disease, and diabetes, medications including RAAS blockers, diuretics, and statin.
Model 3: Model 2 plus laboratory parameters including hemoglobin, albumin, total cholesterol, log transformed hs-CRP
Model 4: Model 3 plus dietary intake including energy, fiber, protein, sodium.
PATIENT-REPORTED MENTAL HEALTH PROBLEMS, SUICIDE IDEATION, AND CLINICAL OUTCOMES IN ADULTS WITH NON-DIALYSIS CKD: RESULTS OF THE KNOW-CKD STUDY

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Background and Aims: Mental health is important for health and well-being at every stage of life and disease. Mental health problems are common and bothersome in chronic kidney disease (CKD). Mental health problems of CKD are poorly understood and evaluated. To address the importance of mental health in CKD, we analyzed a prospective cohort database from prospective CKD cohort.

Method: We analyzed 1897 participants from the KNOW-CKD cohort. We evaluated 4 items as indicators of patient-reported mental health: sleep duration, perceived stress, depressive symptoms, and suicidal ideation. To facilitate interpretation of the mental health problems in CKD, we measure a scaled effect size (ES) for the Kidney Disease Quality of Life Short Form (KDQOL-SF) differences among the groups of mental health problems. We investigated the association between patient-reported mental health problems and clinical outcomes of incident end-stage kidney disease (ESKD) all-cause death in non-dialysis CKD.

Results: The mean age was 53 ± 12 years and 62% were male. The participants had mental health problems of inadequate sleep duration (17.4%), subject distress (27.3%), experience of depression (13.2%), and suicide ideation (16.8%), but had not well taken care (psychiatric counselling 1.9%, antidepressant therapy 2.8%). The 4 item indicators of mental health showed large effect size between-groups KDQOL mental component summary (ES = 1.67). In the fully adjusted Cox proportional model, poor mental health (≥2 mental health problems) was associated with high risk of ESKD [HR = 1.46; 95% CI (1.18~1.08)] and death [HR = 1.55; 95% CI (1.04~2.32)] compared to good mental health (no mental health problems). Among 4 item indicators of patient-reported mental health, suicide ideation was the most predictive indicator of clinical outcomes.

Conclusion: Mental health problem is common and undertreated in CKD. Poor mental health is associated with high risk of ESKD and death in non-dialysis CKD and the single question of suicide ideation is significantly associated with high risk of ESKD and death. It suggests that the evaluation and management of mental health problem is important to the clinical outcomes in CKD.

Figure 1: Frequency of patient-reported mental health by (A) sex, (B) age, and (C) eGFR stage.

Figure 2: Kaplan-Meier curve of time to (A) end-stage kidney disease and (B) all-cause death according to patient-reported mental health and suicide ideation.
THE 2021 CKD EPI GLOMERULAR FILTRATION RATE ESTIMATING EQUATION AND RISK OF HOSPITALIZATION FOR KIDNEY DISEASE

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Background and Aims: The revised Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) equation for estimated glomerular filtration rate (eGFR) reduced CKD prevalence among Asians, but few studies have evaluated its impact on healthcare utilization. We aimed to evaluate the impact of the 2009-eGFRcr(ASR) [1] and 2021-eGFRcr(AS) [2] equations on the risk of hospitalization for kidney disease among multi-ethnic Asians.

Method: Retrospective cohort study of adults who consulted at Singapore's largest healthcare cluster of public healthcare institutions and had a baseline serum creatinine performed in 2014. eGFR was calculated using both eGFRcr(ASR) [1] and 2021-eGFRcr(AS) [2] equations and categorized as G1 (≥ 90 ml/min/1.73 m²), G2 (60-89 mL/min/1.73 m²), G3A (45-59 mL/min/1.73 m²), G3B (30-44 mL/min/1.73 m²), G4 (15-29 mL/min/1.73 m²), G5 (< 15 mL/min/1.73 m²). Electronic medical records were used to identify baseline demographic and clinical information, and the outcome of hospitalization for kidney disease including acute kidney injury, chronic kidney disease, dialysis or transplant in the next three years until December 2017. Multi-variable logistic regression models were used to compare the impact of the eGFR equations on risk of hospitalization for kidney disease. Model discrimination was assessed using the area (AUC) under a receiver operating characteristic (ROC) curve.

Results: Among 33007 Asian adults included in the study, the median age was 69.0 years (interquartile range 63.0, 76.0). The majority were Chinese (79.5%; Indian 7.2%, Malay 10.2% and other race 3.2%), female (53.3%), had diabetes (56.4%) and received statin therapy (71.6%) at baseline. Hospitalization for kidney disease occurred in 1915 (7.1% of 26874 individuals) after excluding those with missing covariates (n = 5133). Hospitalization incidence increased with worsening kidney function (Table 1) regardless of the estimation equation used. After adjusting for age, sex, ethnicity, comorbidities (cardiovascular disease, diabetes, hypertension, cancer, systolic and diastolic blood pressure, body mass index) and medications (statin, ACE inhibitor, angiotensin receptor blocker, loop and thiazide diuretic), eGFR categories were independently associated with hospitalization for both eGFR equations (Table 2). Compared
to G1, the risks of hospitalization for G2, G3A, G3B and G4 were incremental
at approximately 2, 6, 10 and 20 times, respectively, while the risk of
hospitalization for G5 was 100 times that of G1. The AUCs were 0.859 (95% CI:
0.849-0.869) for the model with eGFRcr (ASR) and 0.861 (95% CI: 0.852-
0.871) for 2021-eGFRcr (AS) but the difference was not significant (p = 0.11).
Conclusion: Lower eGFRs ascertained by both the 2009 eGFRcr(ASR) and
2021-eGFRcr(AS) equations were independently associated with greater risks
of hospitalization for kidney disease. The revised 2021-eGFRcr(AS) equation
did not significantly alter model discrimination.

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PRE-DIALYSIS TRAJECTORIES OF ESTIMATED GFR AND
CONCURRENT TRENDS OF CKD-RELEVANT BIOMARKERS
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Background and Aims: The glomerular filtration rate (GFR) decline varies
in patients with advanced chronic kidney disease (CKD), and the concurrent
changes in CKD-related biomarkers are unclear.
Method: We adopted a group-based trajectory model to categorize CKD patients by their pre-dialysis eGFR trajectory and then analyzed the concurrent changing trends of CKD-relevant biomarkers, including urine protein-creatinine ratio (UPCR), albumin, and uric acid.
Results: Using longitudinal data from two years before dialysis initiation, 1,758 CKD patients were included. We identified three distinct eGFR trajectories: persistently low eGFR levels, progressive loss of eGFR, and accelerated loss of eGFR. Eight of the 15 biomarkers showed distinct patterns among the trajectory groups. Compared to the group with persistently low eGFR values, the other two groups were associated with a more rapid increase in the serum urea level and UPCR, especially in the year before dialysis initiation, and a more rapid decline in hemoglobin and platelet counts. Rapid eGFR decline was associated with lower levels of albumin and potassium, and higher levels of MCHC and WBC. The albumin level in the group with an accelerated loss of eGFR was below the normal range. Rapid eGFR decline was associated with lower levels of albumin and potassium, and higher levels of MCHC and WBC. The albumin level in the group with an accelerated loss of eGFR was below the normal range. Overall, there was a total of 691 (39.3%) deaths observed during the follow-up period. In the 2-year and 5-year follow-up, 302 (17.2%) and 549 (31.2%) deaths were observed, respectively. The corresponding median follow-up times were 2 years (IQR:1.6 – 2.0) and 3.3 years (IQR:1.6 –5.0). Kaplan–Meier survival plots showed that the eGFR trajectory was significantly associated with the risk of mortality two years and five years after dialysis, with the log-rank test P = .0057 and P = .0001, respectively.
Conclusion: The changes in CKD biomarkers were delineated with disease progression. The results provide information to clinicians and clues to elucidate the mechanism of CKD progression.
Table 1: Event rates for ESKD were low in general (0.03 to 0.51 per 100 PY) except for individuals with eGFR < 30 ml/min (2.1 to 3.5 per 100 PY). Annual monitoring of eGFR was high in all groups (>90%) with increasing frequency in individuals with impaired kidney function, and measurement of UACR was low in groups with non-diabetic CKD (10-30%). Antihypertensive treatment was frequently prescribed in eGFR < 30 ml/min; overall 87.6% and 94.8% with coexisting diabetes and 92.8% with coexisting heart failure. The use of RAS inhibition was more used in diabetes and in heart failure (>50%) but less with low eGFR. Statin therapy was used in approximately 50% of individuals with diabetes, regardless of CKD group, but was used to a much less extent in non-diabetic CKD (20-24%).

#2976
CHRONIC KIDNEY DISEASE WITH COMORBIDITY IN PRIMARY CARE: CARDIORENAL TREATMENT, QUALITY OF CARE AND PROGNOSIS
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Background and Aims: Diabetes, heart failure, hypertension and cardiovascular disease are common in primary care, and frequently coexist with impaired kidney function (CKD), further increasing risk of cardiovascular and renal events as well as premature death. These comorbidities therefore call for more complex treatment regimens and monitoring. Our aim was to describe the prevalence, management, and prognosis of individuals with CKD and additional comorbidity in a large primary care cohort.

Method: Individuals were included from the Copenhagen Primary Care Laboratory (CopLab) Database, which contains 112 million biochemistry results from persons followed in primary care between 2000 and 2015 and divided into three groups based on (CKD-EPI) eGFR (>60 ml/min, 30-59 ml/min and <30 ml/min) with or without comorbidity in the form of diabetes or heart failure. We included all individuals with at least two measurements of creatinine. The date of the second measurement of creatinine was considered index date (baseline). The database has been combined with pharmacological data (The Danish National Prescription Registry), outpatient clinic visits and hospitalizations (The Danish National Patient Registry - NPR), and mortality information (The Danish Civil Registration System). Heart Failure was defined by ICD-codes in NPR from outpatient clinic visits and hospitalizations and we calculated crude event rates for a range of outcomes according to comorbidity. Diabetes was defined as at least one measurement of plasma or serum glucose ≥11 mmol/l or HbA1c ≥48 mmol/mol in CopLab. We evaluated monitoring of eGFR, albuminuria (UACR) and use of guideline-recommended pharmacological therapy (i.e. RAS-blockers and statins) in each group.

Results: In the total primary care population of 171,134 individuals of which 63.8% were female, 8.3% had impaired kidney function (eGFR <60 ml/min), and measurement of UACR was high in all groups (>90%) with increasing frequency in individuals with impaired kidney function, and measurement of UACR was low in groups with non-diabetic CKD (10-30%). Antihypertensive treatment was frequently prescribed in eGFR < 30 ml/min; overall 87.6% and 94.8% with coexisting diabetes and 92.8% with coexisting heart failure. The use of RAS inhibition was more used in diabetes and in heart failure (>50%) but less with low eGFR. Statin therapy was used in approximately 50% of individuals with diabetes, regardless of CKD group, but was used to a much less extent in non-diabetic CKD (20-24%).

Conclusion: Our data from a large primary care cohort demonstrate a high prevalence of coexisting diabetes and/or heart failure with CKD, increasing the risk for adverse outcomes. The quality of CKD care in general practice may be improved, especially in the non-diabetic population.
ASSOCIATION BETWEEN BODY MASS INDEX, WAIST CIRCUMFERENCE AND CLINICAL OUTCOMES IN KOREAN ADVANCED CHRONIC KIDNEY DISEASE PATIENTS

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Background and Aims: This study analysed the association between body mass index (BMI) and waist circumference (WC) with all-cause death, 3-point major cardiovascular event (MACE), end-stage kidney disease (ESKD) and total composite events in nation-wide cohort of Korean advanced chronic kidney disease (CKD) patients.

Method: This nationwide cohort study, using the National Health Insurance Database, included adult health examinees who received two or more check-ups from 2009 to 2012. Among them, CKD patients (N = 325,657, stage G3a, G3b and 4) were identified. Patients were classified into three groups for BMI (<18.5, 18.5-25 [reference] and ≥25) and four groups for WC (female; <75 cm or male; <85 cm [WC1], male; 75 cm ≤ WC <85 cm or male; 85 cm ≤ WC <95 cm [reference], female; 85 cm ≤ WC <95 cm, male; 95 cm ≤ WC <105 cm [WC2] and male; ≥95 cm, male; ≥105 cm [WC3]). Risks were evaluated using Cox proportional hazard analysis.

Results: Patients (58.6±7.7 years) had mean eGFR of 54.32±5.83mL/min/1.73 m². The underweight (BMI<18.5) group had increased risks of death [HR 1.75%, 95% CI (1.573-1.964)] and total events [HR 1.24, (1.144-1.353)]. Overweight (BMI≥25) group showed lower risks of death [HR 0.888, (0.86-0.917)], ESKD [HR 0.855, (0.788-0.927)] and total events [HR 0.975, (0.956-0.995)]. However, the risk was increased for 3-point MACE [HR 1.056, (1.031-1.081)]. For the association between WC and clinical outcomes, the low WC group (WC1) had increased risk of death [HR 1.129, (1.089-1.171)] and reduced risk for 3-point MACE [HR 0.92, (0.894-0.947)]. In higher WC groups, increased risks were observed for death [WC2: HR 1.052, (1.008-1.098), WC3: HR 1.32, (1.213-1.437)], 3-point MACE [WC2: HR 1.071, (1.038-1.104), WC3: HR 1.104, (1.036-1.176)] and total events [WC2: HR 1.049, (1.022-1.077), WC3: HR 1.12, (1.062-1.181)].

Conclusion: In CKD patients, both lower BMI and WC were risk factors for mortality and ESKD. However, compared to the reference group, higher BMI group exhibited better outcomes while higher WC groups exhibited poorer outcomes. As increased WC is more specifically related to central obesity, we need different approaches to interpreting clinical risks associated with different BMI and WC criteria.

PRIMARY GLOMERULAR DISEASES AND LONG-TERM RISKS OF CKD PROGRESSION, CARDIOVASCULAR EVENTS AND DEATH: A SWEDISH NATIONWIDE COHORT STUDY

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Background and Aims: Although glomerular diseases are the third most frequent cause of end-stage kidney disease worldwide (after diabetes and hypertension), little is known about their long-term risks and complications.

Method: Using data from the Swedish Renal Registry (SRR-CKD) 2005-2021, we compared clinical outcomes between patients with the four most frequent primary glomerular diseases (IgA nephropathy [IgAN], focal segmental glomerulosclerosis [FSGS], minimal change disease [MCD] and membranous nephropathy [MN]) and patients with CKD attributed to non-inflammatory etiologies (i.e. without systemic auto-immune, inflammatory, infectious, hematologic malignancy, genetic disease, or polycystic kidney disease). Poisson models were used to estimate adjusted incidence rate ratios (IRR) of all-cause and cause-specific hospitalizations (cardiovascular-, acute kidney injury-, thromboembolism- and infection-related). Cox proportional hazards models were used to estimate adjusted hazard ratios (HR) of kidney replacement therapy (KRT), major adverse cardiovascular events (MACE) and death.

Results: We identified 2967 patients with primary glomerular disease (71% men, age 57 years, eGFR 28 mL/min/1.73 m², uACR 63 mg/mmol) and 40026 patients with a non-inflammatory CKD (64% men, age 74 years, eGFR 22 mL/min/1.73 m², uACR 20 mg/mmol). As compared to non-inflammatory CKD, patients with primary glomerular diseases were younger, had a lower prevalence of cardiovascular disease, higher eGFR but higher albuminuria. Over median follow-up of 6.3 [3.3-9.9] years, there were median 0.3 [1.07.0] hospitalizations per patient, 9890 (23%) KRT, 11708 (27%) MACE, and 21091 (49%) deaths. As compared to non-inflammatory CKD, patients with primary glomerular disease had a lower risk of all-cause (IRR 0.77 [0.75-0.79]), and all-cause-specific hospitalizations, MACE (HR 0.56 [0.58-0.63]) and death
Figure 1: Adjusted hazard ratios of long-term outcomes associated with primary glomerular disease vs non-inflammatory CKD.
needed to see where we currently stand, and how to progress from here. With this overview we can identify current knowledge gaps, and potential implementation opportunities. Moreover, it will provide guidance as to where future research should be directed. Therefore, the aim of this study was to map the body of existing prognostic models within nephrology and detail the range in outcomes and populations that they cover, as well as their methodological rigour. To do so, we performed a scoping review of studies developing, validating or updating a prognostic model for patients with chronic kidney disease (CKD) or those receiving kidney replacement therapy (KRT).

**Method:** A framework for scoping reviews by Arksey and O'Malley was used and the PRISMA extension for Scoping Reviews was adhered to for transparent reporting. A systematic search yielded 3728 studies for screening, of which 596 were finally included. Of these, 29.5% concerned a CKD population, 31.4% a dialysis population, and 39.1% a kidney transplantation population. Many studies had a sample size of less than 500 participants (41.4%). Although a measure of discrimination of the model was usually presented (79.5%), a measure of calibration was presented in less than half of the studies (43.5%). Of the 411 studies in which a prognostic model was developed, most performed only internal validation (57.9%) or no validation at all (27.7%). Moreover, in almost half of the development studies (43.5%) no usable version of the model was reported, meaning that insufficient information was reported to apply the model in a new setting. For CKD populations, the majority of models predicted disease progression (n = 78), followed by models predicting mortality (n = 22) and cardiovascular events (n = 13). For dialysis populations, most models predicted mortality (n = 79), cardiovascular events (n = 20), and vascular access related outcomes (n = 15). Finally, models originally developed for kidney transplantation populations mainly predicted graft survival (n = 59), recipient survival (n = 39), and delayed graft function (n = 24). Models for non-traditional clinical outcomes, like health-related quality of life and symptom burden, were scarce. If validated or updated at all (n = 199), most models (n = 123) were externally validated and/or updated only once. The rest (n = 76) were validated and/or updated more, with a median (IQR) of 2 (2-3), 2 (2-3), and 3 (2-4) within the CKD, dialysis, and transplantation populations, respectively.

**Conclusion:** A substantial amount of nephrological prognostic research has been performed, but to minimize the gap between research and patient care additional steps have to be undertaken. Methodological rigour, external validation, updating, and impact assessment are of paramount importance. In addition, the current body of literature focuses on traditional clinical outcomes, and models for patient-reported outcomes are scarce. Opportunities to improve implementation of prognostic models in nephrological care are described in Box 1.

Box 1: Implementation opportunities and future suggestions.

#2929

FACTORS ASSOCIATED WITH QUALITY OF LIFE IN KIDNEY FAILURE MANAGED CONSERVATIVE AND WITH DIALYSIS: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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**Background and Aims:** Internationally, chronic kidney disease (CKD) affects over 10% of the general population. As patients approach CKD Stage 5, they are faced with the decision of whether to proceed with dialysis or conservative, non-dialysis, kidney management (CKM). Regardless of pathway, worsening CKD is associated with poorer self-perceived health-related quality of life (HRQOL). Psychological factors such as depression and anxiety have been linked with poorer HRQOL. Quality of life is a major consideration for many patients. Patients’ experiences of disease and significant contributors to HRQOL should be recognised as an important area for healthcare providers to identify, understand and target. The primary aim is to determine if anxiety or depressive symptoms are significantly associated with HRQOL, in patients with CKD Stage 5. The secondary aim is to determine which patient-associated factors (such as comorbidities, symptoms or biochemical parameters) are associated with HRQOL in patients with CKD Stage 5.

**Method:** Patients that attend the St George Hospital Kidney Supportive Care (KSC) clinic complete surveys of their functional ‘domains’ and quality of life (EQ-5D-5L, EuroQOL Research Foundation, 2019) and symptom surveys (IPOS-Renal, Cicely Saunders Institute, 2016) at the beginning of each clinic visit. Demographic data, comorbidities and biochemical data are also obtained from the St George Hospital electronic medical records system and entered into the KSC database, with corresponding survey data. We included all patients from St George and Sutherland Hospitals that attended the KSC Clinic between 1 July 2015 and 30 June 2022 with CKD Stage 5, who were managed with either CKM or dialysis, and completed EQ5D5L and IPOS-Renal surveys at their first KSC visit. The primary outcome is self-perceived health-related quality of life score, measured using EQ-VAS, a continuous 100-point scale on the EQ-5D-5L survey. We performed multivariable linear regression analysis with pre-specified variables including age, sex, eGFR (for those on CKM), "Feeling depressed," (IPOS-Renal) “Feeling anxious” (IPOS-Renal) and “Anxiety/depression" (EQ5DSL), for the CKM and dialysis pathways. Statistical analyses were performed with IBM SPSS Statistics V26.0. P-values of <0.05 were regarded as significant.

**Results:** We included 339 patients (216 patients on CKM and 123 patients on dialysis). Patients receiving CKM were significantly older than those on dialysis, with a median age of 83 years, compared to 73 years. Most patients on dialysis received haemodialysis (85.4%). For patients receiving CKM, variables independently associated with poorer EQ-VAS were difficulty performing usual activities (EQ5DSL), drowsiness (IPOS-Renal) and shortness of breath (IPOS-Renal) (Figure 1). For patients receiving dialysis, variables independently associated with poorer EQ-VAS were reduced ability to perform self-care (EQ5DSL) and lack of energy (IPOS-Renal) (Figure 2). Anxiety and depressive symptoms were not significantly associated with poorer EQ-VAS for either CKM or dialysis patients.

**Conclusion:** We did not find an association between anxiety and depressive symptoms and poorer EQ-VAS for patients with CKD Stage 5. For patients receiving CKM, symptoms that significantly reduce EQ-VAS include shortness of breath, difficulty performing usual activities, drowsiness and lack of energy.
of breath and drowsiness. Impaired functional ability significantly reduced EQ-VAS in patients with CKD Stage 5 managed with and without dialysis. Optimization of multidisciplinary teams within KSC units are likely to be of benefit.

**Figure 1:** Factors associated with HRQOL in CKD Stage 5 not on dialysis.

**Figure 2:** Factors associated with HRQOL in CKD Stage 5 on dialysis.

#2996  
EARLY DECLINES IN KIDNEY FUNCTION AND ADVERSE OUTCOMES IN YOUNG ADULTS  
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**Background and Aims:** Whether early eGFR declines (eGFR below age-expected values) in younger adults are associated with adverse outcomes is unknown. We aim to estimate the association of an early eGFR decline with adverse outcomes by age group (18-39, 40-49, 50-65 years).

**Methods:** We included 8.9 million adults (aged 18-65) with ≥1 eGFR value using linked healthcare datasets in Ontario from January 2008-March 2020. The association of eGFR categories from <60 to >120 mL/min/1.73 m² and adverse outcomes (death, cardiovascular outcomes, end-stage kidney disease) was examined using adjusted Cox models. Comparisons were relative to age normalized measured GFR categories (100-110 mL/min for 18-39, 90-100 mL/min for 40-49, 80-90 mL/min for 50-65).

**Results:** The mean age, eGFR and median followup were 41 years, 104 mL/min and 9.2 years, respectively. 17.3%, 18.9%, and 17.7% had an eGFR below normal for ages 18-39, 40-49, and 50-65, respectively. The risk of an adverse event increased in a stepwise manner with eGFR values below the referent and occurred at higher eGFR values in those 18 to 39 [eGFR 70-80, age 18-39: incidence 4.37 events per 1000 person-years [p-y], HR 1.54 (1.46-1.61); age 40-49: incidence 9.78 per 1000 p-y, HR 1.18 (1.15-1.21); age 50-65: incidence 24.0 per 1000 p-y, HR 1.11 (1.10-1.12)] (see Figure 1). Results persisted for each outcome individually, and after using repeated eGFR, using a common referent, and adjusting for multiple covariates.

**Conclusion:** Young adults (18-39) with an early eGFR decline were at a higher risk of adverse events and this occurred at higher eGFR levels relative to middle-aged and older adults.
Figure 1: Incidence rates (events per 1000 person-years) and adjusted hazard ratios (HRs, 95% CI) for any adverse outcome (first of all-cause mortality, cardiovascular outcomes, end-stage kidney disease) relative to age-specific eGFR reference ranges, by age-group.
ASSOCIATION BETWEEN INCIDENT DEPRESSION AND CLINICAL OUTCOMES IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background and Aims: Depression is highly prevalent and related to increased morbidity and mortality in patients on dialysis, but less is known among patients with earlier stages of CKD. This study investigated the associations between depression and clinical outcomes in patients with CKD not receiving dialysis.

Method: We identified 157,398 adults with CKD stages 3–5 not previously diagnosed with depression from the Stockholm CREAtinine Measurements (SCREAM) project. The primary outcomes included hospitalization, CKD progression (>40% decline in eGFR, initiation of kidney replacement therapy, or death due to CKD), major adverse cardiovascular events (MACE; myocardial infarction, stroke, or cardiovascular death), and all-cause mortality. Survival analyses were used to estimate the associations between incident depression and adverse health outcomes, adjusting for socio-demographics, kidney disease severity, healthcare utilization, comorbidities, and concurrent use of medications.

Results: During a median follow-up of 5.1 (interquartile range: 2.3–8.5) years, 12,712 (8.1%) patients received an incident diagnosis of depression. A total of 634,471 hospitalizations (4,600,935 hospitalized days), 42,866 MACEs, and 66,635 deaths were recorded, and 9,795 individuals met the criteria for CKD progression. In the multivariable-adjusted analyses, incident depression was associated with an elevated rate of hospitalized days (rate ratio: 1.77, 95% confidence interval [CI]: 1.71–1.83), as well as an increased rate of CKD progression (hazard ratio [HR]: 1.38, 95% CI: 1.28–1.48), MACE (HR: 1.22, 95% CI: 1.18–1.27), and all-cause mortality (HR: 1.41; 95% CI: 1.37–1.45). The association with CKD progression was more evident after one year of depression diagnosis (HR: 1.47, 95% CI: 1.36–1.59). Results were consistent across a range of sensitivity analyses.

Conclusion: Among patients with non-dialysis-dependent CKD stages 3–5, incident depression is associated with poor prognosis, including hospitalization, CKD progression, MACE, and all-cause mortality.

Table 1: Association between incident depression and clinical outcomes.

<table>
<thead>
<tr>
<th></th>
<th>No depression period</th>
<th>Depression period</th>
<th>Crude RR/HR (95% CI)</th>
<th>Adjusted RR/HR (95% CI)</th>
<th>P Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of events</td>
<td>Incidence rate (per 1000 person-years)</td>
<td>No. of events</td>
<td>Incidence rate (per 1000 person-years)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>4,177,673</td>
<td>5,073.9</td>
<td>423,262</td>
<td>8,445.8</td>
<td>1.46 (1.41–1.51)</td>
</tr>
<tr>
<td>Men</td>
<td>1,998,097</td>
<td>5,345.7</td>
<td>164,498</td>
<td>9,889.7</td>
<td>1.64 (1.55–1.74)</td>
</tr>
<tr>
<td>Women</td>
<td>2,179,576</td>
<td>4,847.9</td>
<td>258,764</td>
<td>7,728.5</td>
<td>1.38 (1.31–1.44)</td>
</tr>
<tr>
<td>CKD progression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>9,011</td>
<td>12.5</td>
<td>784</td>
<td>19.1</td>
<td>1.44 (1.34–1.55)</td>
</tr>
<tr>
<td>Men</td>
<td>4,747</td>
<td>14.6</td>
<td>309</td>
<td>23.1</td>
<td>1.49 (1.33–1.67)</td>
</tr>
<tr>
<td>Women</td>
<td>4,264</td>
<td>10.7</td>
<td>475</td>
<td>17.1</td>
<td>1.52 (1.38–1.67)</td>
</tr>
<tr>
<td>MACE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>40,193</td>
<td>54.0</td>
<td>2,673</td>
<td>66.3</td>
<td>1.12 (1.08–1.17)</td>
</tr>
<tr>
<td>Men</td>
<td>19,941</td>
<td>60.0</td>
<td>1,045</td>
<td>83.3</td>
<td>1.33 (1.25–1.41)</td>
</tr>
<tr>
<td>Women</td>
<td>20,252</td>
<td>49.1</td>
<td>1,628</td>
<td>58.6</td>
<td>1.10 (1.05–1.16)</td>
</tr>
<tr>
<td>All–cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>61,221</td>
<td>74.4</td>
<td>5,414</td>
<td>108.0</td>
<td>1.30 (1.27–1.34)</td>
</tr>
<tr>
<td>Men</td>
<td>29,222</td>
<td>78.2</td>
<td>2,196</td>
<td>132.0</td>
<td>1.55 (1.49–1.62)</td>
</tr>
<tr>
<td>Women</td>
<td>31,999</td>
<td>71.2</td>
<td>3,218</td>
<td>96.1</td>
<td>1.24 (1.20–1.29)</td>
</tr>
</tbody>
</table>

Table 2: Association between incident depression and clinical outcomes within or beyond 1 year.

<table>
<thead>
<tr>
<th></th>
<th>No depression period</th>
<th>&lt;1 year after incident depression</th>
<th>≥1 year after incident depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence rate (per 1000 person-years)</td>
<td>Crude RR/HR (95% CI)</td>
<td>Adjusted RR/HR (95% CI)</td>
</tr>
<tr>
<td>Hospitalized days</td>
<td>5,073.9</td>
<td>12,806.0</td>
<td>1.45 (1.40–1.51)</td>
</tr>
<tr>
<td>CKD progression</td>
<td>12.5</td>
<td>14.2</td>
<td>1.10 (0.93–1.29)</td>
</tr>
<tr>
<td>MACE</td>
<td>54.0</td>
<td>83.1</td>
<td>1.49 (1.39–1.60)</td>
</tr>
<tr>
<td>All–cause mortality</td>
<td>74.4</td>
<td>129.8</td>
<td>1.69 (1.61–1.78)</td>
</tr>
</tbody>
</table>
ACCURACY OF ESTIMATED GLOMERULAR FILTRATION RATE EQUATIONS IN PATIENTS WITH DISCORDANCES BETWEEN CREATININE AND CYSTATIN C-BASED ESTIMATIONS

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Background and Aims: Cystatin C is recommended for use along with creatinine in estimating glomerular filtration rate (eGFR) when precise estimates are needed for clinical decision-making. Although eGFR based on both creatinine and cystatin (eGFRcr-cys) is the most accurate in research studies, it is uncertain as to whether this remains true in real-world settings, particularly when there are large discordances between eGFR based on creatinine (eGFRcr) and that based on cystatin C (eGFRcys).

Method: We included 6185 adults from the Stockholm Creatinine Measurements (SCREAM) project referred for plasma clearance of iohexol in Stockholm, Sweden, who had 9404 concurrent measurements of creatinine, cystatin C and iohexol clearance. The performance of eGFRcr, eGFRcys and eGFRcr-cys was assessed against mGFR with bias, P30 and correct classification of GFR strata. We stratified analyses within three categories: eGFRcys at least 20% lower than eGFRcr (eGFRcys < eGFRcr), eGFRcys within 20% of eGFRcr (eGFRcys ≈ eGFRcr) and eGFRcys at least 20% higher than eGFRcr (eGFRcys > eGFRcr). Bias was expressed as the median difference in estimated GFR minus mGFR, with negative biases indicating underestimation of mGFR. P30 described the percentage of individuals with eGFR within 30% of mGFR. Correct classification of GFR categories was defined as agreement of eGFR and mGFR categories using the KDIGO GFR categories (<15, 15-29, 30-44, 45-59, 60-89 and ≥90 ml/min/1.73 m²).

Results: eGFRcr and eGFRcys were similar in 4226 (45%) of samples, and there all three estimating equations displayed similar performance (Table 1). In contrast, eGFRcr-cys was much more accurate in cases of discordance. For example, when eGFRcys < eGFRcr (47% of samples), median biases were 15.0 (overestimation), −8.5 (underestimation) and 0.8 ml/min/1.73 m² for eGFRcr, eGFRcys and eGFRcr-cys, respectively; P30 was 50%/73%/84%, respectively; and correct classification was 38%/45%/62%, respectively. When eGFRcys > eGFRcr (8% of samples), median biases were −4.5, 8.4, and 1.4 ml/min/1.73 m². Findings were consistent among individuals with cardiovascular disease, heart failure, diabetes mellitus, liver disease and cancer (Figure 1).

Conclusion: When large discordances between eGFRcr and eGFRcys are found in clinical practice, eGFRcr-cys is more accurate than either eGFRcr or eGFRcys.

Table 1: Bias, P30 and correct classification of different CKD-EPI eGFR equations stratified by the magnitude and direction of the discordance between eGFRcr and eGFRcys.

<table>
<thead>
<tr>
<th>eGFRcys</th>
<th>eGFRcr-cys</th>
<th>eGFRcys &gt; 20% lower than eGFRcr</th>
<th>eGFRcys within 20% of eGFRcr</th>
<th>eGFRcys &gt; 20% higher than eGFRcr</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFRcr</td>
<td>eGFRcys</td>
<td>15.0 (14.6 to 15.5)</td>
<td>4.5 (4.1 to 4.8)</td>
<td>−4.5 (−5.3 to −3.8)</td>
</tr>
<tr>
<td>Bias (ml/min/1.73 m²)</td>
<td>P30</td>
<td>49.7 (48.3 to 51.2)</td>
<td>86.0 (84.9 to 87)</td>
<td>85.9 (83.2 to 88.3)</td>
</tr>
<tr>
<td>Correct classification</td>
<td>38.1 (36.7 to 39.5)</td>
<td>66.5 (65.1 to 67.9)</td>
<td>61.9 (58.3 to 65.4)</td>
<td></td>
</tr>
<tr>
<td>eGFRcys</td>
<td>Bias (ml/min/1.73 m²)</td>
<td>−8.6 (−9 to −8.3)</td>
<td>2.1 (1.7 to 2.4)</td>
<td>8.4 (7.3 to 10)</td>
</tr>
<tr>
<td>eGFRcr-cys</td>
<td>P30</td>
<td>72.9 (71.6 to 74.2)</td>
<td>90.4 (89.5 to 91.3)</td>
<td>71.8 (68.4 to 75.1)</td>
</tr>
<tr>
<td>Correct classification</td>
<td>45.4 (43.9 to 46.8)</td>
<td>69.2 (67.8 to 70.5)</td>
<td>62.9 (59.4 to 66.6)</td>
<td></td>
</tr>
</tbody>
</table>

Abstracts
Figure 1: Bias of eGFR$_{cr}$, eGFR$_{cys}$, and eGFR$_{cr-cys}$ across subgroups, stratified by the extent of discordance between eGFR$_{cr}$ and eGFR$_{cys}$. 
#3393

**PATIENT-REPORTED OUTCOMES IN EARLY VERSUS ADVANCED CHRONIC KIDNEY DISEASE: EVIDENCE FROM BASELINE DATA IN THE DISCOVER CKD PROSPECTIVE STUDY**

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**Background and Aims:** Chronic kidney disease (CKD) negatively impacts patients’ psychological and social wellbeing. Prior studies have suggested that CKD progression is associated with worsening of health-related quality of life (HRQoL), but these studies were limited in terms of racial and geographic composition. We compared patient-reported outcomes, including symptom (HRQoL), but these studies were limited in terms of racial and geographic composition. We compared patient-reported outcomes, including symptom burden, work productivity and HRQoL of patients with early versus advanced CKD, based on contemporary data from DISCOVER CKD, a multinational non-interventional cohort study of patients with CKD.

**Methods:** DISCOVER CKD (clinicaltrials.gov identifier: NCT04034992) is an ongoing study that aims to generate real-world evidence on the clinical management and experiences of patients with CKD. The study adopted a hybrid design comprising both retrospective and prospective cohorts. For the prospective phase, patients were recruited from the USA, Japan, Sweden, Italy, Spain, and the UK. Clinical data were extracted manually from existing patients’ health records into a standardised case report form. HRQoL was measured via the Short Form (SF)-36 questionnaire, work productivity was assessed with the Work Productivity and Activity Impairment (WPAI)-CKD questionnaire. Symptoms were recorded using a mobile phone application. In this analysis, early CKD was defined as stages 2-3 CKD and advanced CKD as stages 4-5 CKD (inclusive of dialysis patients). For each outcome, baseline scores were compared between patients with early and advanced CKD using an ANCOVA model with adjustment for age, sex, diabetes, hypertension and renin-angiotensin-aldosterone system inhibitor use. P<0.05 was considered statistically significant. DISCOVER CKD received research ethics board approval and informed consent was obtained from all patients.

**Results:** A total of 1051 patients with CKD (early CKD, 69.2% [N = 727]; advanced CKD, 30.8% [N = 324]) were enrolled in the prospective phase of DISCOVER CKD. The population was racially diverse with approximately one-third being non-White. The mean age was 62.5 years (early CKD, 63.4 years: advanced CKD, 60.6 years) and 37% (early CKD, 37.7%; advanced CKD, 35.2%) were female. The mean WPAI-CKD scores for percentage work time missed, activity impairment, impairment at work and overall work productivity loss were significantly higher in patients with advanced CKD compared to those with early CKD, suggesting greater work and activity impairment (Figure 1). The mean symptom scores for fatigue, pruritis, problems with sleep, nausea, muscle cramping and overall feel about health were all significantly higher in the advanced CKD population (Table 1). Of note, anxious and depressed feelings were similar for early and advanced CKD.

**Conclusion:** In this multinational cohort of patients with CKD, those with advanced disease appeared to experience greater symptom burden, lower HRQoL, and higher work and activity impairment. These findings highlight the need for early detection and treatment of CKD and its reported symptoms to reduce the likelihood of disease progression, which could adversely impact patients’ QoL.

![Figure 1: Comparison of baseline work productivity and activity impairment scores for patients with early and advanced CKD.](image)

*Statistically significant difference based on ANCOVA model adjusting for age, sex, diabetes, hypertension, and renin-angiotensin-aldosterone system inhibitor use; Scores range from 0 to 100% with higher scores indicating greater impairment and less productivity. CKD, chronic kidney disease; WPAI, Work Productivity and Activity Impairment.*
INFLUENCE OF CHRONIC KIDNEY DISEASE AND GLOMERULAR FILTRATION RATE ON THE COURSE OF ACUTE SARS-COV-2 INFECTION AND POST-COVID PERIOD

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Background and Aims: According to international data available in the literature, chronic kidney disease (CKD) may have a significant impact on the course and outcome of COVID-19. Moreover, kidney pathology have been suggested to aggravate the course of the post-COVID period. The aim of the study was to investigate the effect of CKD and glomerular filtration rate (GFR) on the course of acute infection and post-COVID period.

Method: An international register “Dynamics analysis of comorbidities in SAES-CoV-2 survivors” (ACTIV) (NCT04492384) was established to assess the characteristics of the course of NCI in the Eurasian region. Specialists from 7 countries participated in the register. ACTIV is a multicenter, non-interventional, real-world clinical practice registry that included men and women over 18 years of age with a confirmed diagnosis of COVID-19. The analysis presented is based on data from 4946 patients with an estimated GFR of ≥90 ml/min/1.73 m² - 3591 (42.3%) patients, 89-60 ml/min/1.73 m² - 141 (1.7%) patients, <60 ml/min/1.73 m² - 94 (1.1%) patients. GFR was calculated using the 2021 CKD-EPI formula. The post-COVID period was analyzed using data from telephone interviews that included 3099 patients at 3 months, 2493 patients at 6 months, and 1782 patients at 12 months after recovery from COVID-19.

Results: During the acute infection, patients with a GFR of 59-15 ml/min/1.73 m², had more severe lung tissue damage (stage 3-4 according to computed tomography (CT), p < 0.001) and worse oxygenation (SpO2 75-94% and less than 75%, p < 0.001); increased respiratory rate (over 22 per minute, p < 0.001); and higher body temperature (more than 38.6°C, p < 0.001) compared with patients with GFR over 60 ml/min/1.73 m². In addition, CKD increased the odds of death in hospitalized patients by 3.94-fold compared with patients without CKD (95% confidence interval (CI) 3.15-4.89, p < 0.001). The data of the deceased patients showed that most of them had a GFR of 89-60 ml/min/1.73 m², which corresponds to stage 2 CKD (Table 1). CKD was a risk factor for increased odds of death in the post-COVID period: 4.88-fold (95% CI 2.49-9.13; p < 0.001) within 3 months; 4.24-fold (95% CI 0.60-16.3; p = 0.126) within 6 months and 8.36-fold (95% CI 1.73-29.3; p = 0.012) within 12 months after recovery from SARS-CoV-2.

#4690

Table 1: Comparison of baseline symptom and SF-36 scores for patients with early and advanced CKD.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Early CKD Patients</th>
<th>Advanced CKD Patients</th>
<th>Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>3.90 (1.659)</td>
<td>2.81 (1.025)</td>
<td>-1.09</td>
<td>0.008*</td>
</tr>
<tr>
<td>Pruritus (itching)</td>
<td>3.65 (1.659)</td>
<td>2.14 (0.256)</td>
<td>-1.51</td>
<td>0.044**</td>
</tr>
<tr>
<td>Problems with sleep</td>
<td>2.95 (0.203)</td>
<td>2.14 (0.256)</td>
<td>-0.81</td>
<td>0.006***</td>
</tr>
<tr>
<td>Night sweats</td>
<td>4.00 (1.659)</td>
<td>1.24 (0.256)</td>
<td>-2.76</td>
<td>0.006***</td>
</tr>
<tr>
<td>Constipation</td>
<td>2.00 (1.659)</td>
<td>1.24 (0.256)</td>
<td>-0.76</td>
<td>0.006***</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>1.56 (0.107)</td>
<td>1.24 (0.256)</td>
<td>-0.32</td>
<td>0.006***</td>
</tr>
<tr>
<td>Headache</td>
<td>2.51 (0.107)</td>
<td>1.24 (0.256)</td>
<td>-1.27</td>
<td>0.006***</td>
</tr>
<tr>
<td>Muscular cramping</td>
<td>2.51 (0.107)</td>
<td>1.24 (0.256)</td>
<td>-1.27</td>
<td>0.006***</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>2.51 (0.107)</td>
<td>1.24 (0.256)</td>
<td>-1.27</td>
<td>0.006***</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.00 (1.659)</td>
<td>1.24 (0.256)</td>
<td>-0.76</td>
<td>0.006***</td>
</tr>
<tr>
<td>Anxious or worried feelings</td>
<td>1.51 (0.012)</td>
<td>1.24 (0.256)</td>
<td>-0.27</td>
<td>0.006***</td>
</tr>
<tr>
<td>Overall feeling of health</td>
<td>1.51 (0.012)</td>
<td>1.24 (0.256)</td>
<td>-0.27</td>
<td>0.006***</td>
</tr>
</tbody>
</table>

Influenza of chronic kidney disease and glomerular filtration rate on the course of acute SARS-CoV-2 infection and post-COVID period
Conclusion: CKD could be a predictor of a more severe acute period of COVID-19 and also significantly impact mortality within 12 months after recovery from SARS-CoV-2.

#5424
SYMPTOM CONTROL WITH CURRENTLY AVAILABLE IMMUNOGLOBULIN A NEPHROPATHY TREATMENT: RESULTS FROM A REAL-WORLD SURVEY IN EIGHT COUNTRIES
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1The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, P.R. China; 2Novartis Pharma AG, Basel, Switzerland; 3Novartis Pharma AG, Basel, Switzerland; 4Novartis Healthcare Private Limited, Hyderabad, India and 5Adelphi Real World, Bollington, United Kingdom

Background and Aims: Immunoglobulin A nephropathy (IgAN) is the most prevalent form of primary glomerulonephritis worldwide with an estimated annual incidence of 25 cases per million people. Many patients are not diagnosed until they develop kidney dysfunction, such as hematuria and proteinuria. Proteinuria >1 g/day is associated with a high risk of progression. The aim of the present study is to describe symptom control and consider treatment satisfaction for patients undergoing treatment for IgAN.

Method: Data were drawn from the Adelphi IgAN Disease Specific Programme (DSP)7,8, a point-in-time survey of IgAN-treating nephrologists and their consulting patients conducted in the United States (US), Europe (EU: France, Germany, Italy, Spain, United Kingdom [UK]), Japan, and China, from June to October 2021. Nephrologists completed structured online patient record forms for successive patients presenting with IgAN including demographics, clinical characteristics and treatment patterns. Patients voluntarily completed questionnaires that corresponded with the nephrologist records, with questions about their IgAN on that day regarding symptoms experienced, disease severity, and treatment satisfaction. Patients who were receiving IgAN treatment at the time of survey are included in the presented analysis.

Results: The mean (standard deviation [SD]) age of patients (n = 869) was 42 (13.7) years and 57% were male. IgAN symptoms were deemed severe by 10% of patients at the time of survey and 14% before the initiation of their current treatment. Overall, 91% of patients reported having symptoms of IgAN at the time of survey, the most common were: foamy urine, feeling tired or lack of energy, and swelling, with many patients in China reporting hematuria. The top reported most bothersome symptoms were fatigue, swelling, and high blood pressure, with many patients in China also reporting proteinuria. Satisfaction with their current treatment was reported by patients; 61% reported that they were satisfied, 27% said they were neither satisfied or dissatisfied, and 12% said they were dissatisfied with their medication. This dissatisfaction was due to their current medication not working quickly enough (54%, n = 103) or that it had not helped with their IgAN symptoms (45%, n = 103). This was consistent with the physician-reported data; where proteinuria was reported across treatment lines (L), levels remained high amongst patients (mean [SD] proteinuria [g/day]) at L1: 2.2 (2.3), n = 629; L2: 1.8 (2.0), n = 257; L3: 1.9 (1.4), n = 95) and estimated glomerular filtration rate (eGFR) continued to fall (mean [SD] eGFR [mL/min/1.73m²]) at L1: 77.1 (29.6), n = 615; L2: 72.2 (30.3), n = 246; L3: 66.9 (31.1), n = 96).

Conclusion: Despite treatment, most patients with IgAN continued to experience symptoms. Many of these symptoms were considered bothersome by patients, including fatigue, swelling and high blood pressure which may have an impact on their everyday lives. These data highlight an unmet need for effective IgAN management and future treatments should aim to target better symptom relief and disease progression.

#5478
REAL-WORLD SIGNS AND SYMPTOMS AT DIAGNOSIS IN PATIENTS WITH C3 GLOMERULOPATHY - INTERIM RESULTS FROM A MULTI-COUNTRY STUDY
Clare Proudfoot1, Katharina Pannagl2, Jennifer Nguyen3, Andrea King1, Kathleen Murphy4, Jonathan Decourcy2 and Richard Lafayette3
1Novartis Pharma AG, Switzerland; 2Novartis Pharmaceuticals UK Ltd., London, United Kingdom; 3Novartis Pharmaceuticals Corporation, East Hanover, United States of America, 4Adelphi Real World, United Kingdom and 5Stanford University Medical Center, Stanford, United States of America

Background and Aims: C3 glomerulopathy (C3G) is a rare form of glomerulonephritis, with an estimated incidence of 1 – 2 million per year. C3G is associated with a high risk of disease progression with approximately 50% of patients reaching kidney failure within 10 years of diagnosis. Common signs and symptoms include proteinuria, hematuria, edema and hypertension. The aim of this analysis was to better understand the clinical characteristics of C3G patients from the US, Europe and Asia, at the time of diagnosis.

Method: An analysis was conducted using interim data from the Adelphi C3G Disease Specific Programme (DSP), a cross-sectional survey of C3G-treating nephrologists in US, EUS (France, Germany, Italy, Spain, UK), China and Japan (study ongoing since August 2022; interim analysis based on data until November). Nephrologists completed structured forms administered via online links for consecutive patients presenting with C3G. The forms included demographic and clinical information including signs, symptoms, and lab values amongst others.

Results: In this interim analysis, 88 nephrologists had completed records for 277 patients in this survey, including 95 in US, 120 in EU5, 39 in China and 23 in Japan. Median patient age at diagnosis was 40.9, and 60% were male. 80% had C3 glomerulonephritis (C3GN) and 19% had dense deposit disease (DDD). Median proteinuria at diagnosis was 2.9 g/day, and was ≥1 g/day in 82% of patients. Median eGFR at diagnosis was 50 mL/min/1.73m² (Table 1). In addition to proteinuria, the main clinical signs and symptoms at diagnosis were hematuria, edema, hypertension and fatigue. Pain, appetite loss and sleep problems were also reported. Physicians described disease severity at diagnosis as moderate in 53% and severe in 31% of patients.

Conclusion: This study allows evaluation of a rare disease across geographies. C3G patients experience substantial symptomatic and clinical burden at diagnosis. This symptom burden, high proteinuria, and relatively low eGFR is consistent with physician assessment that the disease is moderate or severe by the time of diagnosis. Facilitating early diagnosis of C3G and rapid initiation of treatment could be beneficial for patients in slowing disease progression.
Table 1: Patient signs and symptoms at diagnosis by geographic region.

<table>
<thead>
<tr>
<th>Signs and symptoms at diagnosis</th>
<th>Geographic region</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Patients</td>
</tr>
<tr>
<td></td>
<td>n = 277</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>229 (83%)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>155 (56%)</td>
</tr>
<tr>
<td>Edema</td>
<td>127 (46%)</td>
</tr>
<tr>
<td>Hypertension (140/90 mmHg)</td>
<td>117 (42%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>95 (34%)</td>
</tr>
<tr>
<td>Discolored urine</td>
<td>52 (19%)</td>
</tr>
<tr>
<td>Pain in back/sides/abdomen</td>
<td>40 (14%)</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>37 (13%)</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>35 (13%)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>32 (12%)</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>29 (10%)</td>
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</table>

Proteinuria at diagnosis

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>n = 224</th>
<th>n = 64</th>
<th>n = 104</th>
<th>n = 34</th>
<th>n = 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 g/24hr</td>
<td>40 (18%)</td>
<td>8 (12%)</td>
<td>9 (9%)</td>
<td>9 (26%)</td>
<td>14 (64%)</td>
</tr>
<tr>
<td>≥ 1 g/24hr</td>
<td>184 (82%)</td>
<td>56 (88%)</td>
<td>95 (91%)</td>
<td>25 (74%)</td>
<td>8 (36%)</td>
</tr>
<tr>
<td>Median</td>
<td>2.9</td>
<td>3.4</td>
<td>3.2</td>
<td>3.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Interquartile range (IQR)</td>
<td>1.3–5</td>
<td>1.5–5</td>
<td>1.8–5</td>
<td>0.8–7.1</td>
<td>0.0–1.8</td>
</tr>
<tr>
<td>Mean (standard deviation)</td>
<td>3.4 (3.0)</td>
<td>3.2 (2.1)</td>
<td>3.6 (2.3)</td>
<td>4.8 (5.2)</td>
<td>1.1 (1.6)</td>
</tr>
<tr>
<td>Range</td>
<td>0–20</td>
<td>0–10</td>
<td>0–13</td>
<td>0–20</td>
<td>0–8</td>
</tr>
</tbody>
</table>

eGFR at diagnosis

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>n = 233</th>
<th>n = 65</th>
<th>n = 111</th>
<th>n = 36</th>
<th>n = 21</th>
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<tbody>
<tr>
<td>Median</td>
<td>50</td>
<td>50</td>
<td>40</td>
<td>67.2</td>
<td>55</td>
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<tr>
<td>IQR</td>
<td>31.5–75</td>
<td>38–72</td>
<td>25–70</td>
<td>57–82.2</td>
<td>31–79</td>
</tr>
<tr>
<td>Mean (standard deviation)</td>
<td>54.5 (28.9)</td>
<td>53.2 (24.4)</td>
<td>47.9 (27.9)</td>
<td>73.5 (32.2)</td>
<td>60.1 (27.7)</td>
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<tr>
<td>Range</td>
<td>5–163</td>
<td>8–150</td>
<td>5–121</td>
<td>20–163</td>
<td>25–130</td>
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#5673
ESTIMATING AND VALIDATING MEASURES OF CKD PREVALENCE AND INCIDENCE USING OBSERVATIONAL AND CLAIMS DATA IN PERSONS AGED 70+
Tim Bothe¹, Anne-Katrin Fietz², Anna Pöhmann³, Elke Schaeffner¹, Nina Mielke¹ and Natalie Ebert¹
¹Charité - Universitätsmedizin Berlin, Institute of Public Health, Berlin, Germany and ²Charité - Universitätsmedizin Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany

Background and Aims: Estimating prevalence and incidence of chronic kidney disease (CKD) based on claims data often underlies bias and limitations due to uncertainty of diagnostic validity. We investigated CKD prevalence and incidence over time using data from a community-dwelling cohort of individuals aged 70+ linked to individual claims data. We assessed the diagnostic validity of claims-based compared with the eGFR-based CKD definition.

Method: We assessed CKD prevalence and incidence in two data sources: 1) eGFR values of participants aged 70+ (n = 2,069) of the Berlin Initiative Study (BIS), including five biennial study visits from 2009-2019, and 2) claims data of BIS participants matched on person-level. Using eGFR, we defined CKD prevalence as eGFR < 60 ml/min/1.73m² calculated with the creatinine-based CKD-EPI (2009) equation. For each study visit, prevalent CKD cases were considered as incident if eGFR was >60 ml/min/1.73m² in the respective previous study visit. In claims data, in- and outpatient ICD-10 diagnoses (N18.3, N18.4, N18.5, N18.8, N18.9, N19) in the year preceding and/or following the study visit date were used to determine CKD prevalence. Incidence was defined as prevalent cases without a diagnosis in the year preceding the first CKD diagnosis. The denominator for incidence was defined as all persons at risk, i.e., who were not prevalent in a respective previous study visit and still under observation. We assessed the diagnostic validity of claims-based CKD prevalence and incidence using eGFR data as a reference. Analyses were stratified by sex.

Results: Between 2009 and 2019, CKD prevalence increased from 0.42 to 0.51 based on eGFR and from 0.30 to 0.43 based on claims data. Incidence varied between 0.16–0.22 using eGFR and 0.07–0.13 using BIS claims data. There was no clear time trend for incidence in any data source. Diagnostic validity of claims-based CKD prevalence and incidence detection is displayed in Table 1. Sensitivity for prevalence increased while other indicators remained stable over time. Detection of incident cases showed lower sensitivity (0.18–0.30 vs. 0.58–0.70) and PPVs (0.40–0.60 vs. 0.79–0.83) compared to prevalence, respectively. Prevalence and incidence based on claims data were slightly higher in males compared to females (Figure 1).

Conclusion: Using the eGFR-based or claims-based definition of CKD we found an increase in prevalence between 2009 and 2019. This might be due to the introduction of the KDIGO guidelines in 2012. During the same time, CKD incidence rates were stable. Comparing the claims-based with eGFR-based CKD definition, we found a sensitivity of 0.58-0.70 for prevalence and 0.18-0.30 for incidence, indicating that there is a risk of underdetection of CKD when using solely claims data, in particular for incident cases.
Table 1: Sociodemographics, prevalence, and incidence estimates of CKD using individual BIS data (n = 2,069 at baseline; presented are results for follow-ups (FU) 1-4) based on eGFR assessed with the creatinine-based CKD-EPI 2009 equation, and claims data. Results of diagnostic validity of claims-based prevalence and incidence with eGFR as reference are shown as well.

<table>
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<tr>
<td>Number of subjects, n</td>
<td>1,670</td>
<td>1,421</td>
<td>1,130</td>
<td>870</td>
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<tr>
<td>Age (years), mean (SD)</td>
<td>81.3 (6.4)</td>
<td>82.6 (6.1)</td>
<td>83.8 (5.6)</td>
<td>85.1 (5.3)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>906 (53.3)</td>
<td>778 (54.0)</td>
<td>641 (55.0)</td>
<td>533 (57.1)</td>
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<tr>
<td>eGFR (ml/min/1.73²), mean (SD)</td>
<td>62.8 (17.9)</td>
<td>61.8 (17.9)</td>
<td>60.1 (17.5)</td>
<td>58.9 (17.7)</td>
</tr>
<tr>
<td>Prevalence estimates</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>BIS data (based on eGFR)</td>
<td>0.42</td>
<td>0.43</td>
<td>0.47</td>
<td>0.51</td>
</tr>
<tr>
<td>Claims data</td>
<td>0.30</td>
<td>0.36</td>
<td>0.43</td>
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<tr>
<td>Sensitivity</td>
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<td>0.71</td>
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<td>0.87</td>
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<td>0.85</td>
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<td>Positive predictive value</td>
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<td>0.80</td>
<td>0.79</td>
<td>0.83</td>
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<tr>
<td>Negative predictive value</td>
<td>0.75</td>
<td>0.77</td>
<td>0.77</td>
<td>0.74</td>
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<td>Incidence estimates</td>
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<tr>
<td>Person at risk, n</td>
<td>1,081</td>
<td>850</td>
<td>655</td>
<td>490</td>
</tr>
<tr>
<td>BIS data (based on eGFR)</td>
<td>0.17</td>
<td>0.16</td>
<td>0.19</td>
<td>0.22</td>
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<tr>
<td>Claims data</td>
<td>0.08</td>
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<td>0.13</td>
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<tr>
<td>Diagnostic validity</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.18</td>
<td>0.23</td>
<td>0.30</td>
<td>0.19</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.94</td>
<td>0.94</td>
<td>0.92</td>
<td>0.96</td>
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<tr>
<td>Positive predictive value</td>
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<td>0.41</td>
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<td>0.60</td>
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<tr>
<td>Negative predictive value</td>
<td>0.85</td>
<td>0.86</td>
<td>0.84</td>
<td>0.81</td>
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LONG-TERM PROGNOSIS OF HYPOPROTEIC DIET SUPPLEMENTED WITH KETOANALOGUES IN PATIENTS WITH ADVANCED DIABETIC KIDNEY DISEASE AND SEVERE PROTEINURIA

Carmen-Antonia Mocanu¹, Gabriel Mircescu¹,² and Liliana Garneata¹,²

¹Carol Davila University of Medicine and Pharmacy, Internal Medicine and Nephrology, Bucharest, Romania and ²“Dr Carol Davila” Teaching Hospital of Nephrology, Nephrology, Bucharest, Romania

Background and Aims: Studies support the role of low-protein regimens in managing chronic kidney disease (CKD). In addition, some data emphasize the role of low-protein diets (LPDs) in postponing kidney replacement therapy (KRT) in patients with CKD, even in diabetic patients with heavy proteinuria. Although most results seem to be in favor of a LPD in CKD, even in patients with advanced diabetic kidney disease (DKD), there is insufficient data on long-term kidney and patient outcomes. This is a follow-up study aimed to determine the outcomes in kidney survival and patient survival in patients with DKD and severe proteinuria.

Method: The follow-up study included all patients with advanced DKD and severe proteinuria who previously participated in a twelve-month multicentric prospective study looking to assess variations in kidney function and proteinuria. At baseline, 97 patients with DKD, with stable stage 4+ CKD and proteinuria of nephrotic-range, who proved adherent to protein restriction were enrolled and received LPD (0.6 g mixed protein/kg-day) supplemented with ketoanalogues of essential amino acids (Ketosteril®, Bad Homburg, Germany, 1 tb/10 kg dry ideal body weight per day) for 12 months. Ninety-two patients completed the study (5 patients received kidney transplant). The efficacy outcomes were assessed by the decline of kidney function and proteinuria. Safety parameters were evaluated by anthropometric measurements (Body Mass Index), Subjective Global Assessment score and serum albumin. Compliance to the LPD was assessed by urinary urea from a 24-hour urine collection to estimate protein intake (ePI) and a 3-day food diary to estimate the energy intake. After the end of the study, the patients continued to remain compliant to the nutritional intervention. The primary composite endpoint was the need for KRT or patient death. The census moment was either the occurrence of the primary endpoint or the 31st of January, 2023.

Results: At baseline, patients had a median age of 61 years (95% CI 58 to 67), 66% were men, with poorly controlled diabetes assessed by the level of the glycated hemoglobin [8.1% (95% CI 8.0 to 8.3)]. All patients had a good nutritional status (SGA A). The median estimated glomerular filtration rate (eGF) was 12.6 mL/min (95% CI 11.7 to 13.1) and the median proteinuria was 5.2 g/g creatininuria (95% CI 5.0 to 5.2). After 12 months, a significant reduction in proteinuria was observed (67%), as well as a reduction in the kidney function decline by almost 80% compared to the period before the inclusion and a preserved good nutritional status (SGA A). The median follow-up was 105 months (95% CI 103 to 106). After almost 9 years of follow-up, 83.7% of patients remained alive, despite significant comorbidities. The median

Figure 1: Estimates of prevalence and incidence based on eGFR and claims data stratified by sex over all study visits.
survival was 62 months (95% CI 47 to 85). Seventy-six percent of patients required KRT, with a predilection for hemodialysis. The median period of time until KRT was 26 months (95% CI 24 to 29). In a Kaplan-Meier survival analysis, the compliance to the LPD was associated with better kidney survival ($p = 0.03$).

Conclusion: Low-protein diets supplemented with ketoanalogues of essential amino acids seem to be associated with a better kidney outcome on long-term in patients with advanced diabetic kidney disease and heavy proteinuria.

#4188

PREFERENCES FOR PROGNOSTIC INFORMATION PROVISION AMONGST PATIENTS WITH CHRONIC KIDNEY DISEASE: A SURVEY

Jet Milders, Chava Ramspek, Friedo W. Dekker and Merel Van Diepen

Leiden University Medical Center (LUMC), Leiden, Netherlands

Background and Aims: Patients with chronic kidney disease (CKD) often experience various symptoms and have an increased risk for many adverse outcomes. The varying nature of the course of the disease comes with much prognostic uncertainty, and patients have expressed a wish for more information about their future with the disease. However, the extent to which patients want to know more about their future with CKD varies highly per individual. By identifying which topics patients are interested in regarding their prognosis, more attention can be given to these topics in clinical practice and future research. Therefore, the aim of this study was to explore whether CKD patients want to know more about their future, and if so, which topics they find most important in regards to their prognosis.

Method: To gather information on what CKD patients want to know regarding their future, a survey was constructed by an expert panel of researchers and nephrologists. Before distributing the survey, it was tested during a two-phase pilot, in which volunteers of the Dutch patients association provided detailed feedback. Feedback was incorporated into a final version, available both on paper and online in Castor EDC. The survey was developed in Dutch, and was fully anonymous. The final survey consisted of three main sections containing multiple questions: 1) demographic questions, 2) ‘do you think about your future with a kidney disease?’, 3) ‘what would you want to know about your future with CKD?’. The survey was specifically developed for all patients that currently have chronic kidney disease, including patients undergoing any form of dialysis or those that have received a kidney transplant in the past. Descriptive statistics were used to summarize the results.

Results: A total of 145 patients filled in the survey. Respondents had a mean age of 63.0 (SD 14.1) and 49.7% was male. The majority of patients (57.9%) had undergone a kidney transplant in the past and 23 (15.9%) patients were undergoing dialysis at the time of responding. When asked whether patients ever thought about their future with CKD, most replied that they think about it every now and then (57.2%) or often (36.6%), and only nine (6.2%) patients reported that they never think about it. Half of the patients (50.3%) reported that they do not want to discuss their future at all. Furthermore, patients were asked in which scenarios they would be interested in knowing more about their future. Most patients (77.9%) mentioned they currently do not discuss it, but would like to, and 23 (15.9%) patients stated that they do not want to discuss their future at all. They were asked in which scenarios they would be interested in knowing more about their future. Most patients (77.9%) mentioned they always wanted to know more about their future, regardless of whether the information is positive or negative. Contrarily, two patients (1.4%) only wanted to know in case of good news, 32 (22.1%) when the outcomes in question can be prevented, and 37 (25.5%) if it would help them make a treatment decision. Four patients (2.8%) were not sure whether they wanted more prognostic information and four patients (2.8%) preferred not to know anything in terms of prognosis at all. Patients were asked to rate the importance of receiving more prognostic information for nine outcome categories on a scale from 0 to 100. Outcome categories that were rated the highest were laboratory measurements, health complaints, and physical well-being. Per category, patients chose specific subjects that they deemed important in terms of prognosis. The top ten most chosen subjects per patient group (CKD, dialysis, kidney transplantation, and all patients) are presented in Figure 1.

Conclusion: Most patients with chronic kidney disease think about their future, and there is interest in receiving individualised prognostic information on what to expect for a variety of subjects. Based on these research results more attention can be paid to specific prognostic information provision tailored to the preferences of and based on subjects that matter to patients, both in future research and clinical practice.

Figure 1: Top ten outcomes patients wished to receive more prognostic information about.

*CKD = all patients that are not receiving dialysis and have not undergone a kidney transplant, KTx = kidney transplantation
PACE-CKD: FINANCIAL BURDEN AND WORK PRODUCTIVITY OF PATIENTS WITH CKD AND CAREGIVERS: RESULTS FROM A US SURVEY

Steven Chadban1, Ciro Esposito2, Janani Rangaswami3, Mai-Szu Wu4, Richard Hult5, Hesham Elsayed6, Helmut Reichel7, Juan Jose Garcia Sanchez8, Surendra Pentakota9, Thames Kularatne9 and Simon Fifer9

1 Royal Prince Alfred Hospital, Department of Renal Medicine, Sydney, Australia, 2 University of Pennsylvania, Nephrology, USA, 3 George Washington University School of Medicine, Nephrology Division, Washington DC, United States of America, 4 Taipei Medical University, College of Medicine, Taipei, Taiwan, Rep. of China, 5 St George’s Hospitals NHS Foundation Trust, Renal and Transplantation Unit, London, United Kingdom, 6 AIN Shams University, Department of Internal Medicine and Nephrology, Cairo, Egypt, 7 Nephrology Center Villingen-Schwenningen, Villingen-Schwenningen, Germany, 8 AstraZeneca, Biopharmaceuticals Medical, Cambridge, United Kingdom and 9 CaPPr: Community and Patient Preference Research, Sydney, Australia

Background and Aims: Chronic kidney disease (CKD) is a progressive condition, conferring serious mortality and morbidity in patients with advanced disease. Upon reaching end-stage kidney disease (ESKD), dialysis or kidney transplantation is typically required, leading to considerable burden to health care systems worldwide. There is a paucity of data assessing the financial wellbeing and work productivity of patients with CKD and their caregivers, compared to the general population. Therefore, the objective of this study was to conduct a quantitative online survey to estimate the financial burden and work productivity of patients with CKD and their caregivers relative to the general population.

Method: This non-interventional survey included adult patients with a diagnosis of CKD for at least 3 months and unpaid caregivers of CKD patients for a minimum of 1 hour per week in the previous 4 weeks. This study was supported by AstraZeneca.

Funding: This study was supported by AstraZeneca.

The study enrolled 199 patients (median age: 58 years) with CKD and 113 caregivers (median age: 38 years) in the United States. Candidates were enrolled between June and July 2022. In the patient cohort, 32.2% of participants were dialysis-dependent, who predominately received treatment in a clinic or hospital (79.7%) rather than at home. Caregivers most commonly cared for their parent (45.1%) or partner (25.7%); the most frequent role for caregivers was providing transport to/from medical appointments (89.4%). Patients were considered to have 17.8% worse financial wellbeing compared to the general population according to the CFPB scale (52.0 vs 63.2, respectively). Patients receiving dialysis experienced a similar financial burden to non-dialysis dependent patients, with slightly worse FACIT-COST scores (22.9 vs 23.4, respectively). Further, patients and caregivers reported losses to work productivity with dialysis patients (21.6%) reporting higher absenteeism from work than non-dialysis patients (9.6%) when compared to the general population (3.6%). Similarly, care of dialysis-dependent patients reported a higher rate of absenteeism (14.8%) compared to non-dialysis dependent patients (10.6%) and the general population (5.2%). Total activity impairment was higher for dialysis dependent patients (55.5%) than for non-dialysis dependent patients (43.7%) and considerably higher versus the general population (5.7%). Caregivers for dialysis dependent patients had greater total activity impairment (44.3%) than caregivers for non-dialysis dependent patients (34.3%) and the general population (17.3%). Results for patients and caregivers in other countries (United Kingdom, Germany, and Mexico) will also be presented at the congress.

Conclusion: The results of this survey suggest that work productivity is impaired in both CKD patients and their caregivers and is also exacerbated further in patients who progress to dialysis and their caregivers. The survey also provides indications that the financial wellbeing in patients with CKD may be affected in comparison to the general population. Evidence based policy interventions ought to consider the progressive nature of CKD and should aim to reduce the societal burden of disease for patients and caregivers.

Funding: This study was supported by AstraZeneca.

#5059

EXTERNAL VALIDATION OF THE KFRE AND GRAMS PREDICTION MODELS FOR DEATH AND KRT IN A SPANISH POPULATION WITH ADVANCED CHRONIC KIDNEY DISEASE

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Background and Aims: The Kidney Failure Risk Equation (KFRE) is used to predict the risk of kidney replacement therapy (KRT) initiation in the following 2 and 5 years, in patients with chronic kidney disease (CKD) stages G3-G5. The Grams model is applied exclusively to stage G4-G5 patients who have a higher risk of dying or requiring KRT. This model predicts both events, KRT and death, at 2 and 4 years, but unlike the KFRE, it considers the patient’s death as a competing event with respect to the start of KRT. It has been suggested that the Grams model makes a more accurate prediction of the onset of KRT in the long term, since by including mortality as a competing event it does not overestimate the risk of KRT. However, there are few external validations of the Grams model to predict mortality in patients with CKD G4+. We performed an external validation of both models with respect to the start of KRT and mortality in a Spanish population with CKD G4+, followed up prospectively during 4-9 years.

Method: We conducted a prospective cohort analysis of incident patients followed in the Advanced Chronic Kidney Disease clinic of the Hospital Universitario Fundacion Alcorcon, Spain between 1-1-2014 and 31-12-2018 who had CKD G4-G5. Clinical data was registered prospectively in a database at each visit to the clinic. Follow-up ended on 31-12-2022. For each patient, the follow-up time ranged from 4 to 9 years. The outcomes were: observed incidence of KRT (haemodialysis, peritoneal dialysis, or pre-emptive kidney transplantation) by 2, 4 and 5 years and death at 2 and 4 years before starting KRT.

Results: We studied 347 patients, 31.1% were women, with a mean age of 72.1 ± 12.7 years, 52.4% with cardiovascular disease and 58.8% diabetics. At the start, the mean eGFR was 20.7 ± 5.0 ml/min and the median urine albumin-to-creatinine ratio was 327 (IQR 52-1118) mg/g. At 2, 4 and 5 years the percentage of patients who required KRT was 20.2%, 38.3% and 45.7% respectively, while 12.7% and 23.6% died at 2 and 4 years respectively, before starting KRT. For KTR both models had an excellent discrimination. For KFRE-2 and Grams-2, the AUC was 0.842 (95% CI 0.801-0.884), and for KFRE-5 the AUC was 0.805 (95% CI 0.751-0.859). For death before KRT the Grams model demonstrated an acceptable discrimination, with an AUC of 0.726 (95% CI 0.646-0.806) and 0.749 (95% CI 0.690-0.809) respectively, for Grams-4 the AUC was 0.842 (95% CI 0.801-0.884), and for KFRE-5 the AUC was 0.805 (95% CI 0.751-0.859).

Conclusion: In a Spanish cohort of patients with CKD G4+, the Grams and KFRE models adequately estimate the risk of KRT. The Grams model provides an acceptable estimate of the risk of death before starting KRT at both 2 and 4 years. It can be considered for treatment planning and information for patients with CKD G4+.
CHANGES IN SERUM CREATININE DURING AND AFTER PREGNANCY IN WOMEN WITH OR WITHOUT CHRONIC KIDNEY DISEASE: AN OBSERVATIONAL STUDY

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Background and Aims: In women with chronic kidney disease (CKD), kidneys may not sufficiently adapt to physiological changes during pregnancy, which may accelerate postpartum loss in renal function. We aimed to characterize pregnant women with or without renal impairment and to describe changes in renal filtration during and until one year after pregnancy.

Method: We performed a descriptive study using primary care data from the United Kingdom-based Clinical Practice Research Datalink (CRPD) GOLD and linked hospital data (2000–2019) in 14’401 pregnancies with ≥2 serum creatinine (Scr) measurements between the year before and after pregnancy. Pregnancies were categorized by means of the median estimated glomerular filtration rate (eGFR) during baseline (proteinuria is not reliably recorded). We captured risk factors for CKD and described changes in Scr levels over time as proxies for renal filtration.

Results: Of 14’401 pregnancies, 84% had a baseline eGFR [ml/min/1.73m^2] of ≥90, 13% between 75–89, 13% between 60–74, and <1% between 15–59. Pre-existing hypertension, diabetes, and/or overweight was prevalent in 66.0% of women with an eGFR < 60 (versus 51.3–54.4% in eGFR ≥ 60). Preterm delivery was recorded in 30.2% of women with an eGFR < 60 (versus 9.4–9.8% in eGFR ≥ 60). In women with a low-normal eGFR between 75–89, median baseline Scr levels (mg/dL [μmol/L]) were 0.92 [81.33] (interquartile range (IQR) = 0.88–0.96 [77.79–84.86]), which decreased by 0.25 [22.1] by week 14/15, remained stable until week 30/31, increased to 0.94 [84.0] [IQR = 0.83–0.99 [73.37–87.52]] until week 3/4 postpartum, and decreased back to baseline by one year postpartum. In women with a moderately low baseline eGFR between 60–74, median baseline Scr levels were 1.05 [92.82] [IQR = 1.01–1.10 [89.28–97.24]] and patterns during pregnancy followed those of women with low-normal
eGFR (decreased by 0.28 [24.7] until week 18/19, plateau until week 38/39). However, Scr levels increased slower in trimester 3 and early postpartum and reached baseline levels at week 9/10 postpartum. Women with a baseline eGFR between 15–59 (median baseline Scr levels = 1.43 mg/dL [126.41 μmol/L], IQR = 1.26–1.72 mg/dL [111.38–152.05 μmol/L]) showed renal adaptation in trimester 1 and 2, but increased Scr levels of 1.71 [151.16] (IQR = 1.32–2.36 [116.69–208.62]) in trimester 3, but sample size was small.

Conclusion: Adaptations of renal filtration were not impaired during or after pregnancy in 1’932 pregnancies of women with a low-normal eGFR between 75–89. In women with a moderately low eGFR between 60–74, the pattern was similar, but potentially prolonged hyperfiltration in trimester 3 and early postpartum requires further investigation. The pattern of renal adaptation in eGFR between 15–59 was similar in trimester 1 and 2. Increased Scr levels in trimester 3 may indicate insufficient renal function but results have to be interpreted cautiously due to small sample size and potentially selective measurements.

THE ASSOCIATION OF EGF SLOPE WITH VISUAL IMPAIRMENT, RETINAL VESSEL DENSITY, AND EYE PATHOLOGIES IN THE EYE DETERMINANTS OF COGNITION (EYEDOC) STUDY

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Background and Aims: Previous studies have identified chronic kidney disease (CKD) as a risk factor for poor ocular health. However, the effect of faster decline in estimated glomerular filtration rate (eGFR) on visual function, retinal markers, and eye conditions is unclear. We therefore examined the association of eGFR slope with visual function measures, retinal vessel density (VD), and common ocular pathologies in a bi-racial general population cohort.

Method: We studied 823 participants with normal kidney function or mild CKD (eGFR ≥ 60 ml/min per 1.73 m^2) at baseline from the Eye Determinants of Cognition (EYEDOC) Study. Exposure was change in eGFR (ml/min per 1.73 m^2 per year) over 4 study visits between 1996 and 2019, calculated using linear mixed-effect models with unstructured covariance matrix. Outcomes (recorded between 2017 and 2019) were visual function (near visual acuity, presenting distance visual acuity, contrast sensitivity), retinal VD in the superficial, intermediate, and deep capillary plexus layers, and common ocular pathologies, such as retinopathy, age-related macular degeneration, and
glaucoma. We used linear regression to model the associations of eGFR slope with visual function and retinal VD. We used logistic regression to study the association of eGFR slope with ocular pathologies. All models were adjusted for age, sex, race, education, smoking, body mass index, diabetes, hypertension, and hyperlipidemia. The models for retinal VD were additionally adjusted for signal strength index.

**Results:** In our study cohort, the mean age was 79 (±4) years with 62% females and 48% African Americans. The prevalence of diabetes and hypertension was 38% and 82%, respectively. The mean [SD] eGFR slope was −1.6 (0.6) ml/min per 1.73 m² per year. A faster eGFR decline of 1 ml/min per 1.73 m² per year was significantly associated with worse near visual acuity (0.04 logMAR [95% CI: 0.00; 0.08], p = 0.03), worse contrast sensitivity (−0.03 log [−0.05; −0.001], p = 0.01), lower VD in the deep capillary plexus layer (−0.99% per mm² [−1.96; −0.02], p = 0.04), and higher odds of retinopathy (odds ratio 2.44 [1.06; 6.63], p = 0.04). Associations of eGFR slope with the remaining measures of visual function and eye conditions were not significant.

**Conclusion:** In our bi-racial general population cohort with an eGFR ≥ 60 ml/min per 1.73 m² at baseline, a faster decline in eGFR was associated with worse visual function, reduced retinal vascular health, and higher odds of retinopathy. Our results support the potential usefulness of eGFR slope for risk assessment of ocular outcomes, even in patients with normal kidney function or mild CKD.

**#5776**

**HIGHER DIETARY NA/K RATIO IS ASSOCIATED WITH AN INCREASED RISK OF CARDIOVASCULAR OUTCOMES IN THE GENERAL POPULATION, BUT NOT IN CKD PATIENTS**

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**Background and Aims:** High sodium and low potassium intake have been recognized as cardiovascular risk factors. The combined effect of sodium and potassium intake, reflected by the dietary sodium-to-potassium ratio (Na/K ratio), may be an even better predictor of cardiovascular disease (CVD). The primary objective of this meta-analysis is to investigate the effect of the estimated dietary Na/K ratio on the composite outcome of cardiovascular events (CVE) and all-cause mortality. As the ideal sodium and potassium intake may be different for chronic kidney disease (CKD) patients, we will compare subjects with and without CKD.

**Method:** We performed a systematic search in MEDLINE and EMBASE databases from January 1946 to December 2022. We included randomized controlled trials and cohort studies with a mean follow-up duration of ≥ 1 year, which reported the association between the estimated dietary Na/K ratio and CVE and/or all-cause mortality. Two reviewers independently assessed the eligibility of identified studies, extracted data, and assessed the risk of bias according to the Cochrane Handbook Guidelines. We compared hazard ratios (HRs) among subgroups with increasing dietary Na/K ratio using the group with lowest estimated dietary Na/K ratio as a reference. We performed a random-effects meta-analysis using these HRs. A sensitivity analysis was performed using the leave-one-out approach. In a subgroup analysis, we compared CKD patients with the general population and adults with a history of CVD. We performed a meta-regression analysis to investigate the impact of the absolute increase in estimated dietary Na/K ratio (Δ Na/K) on the composite outcome, when adjusted for the mean estimated dietary Na/K ratio of the reference group and the follow-up duration of the studies.

**Results:** Of the 8,249 studies initially identified, 16 studies with 404,301 subjects were included in our main analysis. Mean age was 55.2 years, and 49% were male. For estimation of dietary Na/K ratio, 3 studies used spot urines, 3 studies used 24-hour urine collections, and 10 studies used food frequency questionnaires. Mean follow-up duration was 12 years. Higher estimated dietary Na/K ratio was associated with a significant higher risk for the composite endpoint of CVE and all-cause mortality (HR 1.16 [95% CI: 1.10-1.23], p < 0.00001, I² = 41%) (Figure 1). We observed no significant changes in our results using the leave-one-out approach. In the subgroup analysis, we observed that increased estimated dietary Na/K ratio associated with significantly higher CVE and all-cause mortality risk in the general population (10 studies; 387,679 subjects; HR 1.17 [1.10-1.25], p < 0.00001, I² = 48%), and in adults with a history of CVD (5 studies; 15,779 subjects; HR 1.18 [1.11-1.25], p < 0.00001, I² = 49%).

**Figure 1:** Forest plot of the association between the estimated dietary Na/K ratio and the composite outcome of CVE and all-cause mortality in CKD patients, subjects with a history of CVD and the general population. CI, confidence interval.
knowledge gaps by providing observational data on patients' characteristics, risk factors, management patterns, disease progression, and outcomes related to CKD and associated comorbidities namely: T2D, HTN, and HF.

**Method:** The iCaReMe Global Registry (NCT03549754) is a prospective, investigator-led, multinational, observational registry relying on voluntary participation by treating physicians to assess the management and quality of care through socio-demographic and clinical characteristics, disease management patterns (including screening, diagnosis, treatment approaches), healthcare resource utilization and clinical outcomes in patients with CKD, T2D, HTN, and/or HF. Eligible and consented patients were enrolled during routine clinical practice based on the physician's discretion and were followed up per routine clinical care. We present the descriptive analysis of baseline clinical and demographic characteristics of the CKD cohort enrolled in the iCaReMe Global Registry from February 2018 to December 2022.

**Results:** Overall 2977 patients with CKD have been enrolled from 21 countries (Argentina, Costa Rica, Egypt, Ethiopia, Georgia, Greece, Hong Kong, Indonesia, India, Jordan, Kenya, Lebanon, Malaysia, Mexico, Russia, South Africa, Thailand, The Philippines, Turkey, Ukraine, and the United Arab Emirates). At baseline, the mean ± standard deviation (SD) age was 60.4 ± 13.8 years and 54.6% were males. The mean ± SD systolic and diastolic blood pressures of the cohort were 120.4 ± 43.6 and 70.5 ± 25.6 mmHg and the mean ± SD body mass index was 21.6 ± 12.9 kg/m². 68.9% had T2D and 68.3% had hypertension. Diabetic kidney disease and hypertensive kidney disease were the most common etiologies in 78.8% of the patients (Figure 2). Serum creatinine was reported in 85.3% of patients and urine albumin-creatinine ratio (UACR) in 30.5% and only 25.9% had both. The prevalence of KDIGO GFR categories G3-5 based on estimated glomerular filtration rate (eGFR) using CKD-EPI was 72.5% and the prevalence of albuminuria A2/A3 was 75.9%. In total, 7.9% patients were undergoing dialysis. In patients with T2D (n = 2051); 69.1% (1250/1808) had G3-5 GFR category and 76.1% (484/636) had albuminuria stage A2 and A3. In patients with HTN (n = 2033); 77.6% (1367/1761) had G3-5 GFR category and 76.6% (485/633) had albuminuria stage A2 and A3.

**Conclusion:** At baseline most of iCaReMe Registry CKD cohort fall within the KDIGO high or very high risk of outcomes associated with a high prevalence of T2D and HTN. Our results also indicate an underutilization of albuminuria testing despite its critical role in diagnosis, risk stratification and follow up which raises concerns about CKD early detection, management, and prognosis.

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**#6054**

**CLINICAL CHARACTERISTICS AND RENAL RISK OF PATIENTS WITH CHRONIC KIDNEY DISEASE: REAL-WORLD EVIDENCE FROM THE ICAReME GLOBAL REGISTRY**

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**Background and Aims:** Chronic kidney disease (CKD) has emerged as a leading global public health concern due to its growing prevalence and associated morbidity and mortality. Throughout the disease progression, CKD is associated with a substantial health and socio-economic burden on patients, families, and healthcare systems worsened by complex interactions with type 2 diabetes (T2D), hypertension (HTN), and heart failure (HF). To help current and future patients get the best possible care, it is of the greatest importance to better understand how they are managed routinely, but real-world data on coexisting cardiovascular, renal, and metabolic diseases are scarce or non-existent in many countries. The iCaReMe Global Registry aims to address these
MARKERS OF SUBCLINICAL LEFT VENTRICULAR DYSFUNCTION ARE ASSOCIATED WITH MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS WITH PRESERVED EJECTION FRACTION
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Background and Aims: Cardiac dysfunction is frequent in chronic kidney disease (CKD) patients and contributes to high morbidity and mortality in this category. The aim of our study is to evaluate the association between markers of subclinical left ventricular (LV) dysfunction and mortality in CKD patients with preserved left ventricular ejection fraction.

Method: We prospectively enrolled CKD patients (pts) in pre-dialysis. Parameters of cardiac structure and function were evaluated by echocardiography: systolic and diastolic left ventricular (LV) volumes, LV mass index (LVMI), left atrial volume index (LAVI), LV ejection fraction (LVEF), global longitudinal strain (GLS), ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/E’) and ratio between the early maximal ventricular filling velocity and the late filling velocity (E/A). Cardiac functional status was stratified according to NYHA criteria. All patients were followed until death or loss from records. Primary endpoint was all-cause mortality. Secondary endpoints were cardiovascular mortality and a composite cardiac endpoint comprising coronary heart disease, heart failure hospitalization and new-onset arrhythmia.

Results: We prospectively enrolled 39 CKD patients (5 pts CKD stage 2, 27 pts CKD stage 3, 7 pts CKD stage 4) mean age 64.3 ± 10.2 years, men = 28 (71.8%).
At baseline all pts had LVEF >50%; 11 pts (28.2%) were classified as NYHA I, 18 (46.2%) as NYHA II, and 10 pts (25.6%) as NYHA III. endpoint was significantly correlated with LVMI (p < 0.05), in pts with symptomatic heart failure (−15.6 ± 2.6 vs 18.9 ± 2.8, p = 0.05), and in pts with diabetes mellitus (−15.8 ± 1.9) and hypertensive nephropathy (−16.8 ± 2.8) compared with patients with tubulointerstitial diseases (−18.1 ± 2.5) and chronic glomerulonephritis (vs −21.1 ± 3.6) (p < 0.05). E/E’ as a marker of subclinical LV diastolic dysfunction, was significantly higher in pts with symptomatic heart failure (12.2± 3.4 vs 9.5 ± 1.9, p < 0.05), in pts with diabetes mellitus (13.3± 3.5 vs 10.2 ± 2.5, p < 0.05). All-cause mortality was 17.9% (7 events), while cardiovascular mortality was 10.3% (4 events). Composite cardiac endpoint was recorded in 13 pts (33.3%). Baseline profile in patients who died during follow up period included significantly lower eGFR (30.1 ± 10.5 vs 46.1 ± 16.9 mL/min/1.73 m², p < 0.05), higher LAVI (55.5 ± 11.1 vs 37.4 ± 11.9 mm²/m², p < 0.05), higher LVMI (149.8 ±36.1 vs 115 ±28.5 g/m², p < 0.05), and higher E/E’ (15.2 ±3.3 vs 10.7 ± 2.8, p < 0.05). Death was significantly correlated with GLS (p = 0.042), E/E’ (p = 0.002), LVMi (p = 0.008) and LAVi (p = 0.007), while CV mortality was correlated with E/E’ (p = 0.019) and LVMi (p = 0.041). Composite cardiac event was significantly correlated with LVMI (p = 0.01) and LAVI (p = 0.006). Cox regression analysis identified only E/E’ as a predictor for all-cause mortality (p = 0.002) and also for cardiovascular mortality (p = 0.015).

**Conclusion:** In our study population of CKD patients, cardiac imaging parameters of subclinical LV dysfunction (GLS and E/E’) were associated with all-cause mortality. Marker of LV diastolic dysfunction E/E’ proved to be the only predictor of all-cause and cardiovascular mortality. Thus, in CKD patients, evaluation of the cardiac function should focus not only on ejection fraction measurement, but also on the parameters of subclinical LV dysfunction.

**#6774 CAUSAL ASSOCIATION OF COVID-19 AND KIDNEY FUNCTION: A MENDELIAN RANDOMIZATION ANALYSIS**

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**Background and Aims:** Previous observational studies suggest that there are potential associations between COVID-19 and kidney functions. However, whether COVID-19 had causal effects on different kidney traits is currently unclear. We aimed to investigate the causal link between genetically determined COVID-19 and following kidney traits.

**Method:** We performed univariate Mendelian randomization (MR) studies using summary genome-wide association studies (GWAS) statistics of COVID-19 severity (n case/n control: 32,519/2,062,805 for European, n case/n control: 2882/31,200 for Asian) and COVID-19 susceptibility (n case/n control: 122,616/2,475,240 for European, n case/n control: 4459/36,121 for Asian) derived from THE COVID-19 Host Genetics Initiative (r7) as exposure. Phenotypic outcomes analyzed for COVID-19 and following kidney traits. More deeply explorations focused on the association between COVID-19 and kidney traits should be performed with more data would be available in the future.

**#4016 MENTAL HEALTH OF PEOPLE WITH KIDNEY DISEASE AND THEIR SIGNIFICANT OTHERS BEFORE AND AFTER THE COVID-19 VACCINE PROGRAMME**

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**Background and Aims:** The COVID-19 pandemic resulted in widespread psychological experiences, including depression, anxiety, and stress, especially in clinically vulnerable people such as those with chronic kidney disease (CKD). The UK, high rates of infection, severe illness and death, and profound changes to usual activities and healthcare delivery imposed by social distancing and isolation persisted throughout 2020 and only began to abate after the introduction of the COVID-19 vaccination programme early in 2021. We conducted a survey to assess levels of general depression, anxiety, stress and health anxiety in people with non-dialysis CKD (ND-CKD), kidney transplant recipients (KTRs), and their significant others (SOs) at two timepoints: during the Autumn of 2020 when COVID-19 levels and social restrictions were high, and in May 2021 after the majority of the population had been vaccinated. We hypothesised that the mental health status of people affected by CKD would improve after receiving the vaccine.

**Method:** 11 hospital sites in England invited local patients and their SOs to complete an online survey in Autumn 2020, and a follow-up in May 2021. The survey included two validated mental health questionnaires: the Depression, Anxiety and Stress Scale (DASS-21) and the Short Health Anxiety Index (SHAI). Higher scores are indicative of higher levels of depression, stress and anxiety, and health anxiety respectively. One-way ANOVA was used to compare questionnaire scores between the three participant groups, and paired sample t-tests were used to assess changes between the two timepoints for each group.

**Results:** 381 participants completed the Autumn 2020 survey: 123 ND-CKD (61% male, mean age 64 [SD:14] years), 150 KTRs (51% male, 59 [SD:12] years), and 108 SOs (39% male, 60 [SD:13] years). 318 completed the May 2021 follow-up survey. 87 participant groups completed both surveys. In Autumn 2020, people with ND-CKD had significantly higher DASS-21 anxiety scores than SOs (p = 0.029). Both ND-CKD and KTRs had significantly higher health anxiety scores than SOs at baseline (P <0.001), and at follow-up (ND-CKD, P = 0.006; KTR, P = 0.010). In May 2021, 95% of participants had received the COVID-19 vaccine. There were no significant changes in DASS-21 subscale scores or SHAI scores between the Autumn 2020 and May 2021 timepoints for any of the participant groups.

**Conclusion:** Our results show that during the COVID-19 pandemic, people living with ND-CKD and KTRs had higher levels of health-related anxiety than their SOs. As the COVID-19 vaccine programme reduced health risks and allowed relaxation of social restrictions, it may be expected to result in improved population mental health. However, in May 2021, we found no improvement in depression, anxiety, stress, or health anxiety among people living with CKD or their SOs despite nearly all the participants having received the vaccine. It is likely that increased social mixing and marked reduction in public mask-wearing led to persistently high anxiety levels in clinically vulnerable people and those who live with them. Today, the majority of the public have returned to “normal” social behaviour and masks are rarely worn, but COVID-19 remains a threat to people with CKD. There is an urgent need for better mental health support among the kidney community.
SEX DIFFERENCE IN CARDIOVASCULAR RISK IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A POOLED ANALYSIS OF FOUR COHORT STUDIES

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Background and Aims: Progression of chronic kidney disease (CKD) has proven to be faster in men than in women [1-3]. Whether the same holds true for cardiovascular risk remains ill-defined.

Method: We conducted a pooled analysis of 4 cohort studies from 40 nephrology clinics in Italy including patients with CKD (estimated GFR<60 mL/min/1.73 m2 or higher if proteinuria >0.15 g/day). The aim was to compare multivariable-adjusted risk (Hazard Ratio, 95% Confidence Interval) of a composite cardiovascular endpoint (cardiovascular death and non-fatal myocardial infarction, congestive heart failure, stroke, revascularization, peripheral vascular disease, and nontraumatic amputation) in women (n = 1,192) versus men (n = 1,635).

Results: At baseline, women had slightly higher systolic blood pressure (SBP) as compared with men (139±19 vs 138±18 mmHg, P = 0.049), lower eGFR (33.4 vs 35.7 mL/min/1.73 m2, P = 0.001) and lower urine protein excretion (0.30 g/day vs 0.45 g/day in men, P<0.001). Women did not differ from men in age and prevalence of diabetes while having a lower prevalence of cardiovascular disease, left ventricular hypertrophy and smoking habit. During a median follow-up of 4.0 years, 517 fatal and non-fatal cardiovascular events were registered (199 in women and 318 in men). The adjusted risk of cardiovascular events was lower in women (0.73, 0.60-0.89, P = 0.002) than in men; however, the cardiovascular risk advantage of women progressively diminished as SBP (as continuous variable) increased (P for interaction = 0.021; Figure 1). Similar results were obtained when considering SBP categories; when compared to men, women had a lower cardiovascular risk for SBP <130 mmHg (0.50, 0.31-0.80; P = 0.004) and between 130–140 mmHg (0.72, 0.53-0.99; P = 0.038), while no difference was observed for SBP >140 mmHg (0.85, 0.64-1.11; P = 0.232).

Conclusion: Higher BP levels abolish the cardiovascular protection seen in female vs male patients with overt CKD. This finding supports the need for higher awareness of hypertensive burden in women with CKD.

REFERENCES


Abstracts
and ESKD was higher at all stages in Cohort 1 vs. Cohort 2, particularly ESKD which was markedly higher for stage 5 (91.4% vs. 13.6%). Proportion of death was similar in both cohorts and was the highest in stages 4–5.

Conclusion: Substantial differences in kidney outcomes were noted between CKD classifications derived from ICD codes vs. KDIGO criteria, except all-cause mortality which was comparable across both cohorts and increased notably with stage. Changes in kidney function, both progression, regression, and ESKD occurred more frequently in Cohort 1. Our analysis suggests ICD diagnosis and KDIGO criteria might not be used interchangeably in the context of utilizing real-world data sources.

#6871
RISK FACTORS FOR SHORT-TERM CHRONIC KIDNEY DISEASE AFTER A CUTE KIDNEY INJURY WITH RECOVERY OF NORMAL RENAL FUNCTION

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Background and Aims: Acute kidney injury (AKI) is a clinic-biological syndrome encompassing the entire spectrum of acute renal failure that is responsible for a higher short-term risk of developing chronic kidney disease (CKD) even after recovery of normal renal function. The risk of developing new CKD has been estimated at 4 times that of the population without an episode of AKI in several studies. Our objective was to identify its risk factors

Method: We conducted a retrospective descriptive study that included patients hospitalized for AKI with recovery of normal renal function between January 2002 and December 2015 who were followed up to one year after discharge. In order to achieve our objective, we collected data related to the patients’ age, history, multitargeted or not, mechanism of AKI, KDIGO stage, glomerular filtration rate (GFR) at hospital discharge, using a pre-designed form.

Substantial differences in kidney outcomes were noted between CKD classifications derived from ICD codes vs. KDIGO criteria, except all-cause mortality which was comparable across both cohorts and increased notably with stage. Changes in kidney function, both progression, regression, and ESKD occurred more frequently in Cohort 1. Our analysis suggests ICD diagnosis and KDIGO criteria might not be used interchangeably in the context of utilizing real-world data sources.

#4018
CHARACTERISATION OF THE CLINICAL, HUMANISTIC AND ECONOMIC BURDEN OF ANAEMIA IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC LITERATURE REVIEW

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Background and Aims: Chronic kidney disease (CKD) is defined as structural kidney damage and/or decreased kidney function (glomerular filtration rate <60 mL/min/1.73 m²) persisting for ≥3 months [1]. Anaemia is a frequent CKD comorbidity associated with increased cardiovascular (CV) morbidity, mortality, reduced health-related quality of life (HRQoL) and greater healthcare resource utilisation (HRU) [2]. Our systematic literature review provided an overview of the clinical, humanistic and economic burden of anaemia of CKD.

Method: A search was performed in MEDLINE, EMBASE, MEDLINE IN-PROCESS, Cochrane Controlled Trials Register and the Cochrane Database of Systematic Reviews from database inception to 10 April 2022, using predefined criteria to identify cohort, cross-sectional, observational and cost studies, economic evaluations, conceptual model studies, systematic and literature reviews (complemented by grey literature and congress abstract searches and back-referencing relevant review papers [2016–2021]). Full-text selected citations were examined by two independent reviewers. Clinical burden parameters included CKD progression, differences in progression between patients with/without CKD anaemia, time to blood transfusion and association of CKD stage/progression with CV outcomes or mortality. Humanistic burden included HRQoL and caregiver burden. Economic burden was determined by HRU and direct/indirect costs.

Results: Data were extracted from 115 studies (12,109 database records, 79 supplementary items; Figure 1), including patients: pre- or non-dialysis (n = 61), on dialysis (n = 21), mixed non-/on dialysis (n = 19) and unknown dialysis status (n = 14). Incidence of advanced CKD was significantly higher in adult non-dialysis dependent (NDD) patients with anaemia of CKD vs those without (incidence per 1000 person-years: 15 to ∼85 vs 3 to ∼25). Patients with CKD anaemia had a higher risk of disease progression than those without anaemia (n = 21), e.g. non-dialysis stage 1–5 adults with CKD anaemia had ∼double the risk of developing end-stage CKD (hazard ratio [95% confidence interval] CI) = 2.08 [1.50–2.89]). Median time to dialysis initiation was significantly lower in adult NDD stage 1–5 patients with anaemia of CKD vs those without anaemia (45.5 vs 68.3 months p <0.01). A higher proportion of stage 3 adult NDD patients with anaemia of CKD progressed to stage 4 or 5 over follow-up periods of 1, 2 and 3 years vs those without anaemia (40% vs 20%; 60% vs 25%; 75% vs 30%, respectively). Available data from the 43 studies reporting humanistic burden suggested significantly worse HRQoL in patients with vs without CKD anaemia; e.g. non-dialysis adults with CKD anaemia had worse 36-item kidney disease and QoL scores for symptoms/problems, effect- and burden-of CKD. Comparative caregiver burden data in patients with/without CKD anaemia were limited. Limited available evidence from an economic perspective suggested higher HRU in patients with anaemia of CKD vs those without. Patients with anaemia of CKD has ∼2 times greater risk of hospitalisation due to heart failure vs those without (crude incidence rate ratio [95% CI] = 1.9 [1.6–2.1]). Similarly, patients with anaemia of CKD has significantly higher risk of hospitalisations (adjusted relative risk [ARR] [95% CI] = 1.33 [1.31–1.34]) and emergency department visits (ARR [95% CI] = 1.14 [1.12–1.15]) in a multivariate logistic regressions model. No data were available on change in economic parameters over time or on inter-relationships between humanistic/economic burden parameters. There were no published disease models in CKD anaemia; Figure 2 illustrates identified relationships between clinical, humanistic and economic burden parameters.

Table 1: Baseline characteristics and outcomes at 5 years for Cohort 1 and 2 CKD patients and respective sub-cohorts.

<table>
<thead>
<tr>
<th>Cohort 1 (Diagnosed)</th>
<th>No. Of Patients</th>
<th>Male (%)</th>
<th>White (%)</th>
<th>African American (%)</th>
<th>CV history (%)</th>
<th>Regression (%)</th>
<th>Progression (%)</th>
<th>ESKD (%)</th>
<th>Death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>38,472</td>
<td>67 (21)</td>
<td>48</td>
<td>70</td>
<td>18</td>
<td>43</td>
<td>NA</td>
<td>61.6</td>
<td>20.1</td>
</tr>
<tr>
<td>Stage 2</td>
<td>153,784</td>
<td>70 (19)</td>
<td>52</td>
<td>73</td>
<td>18</td>
<td>48</td>
<td>3.5</td>
<td>59.5</td>
<td>18.2</td>
</tr>
<tr>
<td>Stage 3</td>
<td>589,060</td>
<td>74 (16)</td>
<td>48</td>
<td>76</td>
<td>14</td>
<td>51</td>
<td>14.5</td>
<td>25.5</td>
<td>23.3</td>
</tr>
<tr>
<td>Stage 4</td>
<td>163,671</td>
<td>75 (17)</td>
<td>48</td>
<td>71</td>
<td>18</td>
<td>62</td>
<td>64.5</td>
<td>33.0</td>
<td>60.7</td>
</tr>
<tr>
<td>Stage 5*</td>
<td>96,713</td>
<td>66 (20)</td>
<td>53</td>
<td>57</td>
<td>30</td>
<td>61</td>
<td>55.1</td>
<td>NA</td>
<td>91.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cohort 2 (KDIGO Criteria)</th>
<th>No. Of Patients</th>
<th>Male (%)</th>
<th>White (%)</th>
<th>African American (%)</th>
<th>CV history (%)</th>
<th>Regression (%)</th>
<th>Progression (%)</th>
<th>ESKD (%)</th>
<th>Death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>12,298</td>
<td>58 (17)</td>
<td>57</td>
<td>65</td>
<td>26</td>
<td>23</td>
<td>20</td>
<td>8.5</td>
<td>3.1</td>
</tr>
<tr>
<td>Stage 2</td>
<td>25,810</td>
<td>68 (15)</td>
<td>58</td>
<td>72</td>
<td>16</td>
<td>40</td>
<td>7.1</td>
<td>3.4</td>
<td>25.0</td>
</tr>
<tr>
<td>Stage 3</td>
<td>850,824</td>
<td>73 (16)</td>
<td>39</td>
<td>84</td>
<td>10</td>
<td>43</td>
<td>1.7</td>
<td>2.5</td>
<td>7.6</td>
</tr>
<tr>
<td>Stage 4</td>
<td>76,528</td>
<td>76 (15)</td>
<td>41</td>
<td>76</td>
<td>16</td>
<td>61</td>
<td>19.2</td>
<td>26.0</td>
<td>41.5</td>
</tr>
<tr>
<td>Stage 5*</td>
<td>43,908</td>
<td>64 (21)</td>
<td>52</td>
<td>51</td>
<td>36</td>
<td>63</td>
<td>13.8</td>
<td>NA</td>
<td>13.6</td>
</tr>
</tbody>
</table>

*excluding transplant and dialysis; **excluding ESKD.
As the same publication may provide data for different burden domains, the total of clinical, humanistic and economic publications exceeds the total of 115. HRQoL, health-related quality of life; HRU, healthcare resource utilisation; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

No inter-relationships exist for humanistic and economic burden parameters; caregiver burden was reported among all CKD patients regardless of Hb levels. Positive relationships, i.e. if one variable increases the other also increases: green (+); Negative relationships, i.e. if one variable increases the other decreases: red (-). CKD, chronic kidney disease; CV, cardiovascular; Hb, haemoglobin; HRQoL, health-related quality of life; HRU, healthcare resource utilisation.

Based on limited moderate-to-good quality data, we found that patients with CKD anaemia face greater clinical, humanistic and economic burdens than those without anaemia, with significantly worse HRQoL and greater HRU. CKD anaemia was also associated with a higher risk of CKD progression.

REFERENCES
FRAILTY ASSESSMENT TOOLS, SURVIVAL TIME AND TIME TO INITIATE DIALYSIS IN OLDER PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE

Hani Hussien, Mihai Onofriescu, Andra Nastasa, Cristina Popa, Iuliana Teodor, Irina Apascaritei, Andreea Covic, Silvia Corina Cusai and Adrian Covic

University of Medicine and Pharmacy “Grigore T. Popa, Renal medicine, Iași, Romania

Background and Aims: Chronic Kidney Disease (CKD) patients with frailty have been shown to have a shorter survival time compared to non-frail individuals. Additionally, frailty has been linked to earlier initiation of dialysis among CKD patients. Despite the availability of over 50 frailty assessment tools in the literature, few have been applied in studies of older adults with CKD. There is a need for a comprehensive analysis of different frailty tools to identify the most accurate tools that could predict survival time and time to start dialysis in older adults with CKD. The present study compares four commonly used assessment tools of frailty from different categories (self-reporting tools, clinical judgment tools and complex instruments) regarding their association with survival time and time to start dialysis.

Method: Two hundred forty patients with biochemical evidence of CKD Stages 4–5 were included in this prospective cohort study. The inclusion criteria included patients 65 years old or more with two consecutive measurements of estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² separated by more than three months, while exclusion criteria included dialysis dependence, history of kidney transplantation, recent acute kidney injury, initial visit with the provider, amputation, or cerebrovascular accident. The four frailty assessment tools used in the study were Prisma-7 and FRAIL Scale, Clinical Frailty Scale (CFS), and Frailty Phenotype (FP). Patients were followed-up for 36 months for death events or dialysis initiation.

Results: The study population (240 patients) comprised 46% male patients with a mean age of 73.8 ± 6.6 years. Approximately 25% of patients were considered frail using the FRAIL scale, 69% using Prisma-7, and almost 40% using CFS and FP. Except for Prisma-7, “frail” patients, as determined by the FRAIL, CFS, and FP scores (Fig. 1), had significantly shorter survival times, with a mean survival of 24.9 months (Log-rank p < 0.001), 27.3 months (Log-rank p = 0.041), and 26.6 months (Log-rank p = 0.004) respectively. No significant differences were observed in time to dialysis initiation when comparing frail and non-frail patients using any of the frailty assessment tools (Table 1).

Conclusion: The findings suggest that the frailty scores derived from the FRAIL, CFS, and FP tools are better predictors of survival time in frail elderly patients with CKD, while further research is required to determine the most appropriate frailty tool to predict the time to start dialysis in this population.

Table 1: Percentage of frail patients according to different scores and mean survival/ time to dialysis (log-rank p where significantly different); NS - non-significant.

<table>
<thead>
<tr>
<th>“Frail” according to:</th>
<th>Total (N = 240)</th>
<th>Dead (N = 90)</th>
<th>Mean survival (months)(Log-rank p)</th>
<th>Dialysis (N = 60)</th>
<th>Time to dialysis (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRAIL Scale</td>
<td>22.9% (55)</td>
<td>33.3% (30)</td>
<td>24.9 (p&lt;0.001)</td>
<td>28.3% (17)</td>
<td>28.1 (NS)</td>
</tr>
<tr>
<td>Clinical Frailty Scale</td>
<td>43.3% (104)</td>
<td>51.1% (46)</td>
<td>27.3 (p = 0.041)</td>
<td>46.7% (28)</td>
<td>30 (NS)</td>
</tr>
<tr>
<td>PRISMA-7 Score</td>
<td>68.7% (165)</td>
<td>68.9% (62)</td>
<td>28.9 (NS)</td>
<td>80% (48)</td>
<td>30,3 (NS)</td>
</tr>
<tr>
<td>Frailty Phenotype</td>
<td>40.4% (97)</td>
<td>52.2% (47)</td>
<td>26.6 (p = 0.004)</td>
<td>50% (30)</td>
<td>29.1 (NS)</td>
</tr>
</tbody>
</table>
PERFORMANCES OF THE 5-YEAR KIDNEY FAILURE RISK EQUATION IN A TERTIARY SINGLE CENTER CHRONIC KIDNEY DISEASE COHORT (CKD CAREMEAU)

Julien Prouvot1,2, Marion Gerbal1, Pedram AhmadiPoor1, Florian Garo1, Sylvain Cariou1, Sophie Renaud1, Emilie Pambrun1, Pascal Reboul1 and Olivier Moranne1,2

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Background and Aims: Chronic kidney disease (CKD) is a common disease with a heterogeneous course. The Kidney Failure Risk Equation (KFRE) is designed to predict 5-year End stage renal disease (ESRD). This score has shown poor performance in predicting 5-years ESRD in elderly patients, probably because of a competitive risk with death. Indeed, patients with type 2 diabetes are numerous and older than non-diabetic patients, with higher risks of death, and thus a higher competitive risk. In this context, we aimed to evaluate the performance of the KFRE score at 5 years, in a cohort from a tertiary center, according to diabetic status.

Method: The CKD Caremeau (CKDC) cohort is a single-center tertiary cohort of adults seen by a nephrologist for CKD. We studied CKDC patients included between January 2008 and December 2017 and followed them. We excluded patients younger than 45 years. KFRE score covariates were collected at the first visit, and Renal replacement therapy (RRT) (dialysis or kidney transplantation) and death before ESRD were collected during follow-up through December 2022. Multiple imputation (Monte Carlo) was used for missing albuminuria. Score performance was calculated with discrimination (area under curve (AUC)) and calibration (observed versus predicted risks), according to diabetic status, at 5 years.

Results: Of the 3046 patients included, 1288 (42%) had diabetes. 558 (18%) albuminuria were missing and imputed. For diabetic patients, median follow-up time was 5.3 [3.0–7.6] years, median age was 73 [66–80] years, 843 (65%) patients were males, median eGFR was 38 [27–50], median albuminuria was 204 [57–671] mg/g, 177 (14%) developed ESRD, and 398 (30%) died, with a median 5-years KFRE score of 4 [0.65–17.6] %. For non-diabetic patients, median time of follow-up was 5.5 [3.3–8.2] years, median age was 72 [63–81] years old, 1027 (58%) were males, median eGFR was 40 [27–53], median albuminuria was 113 [38–399] mg/g, 205 (12%) experimented ESRD, and 501 (29%) died, with a median 5-year KFRE score of 2 [0.18–14] %. Discrimination was not modified by diabetic status at 5 years (p = 0.67). Calibration was also unaffected by diabetic status, with an overall overestimation at 5 years.

Conclusion: The performance of the KFRE score was not modified by diabetic status, meaning that age is probably more important than diabetic status for the competitive risk of death in CKD patients.
PROPOSING A NEW RENAL OUTCOME WHEN REACHING ESTIMATED GFR OF 30—SIMULATION STUDY USING REAL-WORLD STRATIFIED DATA

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Background and Aims: Patients with renal diseases often have progressive decline in eGFR, with many clinical researches having outcomes of reaching renal death/renal replacement therapy. In the real life, however, patients with eGFR under 15 mL/min/1.73m² (the same unit hereafter) lose their lives more often by cardiovascular diseases before reaching endstage renal disease. Moreover, patients with eGFR below 30 are known to have miscellaneous metabolic derangements including phosphate retention, parathyroid hormone excess, metabolic acidosis, hyperkalaemia and renal anaemia. It appears to be extremely important to recognize that, in order to avoid enfacing plethora of metabolic alterations and cardiovascular disorders that progress after renal function falls below 30, we physicians need to take a step to find ways how to keep patients’ eGFR above 30 for as long time as possible. At the same time, renal clinics are fully booked already; we need to prioritize the patients who have the highest risks in reaching eGFR below 30. This simulation study was performed to draw a trajectory to clarify who are the most eligible patients for nephrologists to intervene.

Method: Before performing the simulations using an inverse transform sampling, a priori statistical distributions were retrieved from the real-world data, i.e., a whole-hospital-wide survey over 4 years; (a) distribution of eGFR: obtained from patients with at least 3 measurements of eGFR over 366 days or more, where a median of eGFR values was used to represent the patient’s renal function, (b) distribution of eGFR slopes: similarly retrieved, which were then stratified in 6 strata with each eGFR range of [30,35)/[35,40)/[40,45)/[45,50)/[50,55)/[55,60). The simulation was performed in 4 steps. In the first step (“random number generating step”), 65,000 pairs of random numbers U1, U2 were generated using a continuous uniform distribution, U[0,1]. In the second step (“eGFR generating step”), eGFR was generated using the clinically-retrieved distribution (a, above) from a random number U1. In the third step (“slope generating step”), a slope in eGFR decline was generated using the a priori stratified distribution (b, above) from a random number U2. In the final step (“estimation step”), renal prognosis, especially an eGFR value 10 years later, was estimated in each of the “65,000 simulated patients”, with or without an effect of nephrology consults. The primary outcome was defined as reaching the eGFR below 30 within 10 years. If this occurred, time until the eGFR 30 was also calculated.

Results: In the strata of simulated patients with eGFR’s [50,55) and [55,60), 35.3% and 34.9% reached their eGFR below 30, over the periods of 4.78 and 4.95 years in average. In these strata, there were marked differences in renal prognosis based on the eGFR slope, where all the patients with the fastest quartile (annual rate of decline faster than 3.09) reached the outcome, while only 4–11% of the patients with slower decline (the remaining 3/4) reached eGFR <30. The number of patients was the largest in the stratum of [55, 60). In the stratum of eGFR [45,50), 45.3% patients, including 100% of faster quartile and 24.5% of slower 3 quartiles, reached eGFR of <30. Assuming the effect of nephrology consultation as attenuating the slope by 1/3, nephrologist intervention most prominently influenced the prognosis of the patients in strata [40,45) and [45,50) in terms of proportion of patients reaching outcomes (decreases by 10.5% and 12.5%).

Conclusion: 1) Reaching an eGFR of <30 mL/min/1.73m² is a newly proposed outcome in clinical research with substantial significance such as avoiding cardiovascular events and metabolic derangements that occur frequently at eGFR below 30. 2) Patients in the fastest quartile in eGFR slope, even those whose baseline eGFR 50–60, are the candidates who merit nephrology consultation.

HEART FAILURE AND DIABETES IN CHRONIC KIDNEY DISEASE

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#2569

Abstracts
Background and Aims: Few studies have investigated the prognosis in chronic kidney disease (CKD) patients with heart failure (HF) and diabetes (DM). In the clinical setting, treating a combination of these conditions is challenging but novel treatments such as SGLT2-inhibitors are now emerging. The aim of this study is to investigate the prevalence and outcomes of survival and major cardiovascular events (MACE) in CKD patients with HF and/or DM before these new treatments were commonly used.

Method: In this retrospective observational study, we extracted data from 26,647 nephrology-referred patients ≥18 years old with eGFR 60 ≤ ml/min/1.73 m² from the Swedish Renal Registry – Chronic Kidney Disease (SRR-CKD) and health registers at the National Board of Health and Welfare in Sweden during an observational period of January 2005 – June 2017. HF and DM was categorized based on International Classification of Disease 10 (ICD-10) diagnostic codes prior to inclusion in the SRR-CKD. Outcomes were death by any cause and MACE, defined as a composite of hospitalization for nonfatal myocardial infarction, coronary heart disease, congestive heart failure, nonfatal stroke or cardiovascular death. Secondary outcome was start of kidney replacement therapy (KRT) defined as start of dialysis or kidney transplantation.

Results: There were 12,910 (47.7%) patients with CKD, 3,458 (12.5%) with CKD + HF, 7,595 (27.3%) with CKD+DM and 3,684 (13.3%) with CKD + HF + DM. Median age was higher in the cohorts with heart failure (CKD + HF and CKD + HF + DM), 77 and 74 years vs 67 and 69 years (CKD and CKD + DM). Most patients were men in all four groups (62-66%). The use of evidence based therapies such as ACE-inhibitors/ARBs, varied across the groups between 62.9, 66.6, 78.5 and 73.7% (CKD, CKD + HF, CKD + DM, CKD + HF + DM). Statins were used in 42.0, 50.7, 71.1 and 73.7% and beta blockers in 53.9, 83.7, 65.9, and 86.1%. Survival data is presented in a Kaplan-Meier curve (Figure 1). Adjusted hazard ratio (HR) for all cause-death was highest in the cohorts with heart failure CKD + HF (2.54 [95% CI 2.40–2.68]) and CKD + DM + HF (3.22 [3.05–3.39]) followed by CKD + DM (HR 1.53 [1.45–1.60]) compared to patients with only CKD. The cumulative incidence of MACE is illustrated below (Figure 2). Adjusted HR for MACE was substantially higher in patients with heart failure, 3.82 (3.62–4.03) and 4.82 (4.59–5.08) for CKD + HF and CKD + HF + DM respectively while it was 1.63 (1.56–1.72) for CKD + DM. The risk of initiation of KRT was similar in all four groups, but risk of death before start of KRT was higher in patients with HF.

Conclusion: In CKD-patients, a heart failure diagnosis comprises approximately three to four times greater risk of death and MACE compared to patients with only CKD. The combination of CKD + HF + DM is the most severe. In all patient groups the use of evidence-based therapies was surprisingly low. This may reflect both deviation from guidelines for CKD-patients and the clinical challenge in treating comorbidities in CKD-patients. The results underlie the importance of identifying CKD-patients with HF and DM early to optimize treatment.

Figure 1: Kaplan-Meier survival curves of survival data. The figure shows the probability of survival in all four groups during the analysis time 10 years. CKD = Chronic kidney disease, HF = Heart failure, DM = Diabetes Mellitus.

Figure 2: Cumulative incidence curve. The figure is showing the cumulative incidence of major cardiovascular events in the four groups. CKD = Chronic kidney disease, HF = Heart failure, DM = Diabetes Mellitus.
**Background and Aims:** The presence of chronic kidney disease (CKD) in patients with type 2 diabetes mellitus (T2DM) leads to elevated medical and economic burden, and with CKD progression, the medical expenditure increases substantially. Information about healthcare utilization and medical expenditures of this patient population is limited in China. This study aims to describe the medical cost and healthcare utilization of patients with CKD and T2DM in a regional database in China.

**Method:** A retrospective, regional EHR-based serial cross-sectional study was conducted in Yinzhou Regional Healthcare Database (YRHCD), Ningbo, China. All adult patients (age \( \geq 18 \) years) with CKD and T2DM were collected between 1st Jan 2017 and 31st Dec 2020, patients were excluded if they did not have serum creatinine (SCr) values or initiated renal replacement therapy. Eligible patients were identified at each calendar year and categorized by CKD stages (G1-G5). Data on demographics, comorbidities and drug prescription were presented for all included patients at baseline and from 2017 to 2020. Annual medical costs and healthcare utilization were described among different CKD stages. Two-part models were built to estimate the medical costs and healthcare utilization in each CKD stage.

**Results:** A total of 16,521 patients with CKD and T2DM were included with a substantial increase between 2017 and 2020. Among all patients, the majority of them were classified in CKD stage 1 and 2. Over 70% of patients aged 65 years or older and approximately 55% were female. >90% of patients had hypertension, followed by peripheral vascular diseases, which increased from 69.2% in 2017 to 82.2% in 2020. Renin–angiotensin system inhibitors (RASI) were the most prescribed medication and metformin ranked the second. In general, the age, proportion of having comorbidities and proportion of drug prescription presented an increasing trend from 2017 to 2020. The proportion of eGFR value \( > 25 \) and \( \leq 75 \text{ mL/min/1.73m}^2 \) in G1 to G4 was 64.4% for baseline and decreased from 58.2% in 2017 to 48.7% in 2020. The general trend of medical costs in all CKD stages increased from 2017 to 2020; for healthcare utilization, the average number of outpatient visits per person per year was over 10.0 times per each CKD stage. The medical cost and healthcare utilization increased substantially in patients with more advanced CKD stages. Mean annual medical costs per patients were 6,084, 8,675, 14,291, and 24,571 CNY (908, 1,294, 2,132, and 3,726 USD) and the mean length of stay were 2.2, 3.3, 6.2, 12.6 and 16.1 days for G1-5 patients respectively in 2020. Patients in G1 and G2 had more outpatient visits compared with hospitalization, the cost of hospitalization raised dramatically in patients with G4-G5 and became a main contributor of total medical cost.

**Conclusion:** Our contemporary study revealed the medical cost and use of healthcare resources increased moderately over time in earlier CKD stages but grew remarkably from G4 stage onwards. The estimates suggested significant correlation between CKD stages and medical costs and healthcare utilization. Our findings further suggest earlier CKD identification and timely treatment may reduce the overall medical and economic burden in this population.

**Table 1: Summary statistics of patients by CKD stages.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>7699</td>
<td>10589</td>
<td>11802</td>
<td>11918</td>
</tr>
<tr>
<td>Age ( \geq 65 )</td>
<td>5510 (71.6%)</td>
<td>7335 (69.3%)</td>
<td>8164 (73.7%)</td>
<td>9032 (75.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>4449 (57.8%)</td>
<td>5967 (56.4%)</td>
<td>6106 (55.1%)</td>
<td>6457 (54.2%)</td>
</tr>
<tr>
<td>CKD stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>1723 (22.4%)</td>
<td>2652 (25.0%)</td>
<td>3011 (27.1%)</td>
<td>3139 (26.3%)</td>
</tr>
<tr>
<td>G2</td>
<td>2407 (26.6%)</td>
<td>3783 (35.7%)</td>
<td>4255 (38.4%)</td>
<td>4645 (39.0%)</td>
</tr>
<tr>
<td>G3</td>
<td>3125 (40.6%)</td>
<td>3537 (33.4%)</td>
<td>3292 (29.7%)</td>
<td>3436 (28.8%)</td>
</tr>
<tr>
<td>G4</td>
<td>256 (3.3%)</td>
<td>412 (3.9%)</td>
<td>376 (3.4%)</td>
<td>471 (4.0%)</td>
</tr>
<tr>
<td>G5</td>
<td>188 (2.4%)</td>
<td>205 (1.9%)</td>
<td>148 (1.3%)</td>
<td>227 (1.9%)</td>
</tr>
<tr>
<td>eGFR ( &gt; 25 ) and ( \leq 75 )/G1-G4</td>
<td>58.2%</td>
<td>52.1%</td>
<td>48.5%</td>
<td>48.7%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7105 (92.3%)</td>
<td>10352 (93.4%)</td>
<td>10352 (93.4%)</td>
<td>11223 (94.2%)</td>
</tr>
<tr>
<td>PVD</td>
<td>5325 (69.2%)</td>
<td>8750 (79.0%)</td>
<td>8750 (79.0%)</td>
<td>9801 (82.2%)</td>
</tr>
<tr>
<td>RASI</td>
<td>5848 (76.0%)</td>
<td>8461 (79.9%)</td>
<td>8461 (71.7%)</td>
<td>9218 (77.3%)</td>
</tr>
<tr>
<td>Metformin</td>
<td>3103 (40.3%)</td>
<td>4718 (42.6%)</td>
<td>4718 (42.6%)</td>
<td>5356 (44.9%)</td>
</tr>
</tbody>
</table>

**Figure 1:** Mean medical cost and length of stay by CKD stages from 2017 to 2020.
RISK FACTORS FOR INPATIENT MORTALITY IN PATIENTS WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE ADMITTED FOR COVID-19 USING A US NATIONAL SAMPLE

Sae Morita¹, Akshay Agrawal², Nehemias Guevara², Arias Carlos¹ and Bessy Flores²

¹SBH Health System, New York, United States of America and ²SBH Health System, United States of America

Background and Aims: Several studies reported that the COVID-19 pandemic has disproportionately affected socioeconomically vulnerable populations. No study evaluated risk factors for inpatient mortality in patients with non-dialysis chronic kidney disease (CKD) admitted with the diagnosis of Covid-19, using a US nationwide sample. This study aimed to elucidate risk factors for mortality in patients with CKD during Covid-19 admissions.

Method: We extracted data from the National Inpatient Sample year 2020, the largest nationally representative inpatient-care database in the US. We created a cohort of all adults with CKD hospitalized for Covid-19 by ICD-10 codes. The outcome was inpatient mortality. We excluded patients with end stage kidney disease on maintenance dialysis and transplant patients. We compared baseline characteristics and used multiple logistic regression to determine risk factors for inpatient mortality in this cohort.

Results: Total of 201,460 admissions with a diagnosis of Covid-19 were detected in patients with non-dialysis CKD. Table 1 showed the baseline characteristics. The mean age was 72.8±0.2 years and females accounted for 43.6%. Of all, White accounted for 52.3%, followed by Black (26.1%) and Hispanic (14.6%). Inpatient mortality was 20.9%. Table 2 showed the results of the multivariable logistic model. Older patients, Males, higher Charlson Comorbidity Index scores were associated with a higher risk of inpatient mortality. White patients had a higher risk compared to Black patients and Native Americans had the highest risk, followed by other ethnic minorities, Hispanic, and Asians. Those from the lowest income households had the highest risk. Admission to a rural, publicly owned hospital and those located in the West and Northeast had higher odds of inpatient mortality.

Conclusion: Our study showed males, race, commercial payment type, lower income, and hospital settings such as regions and location were risk factors for inpatient mortality in patients with non-dialysis CKD. Further studies are needed to evaluate whether differences in clinical practice underly some of these risks.

Table 1: Baseline characteristics in patients with ESRD on HD admitted with diagnosis of COVID-19 by races.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total population (n = 201,460)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>72.8± −0.2</td>
</tr>
<tr>
<td>18–65 years</td>
<td>52.1%</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>48.1%</td>
</tr>
<tr>
<td>Female sex, number (%)</td>
<td>43.6%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>52.3%</td>
</tr>
<tr>
<td>Black</td>
<td>26.1%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14.6%</td>
</tr>
<tr>
<td>Asian</td>
<td>3.0%</td>
</tr>
<tr>
<td>Native Alaskan/Indians</td>
<td>4.2%</td>
</tr>
<tr>
<td>Others</td>
<td>0.3%</td>
</tr>
<tr>
<td>Median household income according to patient’s zip code</td>
<td></td>
</tr>
<tr>
<td>$1–$49,999</td>
<td>35.6%</td>
</tr>
<tr>
<td>$50,000–$65,000</td>
<td>26.4%</td>
</tr>
<tr>
<td>$65,000–$85,000</td>
<td>21.6%</td>
</tr>
<tr>
<td>$85,000-</td>
<td>16.4%</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1–4</td>
<td>51.1%</td>
</tr>
<tr>
<td>&gt; = 5</td>
<td>48.8%</td>
</tr>
<tr>
<td>Hospital ownership</td>
<td></td>
</tr>
<tr>
<td>Government, non-federal</td>
<td>10.5%</td>
</tr>
<tr>
<td>Private, non-profit</td>
<td>74.7%</td>
</tr>
<tr>
<td>Private, investor-owned</td>
<td>14.7%</td>
</tr>
<tr>
<td>Primary payer type</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>73.5%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>8.1%</td>
</tr>
<tr>
<td>Commercial</td>
<td>13.8%</td>
</tr>
<tr>
<td>Self-pay</td>
<td>1.6%</td>
</tr>
<tr>
<td>No pay</td>
<td>0.2%</td>
</tr>
<tr>
<td>Others</td>
<td>0.28%</td>
</tr>
<tr>
<td>Region</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>19.3%</td>
</tr>
<tr>
<td>Midwest</td>
<td>23.4%</td>
</tr>
<tr>
<td>South</td>
<td>41.5%</td>
</tr>
<tr>
<td>West</td>
<td>15.7%</td>
</tr>
<tr>
<td>Location/teaching</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>8.9%</td>
</tr>
<tr>
<td>Urban, non-teaching</td>
<td>18.1%</td>
</tr>
<tr>
<td>Teaching</td>
<td>73.1%</td>
</tr>
<tr>
<td>Bedsize</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>23.8%</td>
</tr>
<tr>
<td>Medium</td>
<td>29.7%</td>
</tr>
<tr>
<td>Large</td>
<td>46.5%</td>
</tr>
</tbody>
</table>

Table 2: Multivariate logistic regression analyses in patients with non-dialysis CKD admitted with the diagnosis of Covid-19 (N = 42,099).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>18 -65</td>
<td>0.44 (0.40–0.47)</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>Ref</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Ref</td>
</tr>
<tr>
<td>Female</td>
<td>0.86 (0.82–0.91)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Ref</td>
</tr>
<tr>
<td>Black</td>
<td>0.88 (0.82–0.95)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.24 (1.14–1.35)</td>
</tr>
<tr>
<td>Asian</td>
<td>1.19 (1.03–1.39)</td>
</tr>
<tr>
<td>Native Americans</td>
<td>1.48 (1.09–2.00)</td>
</tr>
<tr>
<td>Others</td>
<td>1.24 (1.07–1.43)</td>
</tr>
<tr>
<td>Household income</td>
<td></td>
</tr>
<tr>
<td>$1–$49,999</td>
<td>Ref</td>
</tr>
<tr>
<td>$50,000–$65,000</td>
<td>0.86 (0.80–0.92)</td>
</tr>
<tr>
<td>$65,000–$85,000</td>
<td>0.82 (0.75–0.88)</td>
</tr>
<tr>
<td>$85,000-</td>
<td>0.84 (0.77–0.93)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>1–4</td>
<td>0.78 (0.74–0.82)</td>
</tr>
<tr>
<td>&gt; = 5</td>
<td>Ref</td>
</tr>
<tr>
<td>Hospital Owner</td>
<td></td>
</tr>
<tr>
<td>Government, non-federal</td>
<td>1.13 (1.02–1.26)</td>
</tr>
<tr>
<td>Private, non-profit</td>
<td>Ref</td>
</tr>
<tr>
<td>Private, investor-owned</td>
<td>1.02 (0.93–1.12)</td>
</tr>
<tr>
<td>Primary payment type</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>Ref</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1.02 (0.90–1.15)</td>
</tr>
<tr>
<td>Commercial</td>
<td>0.97 (0.89–1.07)</td>
</tr>
<tr>
<td>Self-pay</td>
<td>1.12 (0.88–1.42)</td>
</tr>
<tr>
<td>No pay</td>
<td>0.78 (0.55–1.74)</td>
</tr>
<tr>
<td>Others</td>
<td>1.28 (1.09–1.51)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>1.54 (1.40–1.69)</td>
</tr>
<tr>
<td>Midwest</td>
<td>0.97 (0.89–1.06)</td>
</tr>
<tr>
<td>South</td>
<td>Ref</td>
</tr>
<tr>
<td>West</td>
<td>1.22 (1.11–1.34)</td>
</tr>
<tr>
<td>Teaching status</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>0.77 (0.69–0.87)</td>
</tr>
<tr>
<td>Urban, non-teaching</td>
<td>0.93 (0.86–1.01)</td>
</tr>
<tr>
<td>Teaching</td>
<td>Ref</td>
</tr>
<tr>
<td>Hospital Bedsize</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>0.95 (0.88–1.03)</td>
</tr>
<tr>
<td>Medium</td>
<td>1.07 (0.99–1.15)</td>
</tr>
<tr>
<td>Large</td>
<td>Ref</td>
</tr>
</tbody>
</table>

Abstracts
Background and Aims: Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide, with an estimated annual incidence of 25 cases per million people. Hematuria (tea coloured urine) and proteinuria (foamy urine) are among the most common clinical manifestations of IgAN, however the burden of such symptoms on diagnosis and disease severity is not fully understood. The aim of this analysis was to better understand patient reported symptoms prior to the first nephrologist consultation and diagnosis of patients with IgAN, in the United States, Europe, Japan, and China.

Method: Data were drawn from the Adelphi IgAN Disease Specific Programme (DSP), a point-in-time survey of IgAN-treating nephrologists and their consulting patients, conducted in the United States (US), Europe (EU5: France, Germany, Italy, Spain, United Kingdom [UK]), Japan, and China, between June and October 2021. Nephrologists completed structured online patient report forms for successive patients presenting with IgAN. Patients voluntarily completed questionnaires that corresponded with the nephrologist records, with questions about their IgAN on that day regarding demographics, clinical data, and signs and symptoms.

Results: A total of 991 patients with a nephrologist confirmed IgAN diagnosis completed a self-reported questionnaire. Mean (standard deviation [SD]) patient age was 42.1 (13.8) years, and 57% were male. Patients first noticed their IgAN symptoms at a mean (SD) age of 37.1 (13.1) years. Proteinuria (58%), hematuria (56%), and fatigue (36%) were the top patient-reported symptoms that prompted patients to see a doctor (n = 979). In the EU5, 64% of patients, and in the US 55% of patients, also reported high blood pressure as a sign that prompted them to see a doctor. Patients reported a median (interquartile range [IQR]) time of 12.9 (4.3-25.7) weeks from first experiencing IgAN symptoms to consulting with a doctor, ranging from 8.6 (4.3-25.7) weeks in Europe to 21.4 (4.3-52.1) weeks in Japan. Of those patients who reported a delay between experiencing symptoms and when they visited a doctor, 52% said that they were waiting to see if their symptoms would go away on their own (US: 64%, EU5: 68%, Japan: 34%, China: 49%) and 35% assumed they were just feeling tired or run down (US: 36%, EU5: 22%, Japan: 39%, China: 39%). Most patients reported first visiting either a family doctor/GP (49%) or a nephrologist (34%) for their IgAN symptoms. In China, 20% of patients reported seeing a urologist for their IgAN symptoms (US 0%, EU5 1%, Japan 6%). Median (IQR) patient-reported time from first doctor visit to IgAN diagnosis was 8.0 (4.0-16.0) weeks. This finding was consistent across geographical regions except in Japan, where median (IQR) duration was 12.0 (4.0-24.0) weeks. Waiting for test results (US: 31%, EU5: 35%, Japan: 34%, China: 68%), waiting to be tested (US: 52%, EU5: 59%, Japan: 37%, China: 54%), and waiting for a referral (US: 48%, EU5: 32%, Japan: 48%, China: 32%) were the top patient-reported reasons for a delay in the patient’s IgAN diagnosis. At time of diagnosis, 47% of patients reported ‘mild’, 43% ‘moderate’, and 10% described ‘severe’ IgAN severity (n = 983). 23% of patients in the US reported severe IgAN severity at diagnosis (EU5 14%, Japan 11%, China 7%).

Conclusion: Despite experiencing symptoms, patients with IgAN waited several weeks before consulting a physician. Of those with a delayed diagnosis, over half described their IgAN as moderate or severe. Greater awareness of symptoms of kidney disease may lead to patients seeking help for their symptoms and getting a confirmed diagnosis more quickly. Improvement of the IgAN patient journey pathway in a health care system is important to expedite timely diagnosis of IgAN and subsequent management of the disease.

Abstracts
Table 1: Sociodemographic characteristics, prevalence, and incidence estimates of CKD based on claims data (n = 62,200 per year) from 2012–2018. For each year, samples were drawn equally distributed among five age strata and sex.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of subjects, n</th>
<th>Age (years), mean (SD)</th>
<th>Female, n (%)</th>
<th>Prevalence</th>
<th>Incidence</th>
<th>Person at risk, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>62,200</td>
<td>81.0 (7.4)</td>
<td>31,100 (50.0)</td>
<td>0.18</td>
<td>0.06</td>
<td>50,040 (80.5)</td>
</tr>
<tr>
<td>2014</td>
<td>62,200</td>
<td>81.1 (7.3)</td>
<td>31,100 (50.0)</td>
<td>0.21</td>
<td>0.07</td>
<td>48,382 (77.8)</td>
</tr>
<tr>
<td>2016</td>
<td>62,200</td>
<td>81.1 (7.3)</td>
<td>31,100 (50.0)</td>
<td>0.24</td>
<td>0.08</td>
<td>46,735 (75.1)</td>
</tr>
<tr>
<td>2018</td>
<td>62,200</td>
<td>81.1 (7.4)</td>
<td>31,100 (50.0)</td>
<td>0.26</td>
<td>0.08</td>
<td>44,911 (72.2)</td>
</tr>
</tbody>
</table>

*Estimates were standardized by age and sex based on nationwide demographic distributions (Destatis).
Obesity was defined as body mass index < 25 kg/m² and metabolic syndrome (age-dependent PedsQL for parents as proxies and EQ-5D for adults). PREM questionnaires consisted of 12 questions with 5-point Likert scale answers, encompassing experiences throughout all patient journey (including primary, secondary and tertiary care, and social/rehabilitation services). Higher scores in PREM questionnaire and in EQ-5D indicated worse experiences or worse PROMs evaluation (except for overall health), while higher score in PedsQL indicated better PROMs assessment. Surveys were generated and sent using REDCap system with the entire process integrated into hospital’s electronic medical record system.

Results: 48 (52%) parents and 60 (45%) adult patients completed both questionnaires. In adult patients, median completion times of PREM and PROM surveys were 5.0 and 2.2 minutes, respectively. Among parents, median PREM survey filling time was 1.7 minutes and PBM surveys filling time ranged between 2.7 and 3.8 minutes. Adult patients, who evaluated their mobility worse, reported experiencing more problems throughout diagnosis establishment process ($r = 0.3$, $p = 0.049$) and better experiences in rehabilitation ($r = 0.57$, $p = 0.015$). Worse self-care evaluation and reporting more pain/anxiety correlated with better experiences in psychological support ($r = -0.3$, $p = 0.049$ and $r = -0.34$, $p = 0.026$). Worse overall health self-evaluation associated with worse experiences in diagnosis establishment process ($r = -0.37$, $p = 0.035$). Parents evaluating their children’s physical health as worse reported more negative experiences in diagnosis establishment process ($r = -0.31$, $p = 0.028$), more technical difficulties in the healthcare process ($r = -0.47$, $p = 0.001$) and worse information provision ($r = -0.31$, $p = 0.031$). Similar associations with PREMs were observed with social and global PROMs domains (all $p < 0.05$).

Conclusion: Electronic integrated collection of PREMs and PROMs in patients with chronic kidney disorders is feasible but attempts to promote higher patient engagement are needed. Observed associations between PROMs and PREMs point towards potential benefits of long-term integrated patient feedback collection for targeted healthcare services quality improvement.

OBESITY, METABOLIC SYNDROME AND THE RISK OF ADVERSE CLINICAL OUTCOMES IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Shinyeong Kang, Hyeon Seok Hwang, Jin Sug Kim and Kyungwhan Jeong
Kyuong Hee University Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of South Korea

Background and Aims: Obesity and metabolic syndrome are prevalent disorder in patients with chronic kidney disease (CKD). However, it is unclear whether obesity without metabolic syndrome is associated with higher risk of adverse clinical outcomes in patients with CKD.

Method: We reviewed the National Health Insurance Service database of Korea for people who received ≥2 national health screenings between 2009 and 2011. A total of 68,464 chronic kidney disease patients were identified with consecutive estimated glomerular filtration rate <60 mL/min per 1.73 m². Obesity was defined as body mass index ≥25 kg/m² and metabolic syndrome status was considered as the presence of three or more of the following metabolic factors; waist circumference, blood pressure, fasting blood sugar, triglyceride level, high-density lipoprotein cholesterol level. The primary outcomes were cardiovascular events, end-stage renal disease progression (ESRD) and all-cause mortality.

Results: Compared to non-obese patients without metabolic syndrome, obesity without metabolic syndrome did not increase the risk of cardiovascular event (HR 1.02, 95% CI 0.95–1.11) and progression to ESRD (HR 0.86, 95% CI 0.73–1.02). Risk of all-cause mortality was significantly decreased in these patients (HR 0.88, 95% CI 0.81–0.96). These findings were consistently observed in overweight, obese, morbid obese patients without metabolic syndrome. In addition, while linear increase of HRs for each additional metabolic abnormality was observed, HRs increase for cardiovascular event was significantly slower in obese patients than in non-obese (P for interaction = 0.035).

Conclusion: Obesity without metabolic syndrome did not confer excess risk for cardiovascular complication or ESRD progression and decreased the risk of all-cause mortality. Healthy effect of obesity against mortality risk and metabolic hazard on cardiovascular event is better to be considered in CKD patients.

CHARACTERISTICS OF MEDICATION-INITIATOR COHORTS OF PATIENTS WITH CHRONIC KIDNEY DISEASE AND TYPE 2 DIABETES IN JAPAN: A REPORT FROM FOUNTAIN PLATFORM

Yuichiro Yano1, Hiroshi Kanegasu2, Suguru Okami3, Nikolaus Obergriesser4, Manel Pladevall-Vila5, Alain Gay6, Satoshi Yamashita7, Catherine Johannes8, Natalie Ebert9, Csaba Kovessy9, David Vizzaya10 and Naoki Kashiha11

1Shiga University of Medical Science, Department of Advanced Epidemiology, Otsu, Japan, 2Genki Plaza Medical Center for Health Care, Tokyo, Japan, 3Bayer Yakuhin, Ltd., Medical Affairs & Pharmacovigilance, Osaka, Japan, 4Bayer AG, Integrated Evidence Generation & Business Innovation, Oslo, Norway, 5RTI Health Solutions, Barcelona, Spain, 6Bayer AG, Medical Affairs & Pharmacovigilance, Berlin, Germany, 7RTI Health Solutions, Waltham, MA, United States of America
8Charité-Universitätsmedizin, Institute for Public Health, Berlin, Germany, 9University of Tennessee Health Science Center, Department of Medicine, MEMPHIS, United States of America, 10Bayer AG, Integrated Evidence Generation & Business Innovation, Sant Joan Despi, Spain and 11Kawasaki Medical School, Department of Nephrology and Hypertension, Kureashiki, Japan

Background and Aims: The clinical landscape for the treatment of patients with chronic kidney disease (CKD) and type 2 diabetes (T2D) is rapidly evolving with the introduction of new treatments such as sodium-glucose cotransporter-2 inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonist (GLP-1 RA), and non-steroidal mineralocorticoid receptor antagonists (nsMRA). However, limited information is available regarding the utilization patterns of these new therapies in worldwide clinical practice. The FINEGUST study (EUPAS84188, NCT05526157) is a multinational observational cohort study and part of the FOUNTAIN multi-database research platform. It aims to describe drug utilization and temporal changes of different treatments in adults with CKD and T2D in two time periods (before and after finerenone approval) using secondary data from population-based data sources in Europe, Japan, China, the United Kingdom, and the United States.

Method: In this country-specific analysis, four separate medication-specific cohorts of adults with CKD and T2D, including new users of SGLT2i, GLP-1 RA, steroidal MRA (sMRA), or esaxerenone as a nsMRA available in the study period, were retrospectively identified from the Japan Chronic Kidney Disease Database Extension (J-CKD-DB-Ex) between January 1st 2014 and June 30th 2021 (pre-finerenone period). The presence of T2D and CKD was assessed based on ICD-10 diagnostic codes, and lab measurement values, i.e., serum creatinine to calculate estimated glomerular filtration rate (CKD-EPI) or urine albumin-creatinine ratio (UACR). The CKD stage was categorized based on the KDIGO definition. Patients with type 1 diabetes, kidney cancer or kidney failure at baseline were excluded. The index date was the date of initial prescription of each drug class. Patient characteristics and baseline medication patterns were summarized overall and by presence or absence of UACR results in the previous year.

Results: Of 251,659 patients recorded in J-CKD-DB-Ex in the study period, we identified 6,934, 2,991, 18,974, and 301 patients with recorded use of SGLT2i, GLP-1 RA, sMRA, and nsMRA, respectively. After applying inclusion and exclusion criteria, 1,157 SGLT2-1 (16.7%), 329 GLP-1 RA (11.0%), 1,769 sMRA (9.3%), and 63 nsMRA (20.9%) new users were included in the analysis. The mean age ranged from 66 years in the GLP-1 RA cohort to 74 years in the sMRA cohort (Table 1). All medication classes were most prescribed in patients with CKD stage 3 followed by patients with CKD stage 2. Insulin was most frequently prescribed in the GLP-1 RA cohort (65.3%). Patients in the sMRA cohort were most comorbid based on the prevalence of congestive heart failure (40.2%), coronary heart disease (26.9%), and cerebrovascular disease (16.1%). Compared to patients without UACR measurements, those with a UACR measurement in year prior to the index date were more likely to receive other treatments of interest in combination during the 90 days prior to index (Figure 1). Among the drug classes summarized, angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers were the most prescribed drug class in all cohorts (43.0% in SGLT2i cohort, 28.9% in GLP-1 RA cohort, 30.6% in sMRA cohort, and 50.8% in nsMRA cohort, respectively).

Conclusion: Treatment initiation with either SGLT2i, GLP-1RA, sMRA or nsMRA occurred most frequently in patients with CKD stage 2–3 with variations in characteristics for each medication class, including the patterns of anti-hyperglycemic therapies and cardiovascular complications. Differences by UACR test result availability 1-year prior to index may indicate a possible association between treatment choice and the availability of UACR test results. Subsequent analyses from the FOUNTAIN program, including longitudinal drug utilization patterns and geographic variations across regions, will provide
Table 1: Patient characteristics of each medication-initiator cohort.

<table>
<thead>
<tr>
<th>Table 1: Patient characteristics of each medication-initiator cohort.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SGLT2i</strong></td>
</tr>
<tr>
<td>(N = 1,157)</td>
</tr>
<tr>
<td><strong>Age at index date (years)</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
</tr>
<tr>
<td><strong>CKD stage</strong>, n (%)</td>
</tr>
<tr>
<td>Stage 1</td>
</tr>
<tr>
<td>Stage 2</td>
</tr>
<tr>
<td>Stage 3</td>
</tr>
<tr>
<td>Stage 4</td>
</tr>
<tr>
<td>Stage 5</td>
</tr>
<tr>
<td><strong>Not assessed in the previous year</strong></td>
</tr>
<tr>
<td><strong>UACR results available in the previous year</strong></td>
</tr>
<tr>
<td><strong>ACEi or ARB use, n (%)</strong></td>
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<tr>
<td><strong>Insulin use, n (%)</strong></td>
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<tr>
<td><strong>Hyperkalemia, n (%)</strong></td>
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**Comorbidities**
- Coronary heart disease, n (%) | 171 (14.8) | 50 (15.2) | 475 (26.9) | 11 (17.5) |
- Cerebrovascular disease, n (%) | 79 (6.8) | 25 (7.6) | 264 (16.1) | 7 (11.1) |
- Peripheral vascular disease, n (%) | 47 (4.1) | 15 (4.6) | 78 (4.4) | 1 (1.6) |
- Congestive heart failure, n (%) | 199 (17.2) | 46 (14.0) | 712 (40.2) | 10 (15.9) |

**ARB:** angiotensin receptor blocker; **ACEi:** angiotensin-converting-enzyme inhibitors; **CKD:** chronic kidney disease; **SD:** standard deviation; **UACR:** urine albumin-creatinine ratio. *Based on the International Classification of Disease 10th revision codes and estimated glomerular filtration rate in accordance with KDIGO definition.

Figure 1: Number of additional drug classes* used 90 days prior to index in patients with or without UACR results in year prior to index.

Further insights about the clinical use of different treatment options for patients with CKD and T2D.

**Background and Aims:** Individuals receiving kidney replacement therapy (KRT) are at higher risk of cardiac arrest than the general population. The aim of this systematic review was to evaluate survival outcomes in individuals on different forms of KRT (haemodialysis, peritoneal dialysis or kidney transplantation) following cardiopulmonary resuscitation (CPR) within healthcare settings (hospital or outpatient clinics).

**Method:** A comprehensive literature search of EMBASE, MEDLINE, CINAHL, Web of Science and Central was carried using a pre-defined search strategy with no date or language restrictions. Retrospective and prospective observational studies reporting outcomes following CPR in adults on kidney replacement therapy were included. The study protocol was prospectively registered on PROSPERO: CRD42022336363.

**Results:** Thirteen eligible studies were identified. Due to the heterogeneity of study populations, lack of a standardised outcome set and inconsistent use of control groups, a narrative review was conducted, and a meta-analysis was

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#3538

SURVIVAL OUTCOMES FOLLOWING CARDIOPULMONARY RESUSCITATION IN ADULTS RECEIVING KIDNEY REPLACEMENT THERAPY: A SYSTEMATIC REVIEW AND NARRATIVE SYNTHESIS

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¹North Bristol NHS Trust, Renal Unit, Bristol, United Kingdom,
²Gloucestershire Hospitals Foundation Trust, Renal Unit, United Kingdom and ³University of Bristol Medical School, Department of Population Health Sciences, Bristol, United Kingdom
Figure 1: Bar chart of % Survival following CPR in healthcare setting. Y axis denotes first author, year of publication and number of study participants in corresponding group. Where a control group was used, p-value was taken from publication. Saeed et al (2015) did not report a p-value for unadjusted univariate analysis. Yanget al reported unadjusted annual survival between 2004–2012—the value presented represents the mean of the annual % survival to discharge. Studies by Lafrance et al, Davis et al and Pun et al refer to CPR outcomes in outpatient dialysis clinic settings, the remainder of the presented studies evaluated outcomes following in-hospital CPR. Median % survival was calculated at 22%.

not performed. Crude unadjusted survival rate to discharge from hospital was reported in 11 studies and ranged from 0%—75%. Only two studies reported neurological outcome at discharge, with rates of a favourable cerebral performance category score (CPC 1 or 2) on discharge between 17–20%.

Conclusion: The current evidence is insufficient to guide clinical decision-making regarding resuscitation due to a lack of up-to-date data, uncertainty about outcomes and inconsistent reporting of neurological status after CPR. Additionally, there is a lack of data comparing survival outcomes for people on different types of KRT. There remain unanswered questions regarding the likelihood of favourable outcomes for the KRT population and whether these can be accurately predicted using clinical and demographic features.

#3990

PACE-Ckd: Health-Related Quality of Life of Patients with CKD and Caregivers: Results from a Us Survey

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Background and Aims: The substantial mortality and morbidity burden of chronic kidney disease (CKD) is well described, with the highest burden associated with progression to end-stage kidney disease (ESKD), where kidney replacement therapy (dialysis or kidney transplantation) is indicated. CKD is known to have a detrimental effect on patient health-related quality of life (HRQoL). However, there is a lack of data comparing the impact of CKD on patient and caregiver HRQoL versus the general population. This study aimed to administer validated HRQoL instruments using a quantitative online survey to estimate the HRQoL of patients with CKD and their caregivers compared to the general population.

Method: A non-interventional survey enrolled adult patients with CKD and caregivers. Patients with a diagnosis of CKD for at least 3 months were included. ESKD was defined as patients with CKD stage 5 or receiving dialysis or a kidney transplant. Caregivers were required not to receive formal payment and must have cared for a CKD patient for a minimum of 1 hour a week in the previous 4 weeks. A general population cohort was also enrolled, matching key patient and caregiver demographic characteristics (e.g. age, sex, and area of residence). Patient and caregiver HRQoL were assessed using the EQ-5D-5L instrument. Caregiver HRQoL was also measured by the CarerQoL-7D carer-specific instrument.

Results: This analysis is based on 199 patients with CKD and 113 caregivers in the United States who were enrolled between June and July 2022. Patient and caregiver median age was 58 years and 38 years, respectively. There were 32.2% patients who were on dialysis, while 81.4% caregivers were caring for a patient on dialysis. Most dialysis patients (79.7%) were receiving treatment in a clinic or hospital, with 20.4% of patients receiving it at home. Caregivers typically cared for their parent (45.1%) or partner (25.7%) and their duties would most commonly include driving to/from medical appointments (89.4%). When comparing mean [SD] EQ-5D-5L index scores for patients with CKD with the general population, patients had 33.7% lower utility (0.63 [0.27] vs 0.95 [0.08]) and caregivers had 13.8% lower utility (0.81 [0.22]) vs 0.94 [0.11]) versus the general population. EQ-5D-5L index scores were lower in dialysis-dependent patients (0.59 [0.27]) versus non dialysis-dependent patients (0.65 [0.27]). Patients and caregivers reported problems across all EQ-5D domains (anxiety and depression, mobility, pain/discomfort, selfcare and usual activities) when compared to the general population, with anxiety and depression domains scoring highest. According to the CarerQoL-7D index, caregivers for patients with CKD had worse HRQoL than caregivers for other major illnesses, including hip fractures, breast cancer and dementia, according to published

In total, 3,738 patients were enrolled for analysis from 5,299 patients and fulfilled the inclusion criteria among 12,742 patients who underwent coronary angiography.

Method: C-reactive protein (hs-CRP) levels. As well as potential mediators, including serum albumin and high-sensitivity C-reactive protein (hs-CRP) levels.

Background and Aims: Decreased kidney function is a risk factor for the development of contrast-associated acute kidney injury (CA-AKI) in chronic kidney disease (CKD). Although the relationship between CKD and CA-AKI is well established, the mechanistic link between the two, particularly the extent to which this interaction is mediated by inflammation, remains poorly understood. We examined the association between CKD and CA-AKI, as well as potential mediators, including serum albumin and high-sensitivity C-reactive protein (hs-CRP) levels.

Method: A total of 3,738 patients were enrolled for analysis from 5,299 patients and fulfilled the inclusion criteria among 12,742 patients who underwent coronary angiography (CAG) between 1 January 2007, and 31 December 2016. Multivariable logistic regression and mediation analyses were performed. In addition to the effect as risk factors, direct and indirect effects were also estimated.

Results: Among 3,738 subjects, 414 developed AKI (11.1%). Pre-procedural albumin and Lnhs-CRP (log-transformed) were independently associated with CA-AKI (odds ratio [OR], 95% confidence interval [CI]): 0.320 (0.272–0.378), P < 0.001 and 1.211 (1.132–1.296), P < 0.001, respectively. Direct, and indirect effects were also estimated. Patients with CKD were found to be more likely to exhibit lower serum albumin and higher serum hs-CRP levels. Simple mediation analyses showed that 38.8% and 52.3% of the relationship between CKD and CA-AKI was mediated by the serum albumin and hs-CRP levels, respectively with co-mediation being 13.9%.

Conclusion: These results represent that, in addition to reduced kidney function, inflammatory parameters are also risk factors and mediators of CA-AKI in patients with CKD.

REFERENCES

#4322 MEDIATION ANALYSIS OF THE RELATIONSHIP BETWEEN INFLAMMATION AND CONTRAST INDUCED ACUTE KIDNEY INJURY IN PATIENTS WITH CHRONIC KIDNEY DISEASE
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Background and Aims: Decreased kidney function is a risk factor for the development of contrast-associated acute kidney injury (CA-AKI) in chronic kidney disease (CKD). Although the relationship between CKD and CA-AKI is well established, the mechanistic link between the two, particularly the extent to which this interaction is mediated by inflammation, remains poorly understood. We examined the association between CKD and CA-AKI, as well as potential mediators, including serum albumin and high-sensitivity C-reactive protein (hs-CRP) levels.

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Conclusion: These results represent that, in addition to reduced kidney function, inflammatory parameters are also risk factors and mediators of CA-AKI in patients with CKD.

#4866 PREVALENCE AND SEVERITY OF CHRONIC KIDNEY DISEASE ASSOCIATED PRURITUS IN A DIALYSIS NETWORK IN WEST GERMANY
Thilo Krüger1 and Bastian Schunk2
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Background and Aims: Chronic kidney disease-associated pruritus (CKD-aP) is a troubling and in some cases debilitating problem for patients with CKD and end-stage renal disease with potential impact on patients’ quality of life (QoL). Frequency of CKD-aP with at least a medium intensity has been reported to be present in approximately 40% of dialysis dependent patients in European countries and 26% in Germany. This work intended to update prevalence and disease severity in a large dialysis network in West Germany.

Method: We performed a cross-sectional study addressing maintenance dialysis patients (both hemodialysis and peritoneal dialysis) in 23 dialysis facilities in West Germany with a total of approximately 1,500 dialysis patients. After ethical approval, a questionnaire was distributed to all dialysis patients asking for presence of pruritus and if present about itch duration, dialysis vintage, pruritus severity, communication patterns, therapeutic attempts and impact on quality of life (QoL). Pruritus intensity was assessed using the worst itch numeral rating scale (WI-NRS).

Results: From May to July 2022, 919 patients completed and returned the questionnaire. 31.9% were female, 55.4% male and 12.7% did not disclose their gender. Overall, 223 (23.7%) reported presence of pruritus of any severity with 90.1% having pruritus for at least 6 weeks duration. 159 (17.4%) of all patients reported at least moderate itch intensity (WI-NRS ≥ 4) and 70 (7.7%) a severe itch intensity (WI-NRS ≥ 7). Dialysis vintages of <1 year, 1–2 years, 2–4 years and >4 years were reported by 15.8%, 16.2%, 25.7% and 36.9% of patients with pruritus, respectively. Approx. 71% of all patients with any intensity of pruritus reported to be unaware of origin of pruritus, the remainder gave various reasons with a majority mentioning CKD or dialysis associated reasons. 62 of the 223 with pruritus (27.4%) reported having received treatments of which 14 (22.6%) stated no, 27 (43.5%) partial and 17 (27.4%) good response. Most frequent therapy category mentioned was emollients (14) with a mixed effect; 4 reported no effect, 6 some and 2 a good effect. Of those having received antihistamines, all reported good response (4), 132 (59.2%) of patients with pruritus communicated the presence with someone, 89 of those (67.4%) with their nephrologist. Of the 223 patients with pruritus 214 (96.0%) reported any stage of impact on their QoL in at least one of the categories sleep, social life, household, or work. Highest frequency given was in social life (180/223) and lowest frequency in sleep disturbances (74/223).

Conclusion: Prevalence of CKD-aP of at least medium intensity was lower than previously reported for Germany, continuing the previous trend seen in DOPPS for decreasing prevalences. The patient awareness of association of pruritus to CKD is still low. A positive correlation of itch prevalence in CKD may exist to dialysis vintage. Compared to DOPPS data from 2015, fewer patients communicated itch at all but in case the nephrologist was most frequently addressed. Treatment attempts seem to be still rare and were conducted only in a minority of patients with CKD-aP. Impact of CKD-aP on QoL was usually present.

#5293 THE IMPACT OF SEVERE DEPRESSION ON THE SURVIVAL OF OLDER PATIENTS WITH END-STAGE KIDNEY DISEASE
Background and Aims: Incidence of depression increases in patients with end-stage kidney disease (ESKD). We evaluated the association between depression and mortality among older patients with ESKD, which has not been studied previously.

Method: This nationwide prospective cohort study included 487 patients with ESKD aged > 65 years, who were categorized into minimal, mild-to-moderate, and severe depression groups based on their Beck Depression Inventory-II (BDI-II) scores. BDI-II scores were separated into three symptom domains: affective, cognitive, and somatic depressive symptoms. The association between the depression groups and survival were analyzed using multivariate Cox proportional hazard regression models. Predisposing factors for high BDI-II scores were evaluated using logistic regression analysis. The associations among the three depressive-symptom domains and survival were also analyzed.

Results: The severe depression group showed a higher modified Charlson comorbidity index value and lower serum albumin, phosphate, and uric acid levels than the other depression groups. The Kaplan-Meier curve revealed a significantly lower survival in the severe depression group than in the minimal and mild-to-moderate depression groups (P = 0.011). Multivariate Cox regression analysis confirmed that severe depression was an independent risk factor for mortality in the study cohort (hazard ratio (HR), 1.39; 95% confidence interval (CI), 1.01–1.91; P = 0.041). BDI-II scores were associated with modified Charlson comorbidity index (P = 0.009) and serum albumin level (P = 0.004) in multivariate linear regression. Among the three depressive symptoms, higher somatic symptom scores were associated with increased mortality (HR, 2.45; 95% CI, 1.25–4.79; P = 0.009).

Figure 1: Kaplan-Meier curve for mortality in depression groups.

Table 1: Associations of depression and mortality in Cox proportional hazard regression model.

<table>
<thead>
<tr>
<th>Depression group</th>
<th>Model 1</th>
<th></th>
<th>Model 2</th>
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<th>Model 3</th>
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<th>Model 4</th>
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<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
<td>HR (95% CI)</td>
<td>P value</td>
<td>HR (95% CI)</td>
<td>P value</td>
<td>HR (95% CI)</td>
<td>P value</td>
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<tr>
<td>Minimal</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
<td>Reference</td>
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<td>Reference</td>
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<tr>
<td>Mild-to-moderate</td>
<td>1.07 (0.78–1.48)</td>
<td>0.667</td>
<td>1.12 (0.81–1.55)</td>
<td>0.503</td>
<td>0.98 (0.71–1.37)</td>
<td>0.922</td>
<td>0.98 (0.70–1.38)</td>
<td>0.918</td>
</tr>
<tr>
<td>Severe</td>
<td>1.53 (1.13–2.09)</td>
<td>0.007</td>
<td>1.49 (1.09–2.03)</td>
<td>0.012</td>
<td>1.39 (1.02–1.90)</td>
<td>0.038</td>
<td>1.39 (1.01–1.91)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Model 1: unadjusted.
Model 2: adjusted for age and sex.
Model 3: adjusted for age, sex, and mCCI.
Model 4: adjusted for age, sex, mCCI, albumin, phosphate, and uric acid.
Abbreviations: BDI-II, Beck Depression Inventory-II; HR, hazard ratio; CI, confidence interval; mCCI, modified Charlson comorbidity index.
Conclusion: Among older patients with ESKD, severe depression increases mortality compared with minimal or mild-to-moderate depression. And patients with concomitant somatic symptoms require careful management of their comorbidities and nutritional status.

#5392
THE DIAGNOSTIC JOURNEY OF PATIENTS WITH IMMUNOGLOBULIN A NEPHROPATHY: DATA ANALYSIS OF A REAL-WORLD SURVEY
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Background and Aims: Although rare (estimated global annual incidence of 25 cases per million people), immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis. IgAN is associated with a poor prognosis, with 30% or more of patients with >1g/day of proteinuria progressing to kidney failure within 10 years. As poor prognosis is partly due to delayed diagnosis, this analysis aims to describe aspects of the diagnostic pathway for patients with IgAN.

Method: Data were drawn from the Adelphi IgAN Disease Specific Programme (DSP)1,2, a point-in-time survey of IgAN-treating nephrologists and their consulting patients, conducted in the United States (US), Europe (EU5: France, Germany, Italy, Spain, United Kingdom [UK]), Japan, and China, between June and October 2021. Nephrologists completed structured online patient record forms for successive patients presenting with IgAN, including demographics, clinical data, time to diagnosis, reasons for delayed diagnosis, and treatment history. A duration of greater than four weeks between first consultation with a physician and diagnosis was considered a delayed diagnosis.

Results: A total of 295 nephrologists completed records for 1537 patients which had data characterizing the time from first consultation and diagnosis. Mean (standard deviation (SD)) patient age was 43.0 (15.0) years, and 59% were male. At diagnosis, mean (SD) proteinuria (n = 1254) was 2.3 (2.4). Median time from first physician consultation to confirmed IgAN diagnosis varied by physician speciality. When patients initially consulted a nephrologist regarding their IgAN symptoms, median (interquartile range) duration from first consultation to diagnosis was 2.4 (0.7-5.6) weeks (n = 582). For family doctors/ General Practitioners (GPs)/ Primary Care Physicians (PCPs) (n = 656), this was 6.6 (3.0-13.8) weeks, for internal medicine/ internists (n = 120) and urologists (n = 113) the duration was 4.4 (1.3-9.4) and 1.5-12.5) weeks. Most patients were diagnosed by a nephrologist (US 95%, n = 263; EU5 96%, n = 491; Japan 99%, n = 236; China 85%, n = 547) and these were typically performed by a nephrologist in most countries (US 99%, n = 233; EU5 81%, n = 397; Japan 95%, n = 231; China 97%, n = 464) except in the US, where 40% of cases were done by a radiologist. However, some patients were unable to undergo a biopsy (6%, n = 1531) and in some cases the physician chose to diagnose the patient using non-invasive methods (8%, n = 1531).

Conclusion: Most of the patients with IgAN in this survey were diagnosed by a nephrologist using a kidney biopsy. These data suggest that initially consulting a family doctor/ GP/ PCP led to a delayed diagnosis for patients. This may be due to the time taken for onward referral to a nephrologist. China had the highest proportion of patients diagnosed within 4 weeks from the first consultation (57%) and the highest proportion of patients who first visited a nephrologist regarding their symptoms. The results from this study suggest that speeding up referral from PCPs to nephrologists may reduce the amount of time taken to confirm IgAN diagnosis.

#5807
FACTORS ASSOCIATED WITH KALEMIA IN RENAL DISEASE
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Background and Aims: International recommendations promote a strict potassium diet in order to avoid hyperkalemia in chronic kidney disease patients. However, efficiency of such a dietary counseling has never been demonstrated. The objectives of this study were to define the relationship between kalemia, dietary potassium intake estimated by kaliuresis and renal function and to define the factors associated with kalemia in patients using artificial intelligence.

Method: To this extent, data from patients followed in a nephrology unit, included in the UniverSel study and whose kalemia (measured on the day of urine collection; n = 367) were analyzed. The association between kalemia and thirty-four variables concerning the patients’ characteristics, their biological work-up, their medications and their answers to the UniverSel dietary self-questionnaire on kalemia were assessed using a Bayesian network.

Results: The patients included had a wide range of estimated glomerular filtration rate, but few had stage 5 chronic kidney disease (CKD). Kalemia was negatively and linearly correlated to estimated glomerular filtration rate (p<0.001) but was not correlated to kaliuresis (p = 0.55). Kaliuresis was not correlated to estimated glomerular filtration rate (p = 0.08). Factors associated with kalemia were analyzed using a Bayesian network. The 5 variables most associated with kalemia were, in descending order, estimated glomerular filtration rate, original nephropathy, age, diabetes, and plasma bicarbonate level. RAS-blockers prescription was also associated to kalemia. Consumption of potassium rich food were poorly associated to kalemia.

Conclusion: Our results do not support a strict control of potassium intake in stage 1 to 4 CKD patients. Our results reinforce the interest of a multidimensional management including personalized therapy and strict correction of metabolic acidosis. Lightning dietary restrictions in potassium would improve the quality of life of patients with CKD who are often multi-pathological and already subject to multiple dietary constraints.
#6758
THE CASUAL ASSOCIATION OF ALCOHOL CONSUMPTION AND CHRONIC KIDNEY DISEASE: A MENDELIAN RANDOMIZATION STUDY
Liu Dekai, Lei Tang, Xiaoxi Zeng and Ping Fu
West China Hospital, Sichuan University, Division of Nephrology, Kidney Research Institute, Chengdu, PR. China

Background and Aims: Many previous views believed that alcohol intake increases the risk of chronic kidney disease progression. Even in the previous KDIGO guidelines, alcohol restriction was included in the guidelines. However, in recent years, some research contradicted these views and removed alcohol restriction from the KDIGO guidelines. The causal relationship between alcohol intake and the risk of progression of chronic kidney disease was explored using the methods of Mendelian randomized studies.

Method: Using data from a large sample of genome-wide association studies, the Society for Genome-wide Association Analysis and Sequencing of alcohol and nicotine consumption or use (GSCAN) database (1.2 million individuals) was used to identify independent genetic loci strongly associated with alcohol consumption. Then select the corresponding genetic loci in the CKDGen consortium database (one million individuals) as instrumental variables. One is not to use "MR-PRESSO" package for analysis. Then, two sample Mendelian random methods, such as inverse variance weighting method, approximate maximum method, MR-Egger regression method, weighted median method and weighted model method, are adopted. The other one is to use "MR-PRESSO" bag to detect whether there are outlier points, remove them, and then use the inverse variance weighting method of quantity sample Mendelian random method. The causal relationship between alcohol intake and chronic kidney disease was reflected by the change in eGFR value with increased unit alcohol intake.

Results: A total of 44 single nucleotide polymorphisms (SNPs) were screened as instrumental variables. Without the use of "MR-PRESSO" package, the results obtained by using inverse variance weighting method, approximate maximum method and MR-Egger regression method were not statistically significant. The weighted median method showed that alcohol intake increased by one unit per week. The glomerular filtration rate (eGFR) was increased by 0.015 ml/min (95% CI 0.005-0.026, P = 0.004). Weighted model results showed that an increase of one unit per week in alcohol intake was associated with an increase of 0.017 ml/min in estimated glomerular filtration rate (eGFR) (95% CI 0.005-0.026, P = 0.002). The MR-Egger regression result showed that the genetic pleiotropy did not bias the result (intercept = 0.009, P = 0.507). However, with the removal of six outliers using MR-PRESSO, the inverse variance weighting method showed that an increase of one unit of alcohol intake per week increased the estimated glomerular filtration rate (eGFR) by 0.014 ml/min (95% CI 0.010-0.020, P = 0.004).

Conclusion: This study provides an association between alcohol intake and progression of chronic kidney disease. Overall, increased alcohol intake is protective against progression of chronic kidney disease. Clinically, alcohol intake is associated with many diseases. Although this study concluded that alcohol has a protective effect on the progression of chronic kidney disease, whether increasing alcohol intake can protect kidney function needs to be treated with caution. In addition, the long-term effects of alcohol intake on the progression of chronic kidney disease also need to be studied.

#6904
EVALUATION OF KIDNEY FUNCTION GRAPH SURVEILLANCE ACROSS SOUTH WALES, UK
Owain Brooks1, Aled Richards1, Robert Greening1, Chris Brown1, Lee White1, William Ford2, Juliette Moutel-Davesne2 and Julia Phillips2
1Swansea Bay University Health Board, Department of Nephrology, Morriston Hospital, Swansea, United Kingdom and 2Cardiff University, School of Pharmacy and Pharmaceutical Sciences, Cardiff, United Kingdom

Background and Aims: For people requiring Kidney Replacement Therapy (KRT) late presentation to a nephrologist (within 90 days of initiating KRT) is associated with adverse outcomes. The ASSIST-CKD kidney function graph surveillance (KFGS) quality improvement project was adopted by the Department of Nephrology in South West (SW) Wales, UK in November 2017. Between the end of 2017 and the end of 2020, late presentation rates reduced from 19.5% [1] to 13.5% [2] across the region, having reduced to 9.7% in 2019 [3]. During KFGS, graphs of eGFR over time are generated for patients ≤65 years with eGFR ≤60 ml/min/1.73 m² and ≥65 years with eGFR ≤40 ml/min/1.73 m² with significantly deteriorating kidney function. Alerts are sent to the GP for review and/or referral to nephrology. Over 100,000 graphs have been reviewed in SW Wales. We present demographic and initial outcome data for patients identified by KFGS.

Method: An observational retrospective cohort study analysed data of patients identified through KFGS in SW Wales between 1/11/17 and 1/10/21. Data were extracted from ASSIST-CKD and renal (Vital Data) databases using SQL coding.

Results: Data pertaining to 4811 patients are included for analysis. 44% of patients were male. At initial eGFR the mean age of patients ‘flagged’ was 73 years. The mean [range] initial eGFR was 32 ml/min/1.73 m² [2-50]. The median time [range] from initial eGFR to KFGS alert was 8 days [2-113]. For
those with results within 90 days of initial eGFR the mean initial haemoglobin (HB) was 118 g/l. The mean serum potassium was 4.7 mmol/L. Data for 1144 (24%) patients were included for outcome analysis, where a clear timeline from initial eGFR to KFGS alert, first registration with the nephrology service (registration), and outcome could be established. 3667 patients were excluded from outcome analysis because they were registered before KFGS or were not registered with nephrology, had died or moved out of area after KFGS alert. The median time [range] from alert to registration was 22 days [0-1636]. 20% of patients (n = 232) received CKD education from a specialist nurse. The median time [range] from registration to first contact from a CKD education nurse was 349 days [8-1419]. 34% of patients received IV iron and 31% received an erythropoiesis-stimulating agent (ESA) after alert. The median time [range] from registration to first IV iron and first ESA was 257 [5-1705] and 277 [3-1650] days respectively. 6% (n = 71) of patients required KRT. The late presentation rate was 22%, 21% of patients needing haemodialysis (HD) received their first treatment via an arteriovenous (AV) fistula, 1% via AV graft, 59% via non-tunneled line and 19% via tunnelled line. 44% (7/16) of patients presenting late died within 90 days of starting KRT. 33% (18/55) of patients died within 90 days of starting KRT if they presented to a nephrologist >90 days before starting KRT.

Conclusion: Late presentation rates have reduced in SW Wales since implementing KFGS. The relatively high late presentation rate and low rate of initial definitive access for HD in the present data requires further analysis. eGFR values that prompted alert may denote Acute Kidney Injury (AKI) as opposed to, or as well as CKD progression; increasing the urgency of referral to nephrology. eGFR values pre and post alert will be reviewed to elucidate this. Patients presenting late were more likely to die within 90 days of starting KRT than those presenting early, emphasising the importance of early identification of progressive kidney disease. We aim to compare present data with a cohort referred to nephrology independent of KFGS to inform renal centres of the benefits of KFGS beyond headline late presentation rates, including timely access to specialists. We will consider potentially unwelcome consequences of KFGS, such as inappropriate referral. We cannot draw conclusions of causality between KFGS and outcomes. The GP may not have seen the alert, and there are several reasons why a GP may decide not to refer to nephrology following a KFGS alert.

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#4167

THE HEALTH, SOCIOECONOMIC AND ENVIRONMENTAL IMPACT OF CKD IN THE UK: BUILDING A CONCEPTUAL FRAMEWORK

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Background and Aims: The past three decades have seen an increase in the prevalence and mortality rate of chronic kidney disease (CKD). It is estimated that between 1990 and 2017, the global all-age prevalence of CKD increased by 29.3%, whilst the mortality rate rose by 41.5%. Over this period, CKD became the 12th leading cause of death worldwide, with an estimated 1.2 million deaths attributed to the disease in 2017 [1]. With global prevalence currently estimated at 10% [2], CKD is a leading cause of disability, accounting for 35.8 million disability-adjusted life years (DALYs) in 2017 [3]. This growing burden of the disease calls for robust healthcare policy interventions to improve disparities in health, socioeconomic, and environmental outcomes. The aim of this research is to build a Healthcare Policy framework for CKD that will analyse the drivers and components of the burden of disease in terms of clinical, socioeconomic and environmental outcomes. It will also incorporate current knowledge of best practices and challenges in the organisation of healthcare services to mitigate these burdens. The framework will facilitate the analysis of the burden of disease attributable to CKD and be used to inform further research on areas in which policies could be implemented to optimise CKD prevention, early detection, and treatment at different stages of CKD and different levels of health systems. The framework presented here reflects the UK context but can be adapted for different country contexts.

Method: The framework development included two stages. First, a scoping review of the literature in this field was conducted. The literature review included peer-reviewed articles, grey literature, policy documents, academic reports and congress and conference reports. The second stage saw the validation of the framework by a multidisciplinary expert panel in the UK. This expert panel was composed of eight UK experts in the fields of nephrology, public health, primary care, organ donation and transplantation, and other disciplines.

Results: The framework outlines a holistic patient pathway from pre-CKD development to kidney failure along with the corresponding interdisciplinary level of care. The framework stresses the need to implement a population-wide approach focused on preventative care strategies, chiefly on the risk reduction of kidney failure. Underlying aetiologies and disparities in access to care were found to be inherently linked to disease progression and health outcomes. Data systems were identified as vital to ensuring continuity of care between primary and specialty care which in turn could lead to improved patient outcomes. The use of greener energies coupled with a reduction in the incidence of renal failure requiring dialysis could reduce substantially the environmental footprint of this disease. The burden of disease reflects the sum of the individual and system-level impact and outcomes of CKD which are labelled as economic, social, and environmental (Fig. 1).

Conclusion: The conceptual framework underscores how underlying aetiologies, socioeconomic factors, and fragmentation of care are reflected in disparities in healthcare access, particularly in marginalised and underserved populations. The environmental footprint of this disease could be reduced through optimal standard of care. The framework can inform future research to model the burden of CKD in terms of clinical, societal, economic, and environmental outcomes in the UK and the targeting of policy interventions to mitigate these burdens across different country contexts.

REFERENCES

USING THE KIDNEY FAILURE RISK EQUATION TO PREDICT END-STAGE KIDNEY DISEASE IN CKD PATIENTS OF SOUTH ASIAN ETHNICITY: AN EXTERNAL VALIDATION STUDY
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Background and Aims: The Kidney Failure Risk Equation (KFRE) predicts the 2- and 5-year risk of needing kidney replacement therapy (KRT) using four risk factors – age, sex, urine albumin-to-creatinine ratio (ACR), and creatinine-based estimated glomerular filtration rate (eGFR). Although the KFRE has been recalibrated in a UK cohort, this did not consider minority ethnic groups. Further validation of the KFRE in different ethnicities is a research priority. The KFRE also does not consider the competing risk of death, which may lead to overestimation of KRT risk. This study externally validates the KFRE for patients of South Asian ethnicity and compares methods for accounting for ethnicity and the competing event of death.

Method: Data were gathered from an established UK cohort containing 35,539 individuals diagnosed with chronic kidney disease. The KFRE was externally validated and updated in several ways taking into account ethnicity, using recognised methods for time-to-event data, including the competing risk of death. A clinical impact assessment compared the updated models through consideration of referrals made to secondary care.

Results: The external validation showed risk of KRT differed by ethnicity. Model validation performance improved when incorporating ethnicity and its interaction with ACR and eGFR as additional risk factors. Further, accounting for the competing risk of death improved prediction. Using a criteria of 5 year ≥5% predicted KRT risk, the competing risks model resulted in an extra 3 unnecessary referrals (0.59% increase) but identified an extra 1 KRT case (1.92% decrease) compared to the previous best model. A hybrid criteria of predicted risk using the competing risks model and the previous guidelines should be used in referrals to secondary care.

Conclusion: The accuracy of KFRE prediction improves when updated to consider South Asian ethnicity and to account for the competing risk of death. This may reduce referrals whilst identifying risks of KRT and could further individualise the KFRE and improve its clinical utility. Further research should consider other ethnicities.

THE CLINICAL AND ECONOMIC BURDEN OF CHRONIC KIDNEY DISEASE IN GREECE
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Background and Aims: Chronic Kidney Disease (CKD) is a progressive disorder with a substantial clinical and economic burden. This burden is expected to grow, mainly because of the ageing population, and the increasing incidence of diabetes mellitus and arterial hypertension. The objective of this study is to provide insights into the clinical and economic burden of CKD in Greece.

Method: A cost of illness (COI) study has been performed to approximate the burden of CKD in Greece from the perspective of EOPYY (National Organization for Health Care Services Provision), with reference year 2022. The COI model employs a prevalence-based approach using national and international sources and approximates the annual direct cost of CKD. The direct costs included in this analysis are categorized into primary care, medication, hospitalization and renal replacement therapy (RRT) costs.

Results: It has been estimated that there are about 1,115,991 patients with CKD (stages 1–5) in Greece, most of them in stage 3 (about 534,694), and about 15,337 receiving RRT or having received a kidney transplant. In 2032 this population is expected to increase to approximately 1,249,475 patients. The total annual direct cost of CKD was estimated at €845,936,094. The main cost driver was RRT, which accounted for roughly 49% (417 millions) of total cost of care, followed by hospitalizations 29% (246 millions) and medications 17% (143 millions). The progression of the disease is strongly correlated with an increase in the annual management cost. About 1.4% of the CKD population (RRT group) spent about half of the total CKD budget or more than 4% of the total public health expenditure, higher than other European countries.

Conclusion: CKD is creating a high and growing clinical and economic burden, largely driven by the RRT cost. There is an urgent need for public health strategies aiming at early detection and management of CKD.
RETROSPECTIVE SINGLE-CENTER EXPERIENCE
KIDNEY DISEASES IN PATIENTS WITH MALIGNANCY: A UTILITY OF KIDNEY BIOPSY AND SPECTRUM OF BIOPSY PROVEN

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Background and Aims: Kidney biopsy may improve diagnostic accuracy and aid in the management of cancer patients with kidney diseases. However, literature on the utility of kidney biopsy in cancer patients and survivors is lacking. We aimed to evaluate the clinical characteristics of cancer patients who underwent kidney biopsy, as well as the histological spectrum of biopsy proven kidney diseases in this cohort.

Method: This was a single-center retrospective study of all patients who had native kidney biopsies at the Singapore General Hospital between 1st October 2015 to 31st December 2022. Demographic, clinical, laboratory and histological data were retrieved from electronic medical records to identify patients with solid-organ or hematological malignancies who underwent kidney biopsy.

Results: Out of 1208 patients who underwent kidney biopsy between 1st October 2015 to 31st December 2022, 116 (9.6%) patients had diagnoses of solid-organ or hematological malignancies. Approximately two-thirds (79/116; 68.1%) had solid-organ malignancies, of which 21.5% had metastatic disease at time of biopsy. Approximately one-third (36/116; 31.0%) had hematological malignancies, of which 10 (8.6%) had a hematological stem-cell transplant (HSCT). One (0.9%) patient had both solid-organ and hematological malignancies. Sixty-eight (58.6%) patients were in remission at time of biopsy, comprising of 52 (44.8%) and 16 (13.8%) patients with solid-organ and hematological malignancies, respectively. Median age at biopsy was 65.7 years (IQR 56.5, 71.4) and majority was female (61/116; 52.6%). Comorbidities of hypertension, type 2 diabetes mellitus, autoimmunity, and liver transplant were found in 36.2% (42/116), 23.3% (27/116), 8.6% (10/116) and 1.7% (2/116) patients respectively. Median serum creatinine at time of biopsy was 152.0 μmol/L (IQR 101.8, 220.5). Micro-hematuria was present in approximately two-thirds (66.1%) of patients. Nephrotic range proteinuria and nephrotic syndrome were observed in one-quarter (25.9%) and one-third (31.0%) of the patients, respectively. Approximately half (49.1%) of the patients had acute kidney injury at time of biopsy, while one-fifth (19.8%) had progressive chronic kidney disease. A wide spectrum of histological diagnoses was observed. Glomerulonephritides, tubulointerstitial inflammation and/or glomerular endothelial injuries were diagnosed in 60.8% (79/120) of solid-organ and 80.6% (29/37) of hematological malignancies. Amongst patients with active solid-organ malignancies (n = 20), acute tubulointerstitial nephritis (ATIN) (5/20, 25.0%), IgA nephropathy (3/20; 15.0%) and lupus nephritis (3/20; 15.0%) were the most common primary diagnoses. Amongst patients with active hematological malignancies (n = 17), dysproteinemic kidney disease and/or leukemic infiltration was most frequently diagnosed (6/17; 35.3%). Compared to remission status, active malignancy was not associated with an increased likelihood of an overall diagnosis of glomerulonephritides, tubulointerstitial inflammation and/or glomerular endothelial injuries (p = 0.16). Specifically, the incidence of membranous nephropathy was similar in patients with active malignancy and those in remission (p = 0.42). Amongst patients with HSCT, thrombotic microangiopathy (40.0%) was observed most frequently. Overall, onco-therapeutics-related kidney injuries were present in 13 (11.2%) patients, of which ATIN (38.4%) was most commonly encountered, followed by glomerular endothelial injury (30.7%).

Conclusion: Kidney biopsy provides valuable diagnostic information amongst cancer patients. While a broad spectrum of histological diagnoses can be observed, glomerular diseases and onco-therapeutics-related kidney injuries remain the most common.

IMPACT OF THE COVID-19 PANDEMIC ON THE WELL-BEING OF PATIENTS WITH CHRONIC KIDNEY DISEASE
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Background and Aims: Coronavirus Disease 2019 (COVID-19) devastatingly impacted well-being, especially among the socioeconomically vulnerable population. The impacts of the pandemic on specific groups of age, sex, race, type of work, and income have been studied. However, the impacts COVID-19 pandemic on well-being of people with diseases have yet to be well evaluated. We conducted a longitudinal survey for outpatients who visited our Nephrology division and asked about their monthly well-being status for two years. Therefore, we aimed to elucidate the impacts of the pandemic especially on the well-being of patients with chronic kidney disease (CKD).

Method: We conducted a monthly survey for 358 outpatients who visited the Nephrology division of Okinawa Prefectural Nanbu Medical Center and Children’s Medical Center between February 1st, 2020, and December 31st, 2021. Out of these patients, 257 patients were included in this study. All participants were asked questions about their well-being status with a visual analog scale (0-10) regarding their health, socioeconomic satisfaction, human connections, general anxiety, and satisfaction in receiving treatment. We also collected information about their basal demographics, social situation (living with family, marriage, having children, or caregiving), educational status, income level, the activity of daily life, and active diseases. We used a mixed-effects regression model to assess the impacts of the pandemic on longitudinal changing of well-being scores especially among patients with CKD. We also described trajectories of well-being scores for CKD patients and non-CKD patients to visualize the difference in the impacts of the COVID-19 pandemic on them.

Results: Among the 257 analyzed patients, 43.9% were male, and the mean (± standard deviation) of their age was 58.9 (± 19.9). 25% were unmarried, and 59.5% had full-time job. 47.9% had G3b or higher stage CKD (eGFR < 45 ml/min/1.73 m²); 24.5% had diabetes; and 30.7% had collagenous disease. In total, 1,814 answer sheets were collected from the patients. Based on the mixed-effects regression model, especially among female patients with CKD, the pandemic has decreased the well-being regarding their human connections (Fig. 1). Contrarily, male patients with CKD showed an increase in well-being regarding human connections during the pandemic. In female patients with CKD, (1) younger, (2) married, (3) living with a family member, and (4) required caregiving status were associated with lower well-being status regarding human connections. Notably, male patients with CKD had higher well-being status regarding human connections and socioeconomic situation if married and living with family than male patients without CKD.

Conclusion: In patients with CKD, female Japanese patients showed lower well-being score regarding human connections than male patients during the early phase of pandemic. The support and caregiving among families influenced differently for male and female patients with CKD.
SAFETY OF NATIVE AND TRANSPLANT KIDNEY BIOPSY IN A NATIONAL COHORT

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Background and Aims: Safety of kidney biopsy is variably reported in different published series. Since 2014, all native kidney biopsies undertaken in the 9 adult renal units in Scotland have been recorded by the Scottish Renal Registry (SRR) and since 2015 all transplant kidney biopsies were included. In this complete national dataset, we report data on safety of kidney biopsy in a current real world setting.

Method: Major complications of kidney biopsy are recorded using pre-defined terms and include: arteriography and embolisation, arteriography no embolisation, clot retention, blood transfusion only, death within 28 days directly attributable to biopsy, nephrectomy and other. Biopsies are undertaken under ultrasound guidance using 16G or 18G spring loaded biopsy guns. All centres discontinue clopidogrel, DOACs and warfarin. Some centres continue

<table>
<thead>
<tr>
<th>Biopsy Type</th>
<th>Native</th>
<th>Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total biopsies (n)</td>
<td>5095</td>
<td>1884</td>
</tr>
<tr>
<td>% Male</td>
<td>54.7%</td>
<td>59.4%</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>57.2</td>
<td>48</td>
</tr>
<tr>
<td>% Adequate</td>
<td>98.2%</td>
<td>95.1%</td>
</tr>
<tr>
<td>Commonest Indication (% of biopsy type)</td>
<td>AKI query cause (30%)</td>
<td>AKI query cause (37.7%)</td>
</tr>
<tr>
<td></td>
<td>Chronically reduced eGFR (28.1%)</td>
<td>Chronically deteriorating transplant function (25.4%)</td>
</tr>
<tr>
<td></td>
<td>Nephrotic syndrome (19.7%)</td>
<td>Achieved transplant function lower than expected (9.1%)</td>
</tr>
<tr>
<td>Commonest Diagnosis (% of biopsy type)</td>
<td>1. IgA nephropathy (13.1%)</td>
<td>1. Acute Rejection (34.3%)</td>
</tr>
<tr>
<td></td>
<td>2. Tubulointerstitial nephritis (8.5%)</td>
<td>2. Other (23.9%)</td>
</tr>
<tr>
<td></td>
<td>3. Membranous nephropathy (7.2%)</td>
<td>3. Acute tubulodegenerative Change (15.8%)</td>
</tr>
<tr>
<td>Biopsies performed by radiology (%)</td>
<td>31.3%</td>
<td>38.3%</td>
</tr>
<tr>
<td>Biopsies performed by nephrology (%)</td>
<td>61.9%</td>
<td>57.6%</td>
</tr>
<tr>
<td>Median serum creatinine (mg/mmol)</td>
<td>163 (96-271)</td>
<td>212 (156-357)</td>
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<tr>
<td>Mean number of glomeruli</td>
<td>14.6</td>
<td>15.2</td>
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<tr>
<td>Total Complications (% of biopsy type)</td>
<td>121 (2.4%)</td>
<td>26 (1.4%)</td>
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<tr>
<td>Complication Breakdown:</td>
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</tr>
<tr>
<td></td>
<td>Arteriography and embolisation: 6.1/1000</td>
<td>Arteriography and embolisation: 1.6/1000</td>
</tr>
<tr>
<td></td>
<td>Arteriography no embolisation: 5.9/1000</td>
<td>Arteriography no embolisation: 2.7/1000</td>
</tr>
<tr>
<td></td>
<td>Blood transfusion only: 3.5/1000</td>
<td>Blood transfusion only: 3.7/1000</td>
</tr>
<tr>
<td></td>
<td>Clot obstruction: 2/1000</td>
<td>Clot obstruction: 2.7/1000</td>
</tr>
<tr>
<td></td>
<td>Nephrectomy: 0</td>
<td>Nephrectomy: 0.5/1000</td>
</tr>
<tr>
<td></td>
<td>Death: 1.6/1000</td>
<td>Death: 0</td>
</tr>
</tbody>
</table>
aspirin. In some centres biopsy is performed by nephrologists and in others by radiologists.

**Results:** In total, 6979 biopsies in 5755 patients were recorded between 2014 and 2021 (5095 native biopsies and 1884 transplant biopsies), with an adequacy for diagnosis of 98.1%. Table 1 describes the demographics, indications, operator and diagnoses made by biopsy type. Overall, in patients undergoing native kidney biopsy 2.4% suffered a major complication and 1.4% of patients undergoing transplant biopsy. The commonest complication was the requirement for arteriography, with or without embolisation. We included CT angiography in this group. There were 8 deaths within 28 days attributable to renal biopsy.

**Conclusion:** Kidney biopsy remains safe for the vast majority of patients and complications are less likely with transplant biopsy.

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**Abstracts**
Epidemiology Collaboration in 2021. We projected the changes of eGFR, CKD prevalence, and incidence of end stage renal disease (ESRD) and mortality in a large prospective cohort of adult Koreans who had voluntary health check-ups, using current (CKD-EPI 2009) and new equation (CKD-EPI 2021).

**Method:** We included 112,772 adult participants, aged 18 years or older, who had voluntary routine health check-ups including serum creatinine at three medical centers in Korea from 2003 to 2009. We compared the difference of eGFR and predictability of mortality and ESRD between eGFR values calculated by CKD-EPI 2009 and CKD-EPI 2021. Serum creatinine was expressed as the IDMS-traceable creatinine according to the manufacturer’s conversion formula from the original value measured by the alkaline picrate Jaffe kinetic method. The incidence of mortality data was extracted from Statistics Korea and the ESRD data from the ESRD registry of the Korean Society of Nephrology.

**Results:** At baseline study, there were 60,723 males (53.8%). Age was 48.9 ± 12.0 years. The value of IDMS-traceable serum creatinine was 0.86 ± 0.21 mg/dL. Levels of eGFR at baseline study was 93.5 ± 15.6 ml/min/1.73 m² by CKD-EPI2009, and 97.1 ± 15.0 ml/min/1.73 m² by CKD-EPI2021. Values subtracted eGFRs by CKD-EPI2009 from eGFR by CKD-EPI2021 were 3.6 ± 3.2 range: -32.9 to 6.1) ml/min/1.73 m². The difference of eGFR was higher in males compared to females (p<0.001), was the highest in the oldest group among participants aged 18–44 years, 45–64 years, and 65 years or more (p<0.001). Patients with diabetes mellitus (DM) or hypertension showed higher difference of eGFR compared patients without DM or hypertension, respectively (each p<0.001). Patients with eGFR >120.0 ml/min/1.73 m² by CKD-EPI 2009 showed the highest difference between two eGFRs compared to patients with the other values. CKD stage was improved in 11,828 (10.5%) participants using eGFR calculated by CKD-EPI 2021 instead of CKD-EPI 2009, however, only 0.63% of participants with eGFR <60 ml/min/1.73 m² by CKD-EPI equation was reclassified into eGFR ≥60 ml/min/1.73 m² by CKD-EPI 2021.During 11.6 ± 2.0 years, 3354 (3.00%) subjects were dead and 151 (0.13%) subjects had end stage renal disease (ESRD) before death. Any eGFR or stage of CKD was an independent risk factors to ESRD or mortality estimated by Cox’s hazard proportional model adjusted by related factors. AUC to estimate renal survival by eGFRs was not different between eGFRs by CKD-EPI2021 and CKD-EPI2009 [0.739 (0.687-0.790)] vs 0.740 (0.688-0.792), p = 0.170]. AUC to estimate survival by eGFRs calculated through CKD-EPI equation was slightly higher than that by CKD-EPI2021 equation [0.673 (0.604-0.682) vs 0.667 (0.658-0.676), p<0.001], however, the difference of AUC was negligible (standard error of AUC difference by two eGFRs: 0.3% [95% CI: 0.006-0.01])

**Conclusion:** The eGFR calculated by CKD-EPI2021 was higher compared to eGFR calculated by CKD-EPI2009. The power to estimate renal survival was not different between eGFRs by CKD-EPI2021 and CKD-EPI2009.

#4026
ECONOMIC EVALUATION OF ANAEMIA OF CHRONIC KIDNEY DISEASE (CKD): A SYSTEMATIC LITERATURE REVIEW AND MODEL CONCEPTUALISATION

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**Background and Aims:** Anaemia is a common complication of chronic kidney disease (CKD), affecting up to 33% of patients with Stage 5 CKD compared to 8.4% of patients with Stage 1 CKD [1]. Anaemia of CKD is associated with increased risk of cardiovascular events and death, increased healthcare resource utilisation (HRU), and reduced health-related quality of life (HRQoL) [2]. Established treatments for anaemia of CKD include erythropoiesis-stimulating agents (ESAs) [1,2]; however, hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), targeting both erythropoietin production and iron metabolism (the two key mechanisms of anaemia of CKD), are an emerging class of agents in this indication [3]. The cost and HRQoL burden associated with anaemia of CKD treatment is not well characterised.1 Thus, we conducted a systematic literature review (SLR) to evaluate published economic models (including the cost inputs, time horizon, subgroups, and clinical assumptions used) and HRU data in patients with anaemia of CKD. Findings of the SLR will help guide future economic model development and inform economic evaluation strategies as part of health technology assessment submissions to support daprodustat, an HIF-PHI under development for use in both dialysis-dependent and non-dialysis-dependent patients.

**Method:** Relevant publications were identified using structured searching of MEDLINE, Embase, MEDLINE In-Process, Cochrane Controlled Trials Register, and the Cochrane Database of Systematic Reviews from database inception to 10 April 2022 using disease- (e.g. CKD, chronic kidney failure, anaemia) and economic-associated (e.g. economics, economic evaluation, quality-adjusted life-years, model structure) search terms. Additional supplemental searches (conference proceedings [2016–2021], grey literature, and bibliographies) were conducted. Studies were assessed for inclusion or exclusion by two independent reviewers, with any discrepancies resolved by a third reviewer. Objectives were to determine the structure of any published economic models and the availability of health utility data in patients with anaemia and additional complications of CKD, and to examine what cost inputs, time horizons, subgroups, and clinical assumptions are used to inform economic modelling.

**Results:** From 1397 citations identified in the searches, 40 primary studies were included in the final analysis. Review of the data revealed an established approach for modelling the ESA cost-effectiveness (i.e. a Markov model with health states defined according to CKD treatment received or anaemia status): most studies were conducted from a North American or European perspective, time horizons varied, and reporting of cycle length was poor. Only one economic evaluation included an HIF-PHI model: given the different mechanisms of action of ESAs and newer treatments, a modelling strategy focused mainly on a Markov approach may not be the most optimal way of assessing cost-effectiveness in anaemia of CKD where HIF-PHIs are used. Considerations of modelling factors that could influence cost-effectiveness of HIF-PHIs are shown in Fig. 1. While existing models typically only stratified patient populations according to age (<65 vs >65 years), for appropriate modelling of treatment effectiveness, the impact of prior treatments (including response to prior ESAs) was also considered. As in every model, comorbidities may also have a role in effect modification and this impact will need to be considered in economic models of anaemia of CKD treatment. Due to the natural history of anaemia in CKD, innovative modelling techniques that retain the Markov approach and which account for respective haemoglobin levels, CKD stage, and potential kidney transplantation should be incorporated into the economic evaluation (Fig. 2).

**Conclusion:** Adjustment of existing models using the approaches described may provide more reliable estimates of treatment efficacy in a highly heterogenous population of patients with anaemia of CKD.

**REFERENCES**


BURDEN OF KIDNEY DISEASES IN THE GENERAL POPULATION OF THE VAL VENOSTA/VINSCHGAU DISTRICT

Giulia Barbieri1,2, Lucia Cazzoletti1, Roberto Melotti2, Essi Marjatta Hantikainen2, Laura Barin2, Giovanni Gambaro3, Pramstaller Peter4, Maria Elisabetta Zanolin1 and Cristian Pattaro2

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Background and Aims: Chronic kidney disease (CKD) is a public health burden affecting >10% of the population worldwide. Population-based studies are essential to assess CKD prevalence and its determinants. However, questionnaires to survey CKD and other kidney diseases in the general population are scarce. We developed a novel questionnaire to identify several types of kidney disease in the general population and implemented it in a large central-European population study. We integrated questionnaire responses with standard renal biochemical measurements to estimate CKD prevalence in the Val Venosta/Vinschgau district. We aimed to assess the degree of CKD underdiagnosis and to describe the kidney health status of study participants.

Method: Within the Cooperative Health Research In South Tyrol (CHRIS) study, we conducted a cross-sectional assessment of kidney health on 11684 adults (mean age 45 years; females 53.8%) with interviewer-administered kidney questionnaire and measured fasting serum creatinine and albuminuria. The questionnaire covered retrospectively various kidney diseases, including reduced renal function and renal surgeries (Fig. 1). Questions asked if a doctor had ever diagnosed the specific condition and the age at diagnosis. We defined CKD based on combinations of self-reported diagnosis of reduced kidney function (Q6), CKD-EPI 2021 estimated glomerular filtration rate (eGFR) levels, and microalbuminuria (Table 1). Prevalence was estimated via the Clopper-Pearson method and adjusted to the general target population via relative sampling weights. Using factor analysis we explored the underlying correlation structures within and between questionnaire items and laboratory markers.

Results: Participants had median eGFR and urinary albumin-to-creatinine ratio (UACR) of 98.4 ml/min/1.73 m² (IQR: 87.8-108.8) and 5.7 mg/g (IQR: 3.8-10.0), respectively. Overall, 744 reported only one and 179 reported at least two types of kidney diseases (Fig. 1). Glomerulonephritis (n = 359; 3.14%), kidney stones (n = 311; 2.93%) and other kidney diseases (n = 200; 1.91%) were the most frequent types. Males reported kidney stones (M: 3.2%; F: 2.2%; p-value = 0.0116) and renal surgeries (M: 0.9%; F: 0.5%; p-value = 0.0013) more frequently than females. Females reported a higher proportion of glomerulonephritis (M: 0.6%; F: 5.2%; p-value <0.0001). The population-weighted CKD prevalence varied between 0.71% to 9.29% depending on the definition (Table 1), with a KDIGO estimate of 8.79% (95%CI 8.28%-9.31%).
Figure 1: Summary of the responses to the kidney questionnaire. Combinations reported by ≤2 participants were excluded.

Table 1: Comparison of population-weighted CKD prevalence.

<table>
<thead>
<tr>
<th>Definition</th>
<th>Prevalence</th>
<th>95%CI-Lower</th>
<th>95%CI-Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Questionnaire self-rep. reduced kidney function (Q6)</td>
<td>0.71%</td>
<td>0.56%</td>
<td>0.88%</td>
</tr>
<tr>
<td>(2) CKD G3 to G5 (eGFR &lt; 60 ml/min/1.73 m²)</td>
<td>2.56%</td>
<td>2.28%</td>
<td>2.87%</td>
</tr>
<tr>
<td>(3) Microalbuminuria (UACR &gt; 30 mg/g)</td>
<td>7.07%</td>
<td>6.62%</td>
<td>7.55%</td>
</tr>
<tr>
<td>(4) KDIGO: “Moderately increased” to “Very high” risk – (2) or (3)</td>
<td>8.79%</td>
<td>8.28%</td>
<td>9.31%</td>
</tr>
<tr>
<td>Any CKD definition</td>
<td>9.29%</td>
<td>8.77%</td>
<td>9.84%</td>
</tr>
</tbody>
</table>

Questionnaire items showed low sensitivity and high specificity to identify low eGFR or high UACR levels. Factor analysis revealed two clearly separated latent factors: one representing “reduced renal function”, which included eGFR, UACR, and the question Q6 on reduced kidney function; and one representing “all other kidney diseases”.

Conclusion: In the Val Venosta/Vinschgau district, CKD prevalence is aligned to Western-European countries. In general population studies, questionnaire-based CKD assessment may severely underestimate CKD prevalence as compared to eGFR- and UACR-based estimates. Our analysis highlights that the large majority of individuals with CKD according to KDIGO guidelines were unaware of the disease. On the other hand, the questionnaire has allowed identifying several specific kidney diseases that usually go undetected in population studies. The limited discriminant ability of questionnaire items and the identifiable correlation structure support the use of the survey questionnaire as an integrative tool to study the kidney health status in general population.

#4160

PHASE ANGLE (PA), AGE AND MIS AS MORTALITY PREDICTORS IN PATIENTS WITH ADVANCED CKD

Guillermina Barril, Graciela Alvarez, Almudena Núñez, Carmen Sanchez Glez and Ángel Nogueira

Hospital de La Princesa, Nefrología, Madrid, Spain

Background and Aims: Survival study in Advanced CKD patients according to age, MIS and phase angle

Method: We studied 225 patients with ACKD, 153 men (68.3%), xage 70.09±12.72 years. We analyze survival at 120 months and how the Phase angle (PA) and MIS scale influence mortality. We chose these parameters, one of body composition (BIA-vector) and the MIS malnutrition-inflammation scale, since they are described as independent predictive factors.

Results: We defined the cut-off point for PA with the ROC curve, appearing as 3.75 (sensitivity 67% and specificity 55%). With 83 (37.1%) ≤3.75 and 141 (62.9%) greater than 3.75, PA, with significance between men and women p<0.001. Analyzing the % of deaths with PA with PC- 3.75 there is a significant difference between groups p<0.001, Sig difference between men and women p<0.021. We define with COR cut-off point age = 70.5 years sens 85% spec 63% 79 patients (64.6%) died in 120 months, 53/152 (65.1%) men and 45/71 (63.4%) women xage deceased 76.39±9.16 vs 66.63±13.14 years p<0.001. The survival curves for the 3 variables by Kaplan Meier are significant with the established cut-off points (Fig. 1). In the univariate analysis we found that age (CP-70.5 years) p<0.001, and PA (CP-3.75) p<0.04 are significant, but not MIS(CP-5). In the Cox analysis we evaluated age, PA and MIS, with age as a priority, followed by PA and finally the MIS Wald 18.73, 3.77 and 2.26 respectively.

Conclusion: 1-Age, phase angle and MIS are independent mortality risk factors for ACKD patients. 2-In the multivariate model Age and phase angle are predictors of mortality. 3-Independent of age, the phase angle is the best predictor of mortality.
INCIDENCE AND FREQUENCIES OF HYPERKALEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A RETROSPECTIVE DATABASE STUDY FROM US CLINICAL CARE

Sascha van Boemmel-Wegmann1, Chris Bauer2, Johannes Schuchhardt2, Alexander Hartenstein1, Glen James3, Elena Pessina4, Scott Beeman5 and Roberto Pecoits-Filho6,7

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Background and Aims: Hyperkalemia (HK) is associated with significant risks for premature mortality, adverse clinical outcomes, and with a potentially more rapid decline of renal function. Reported numbers on the epidemiology of HK in patients diagnosed with chronic kidney disease (CKD) vary significantly and are unclear in real-world patients across different CKD stages, eGFR and UACR strata. We aimed to evaluate the occurrence of moderate to severe hyperkalemia episodes among a large, representative sample of patients with CKD from the US between 2009 and 2020.

Method: Using Optum Electronic Health Records data, we included patients with CKD between January 2009 and December 2020, who had at least two qualifying estimated glomerular filtration rate (eGFR) (15-60 ml/min/1.73 m²) and/or UACR values ≥ 30 mg/g between 90 and 365 days apart. The second qualifying value was considered confirmatory and set as the index date. Patients had to have 365 days of baseline activity prior to index, be ≥ 18 years of age, and not show any diagnoses, procedures, or lab values of kidney failure or hemodialysis or kidney transplant during baseline. A HK episode was defined in two ways, (1.) as either a combination of two elevated inpatient or outpatient serum potassium values (sK+ ≥ 5.5 mmol/L, not longer than 7 days apart, or (2.) a combination of one elevated sK+ and the initiation of pharmacotherapy (e.g., i.v. calcium or insulin-glucose, nebulized albuterol, potassium binders) or a diagnostic code for HK, not longer than 3 days apart. We calculated relative frequencies and incidences of HK in the overall CKD study population and specific subgroups of interest.

Results: 1,771,900 patients met our selection criteria for CKD, with advanced stages 3 and 4 predominantly represented (85.7% and 10.2%, respectively). The cohort consisted of 57.7% females, 83.8% Caucasian and 9.8% African American. Most common baseline comorbidities were hypertension (68.5%), hyperlipidemia (55.1%) and T2D (34.2%). 69.3% of patients were prescribed antihypertensives, 45.7% statins and 45.6% antiarrhythmics. 99.1% of patients had at least one baseline potassium measurement with values averaging 4.3 mmol/L (median, 4.3; IQR: 4.0-4.55). During an average follow up 3.9 years, 220,339 (12.4%) patients experienced at least one episode of hyperkalemia. Of those, 69.3%, 17.5%, and 13.2% showed one, two, and three or more HK episodes, respectively. Across all patients with CKD, the mean incidence rate was 3.37 (95% CI, 3.36-3.38) cases per 100 patient years (PYs). HK incidence correlated with lower eGFR and increased UACR values, with rates of 1.32 (1.25-1.39), 2.48 (2.40-2.55), 3.00 (2.99-3.01) and 8.80 (8.71-8.88) cases/100 PYs for patients with CKD stage 1, stage 2, stage 3 and stage 4, respectively. Highest incidence rates (13.81; 12.96-14.70) were found in patients with UACR values ≥ 3500, irrespective of their eGFR value. In addition, across disease-related subgroups, significantly higher incidence rates were found in patients co-diagnosed with T2D (5.43; 95% CI, 5.40-5.47) and HF (8.70; 8.62-8.77), and sMRA users (7.66; 7.57-7.76) at baseline.

Conclusion: Our contemporary findings demonstrate that HK is common in patients with CKD undergoing routine clinical care in the US, and it is notable in patients with reduced eGFR and elevated UACR. In addition, HK was more predominant in patients with T2D, heart failure or sMRA use, emphasizing a need for more routine sK+ monitoring in patients with these risk factors. Further research is needed to assess additional intrinsic risks, clinical consequences and management approaches of HK in patients with CKD to further inform clinical practice.

Table 1:

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>N patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>75 (66, 80)</td>
</tr>
<tr>
<td>Female</td>
<td>1,022,051 (57.7)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1,484,694 (83.8)</td>
</tr>
<tr>
<td>African American</td>
<td>173,767 (9.8)</td>
</tr>
<tr>
<td>Asian</td>
<td>20,053 (1.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>93,386 (5.3)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1,213,878 (68.3)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>975,563 (55.1)</td>
</tr>
<tr>
<td>T2D</td>
<td>605,099 (34.15)</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>1,228,357 (69.3)</td>
</tr>
<tr>
<td>Statins</td>
<td>810,065 (45.7)</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>803,537 (45.4)</td>
</tr>
<tr>
<td>Oral antidiabetics</td>
<td>446,953 (25.2)</td>
</tr>
<tr>
<td>Insulin</td>
<td>354,269 (20.0)</td>
</tr>
<tr>
<td>Potassium level, median (IQR)</td>
<td>4.3 (4.0, 4.55)</td>
</tr>
</tbody>
</table>

Abstracts i573

T2DM MODIFIES THE RELATIONSHIP BETWEEN CAC AND ADVERSE KIDNEY OUTCOME IN PATIENTS WITH CKD

Hae-Ryong Yun and Seung Hyeok Han

Yonsei University College of Medicine, Department of Internal Medicine, Seoul, Rep. of South Korea

Background and Aims: Kidney function decline faster in patients with type 2 diabetes mellitus (T2DM) than in those without. We previously showed that coronary artery calcification (CAC) is a strong risk of adverse kidney outcome. Here, we examined whether T2DM could modify the relationship between CAC and the progression of chronic kidney disease (CKD).

Method: 2067 participants from the KoreaN Cohort Study for Outcome in Patients With CKD were enrolled. The main exposures were T2DM and CAC. The primary outcome was CKD progression defined as a composite of a 50% decline in estimated glomerular filtration rate or kidney failure with replacement therapy. Multivariable cause-specific hazard function was

Figure 1:

#4381

Abstracts i573

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employed to determine the association between the main exposures and the primary outcome.

Results: During 8633 person-years of follow-up, the primary outcome occurred in 565 (27.3%) participants. In the multivariable cause-specific hazard model, both T2DM and CAC Agatston score (CACS) > 0 were associated with a 1.80- and a 1.41-fold increased risk of CKD progression compared with counterparts. There was a significant interaction between T2DM and CAC for the primary outcome. In patients without T2DM, CACS > 0 was not associated with the primary outcome compared with CACS of 0. However, in patients with T2DM, CACS > 0 was associated with a significantly higher risk of CKD progression (adjusted hazard ratio 2.12; 95% confidence interval, 1.64–2.75). In addition, a 1-SD increase in CACS was associated with 1.11-fold higher risk of CKD progression. Notably, this association was also significant in patients with T2DM who had CACS of 0. The slope of eGFR decline was steeper in patients with T2DM and the magnitude of decline was greater when CACS > 0.

Conclusion: CAC were more strongly associated with risk of CKD progression in patients with T2DM than in those without. Thus, clinical implication of CAC may differ depending on the presence of T2DM.

Method: SS patients have two kinds of photographs in literatures, before SS nondeformed and after SS deformed. We studied to create face map in SS by using technic in soil survey. 10 face images (5 before SS and 5 after SS) were used. Unsupervised Classification (UC) system of Erdas 8.4 software was used to classify images. Methodology had 3 phases in this research. In first phase, we got the images at same scale by cutting them around faces images. In final phase, we applied coloring on 10 classes of images. We used same color for same class number both ClbSS and ClaSS images. If color classes are in same structure of face (on cheek, forehead, etc), they may be combined.

Results: We have very important results on deformed faces photos in SS (ClaSS). First finding is all ClaSS have specific “hourglass” shapes (figure 4). “Hourglass” is enclosing red area for sample A and B Figure 3, Column 1: photos of patients before SS (raw images), column 2: classified photos of column 1, column 3: classified photos of patients after SS, Figure 5. “Hourglass” is conformity of “Hourglass” form for all ClaSS curved face.

Conclusion: Image processing plays very important role in clinical practices and biomedical researches. SS is a kidney disease and derived from inside of the body but its effects are appearance outside of human body, such as head, face, skull deformations. These symptoms can be put forward by using Image Classification for SS. Moreover, shape of “hourglass” can be an index for SS and this is very specific for SS. “Hourglass” can be an indicator for grading SS. Finally, “hourglass” should be carefully evaluated in SS.
TERTIARY HOSPITAL EXPERIENCE IN AN ESSENTIAL SUBSPECIALTY: ONCONEPHROLOGY
Sheila Bermejo Garcia, Mónica Bolufer, Davide Viggiano, Ana Callejo, Enriqueta Felip, Marina López, Ander Vergara, Irene Agraz Pamplona, Oriol Bestard Matamoros and Maria Jose Soler Romeo
Vall d’Hebron University Hospital, Nephrology, Barcelona, Spain, Vall d’Hebron University Hospital, Oncology, Barcelona, Spain and University of Turin - Campus Luigi Einaudi, Nephrology, Torino, Italy

Background and Aims: Kidney complications of cancer patients and cancer in renal patients have increased in recent years. The objective of this study is to evaluate the characteristics of the patients referred to the Onconephrology Unit from January 2021 to December 2021, studying the cognitive and mood status of these patients.

Method: This is a prospective observational study of the Onconephrology consultation at a University Hospital Center during 2021. Clinical and analytical characteristics of the patients and clinical indication for referral were analyzed. In addition, sleep quality, mood and cognitive status were assessed using validated rating scales (Epsworth, Geriatric Depression Scale and Montreal).

Results: Seventy-four patients were evaluated, mean age was 69.6(±11) years, 41(55.4%) men, 47(63.5%) had hypertension, 18(24.3%) diabetics, and 11(14.9%) were affected by heart disease. In addition, creatinine 1.93(±1.1)mg/dl, eGFR 39.97(±20.3)ml/min, proteinuria 187[29-515.9]mg/g, and 4(5.4%) had microhematuria. The most frequent cancers were intestinal, gynecological and mammary with 12.16%(n = 9) each. The most frequent indication for referral was acute kidney injury (n = 36; 48.7%), followed by chronic kidney disease (n = 27; 36.49%) and proteinuria (n = 5; 6.76%). Rating scales were obtained in 51 patients: 49% (n = 25) were snorers, followed by 17.6% (n = 9) with insomnia and 11.8% (n = 6) with OSAS. 27 patients (36.5%) had cognitive impairment. Mild depression was detected in 13 cases (25.5%) and moderate depression in 11.6% (n = 6). 21 renal biopsies were performed, the most frequent diagnosis was acute interstitial nephritis (71.4%, n = 15) followed by thrombotic microangiopathy (19%; n = 4). A total of 15 patients (20.3%) died during the year.

Conclusion: Most patients referred to Onconephrology are affected by advanced oncological disease and consequently had a high mortality. The most frequent indication for referral was acute kidney injury (48.7%). Comprehensive patient care is important, given the prevalence of depressive syndrome. Onconephrology is an example of a comprehensive and multidisciplinary approach to improve the survival and quality of life of patients with advanced cancer and renal disease.
Method: We obtained data from the 2011–2014 and 2019–2020 Korea National Health and Nutrition Examination Survey (KNHANES). Microalbuminuria was measured based on spot urine albumin-creatinine ratio (UACR). The Framingham risk score (FRS) model was implemented to evaluate the CVD risk. Linear and logistic regression models were used to identify the associations of microalbuminuria status with cardiometabolic predictors and CVD status determined by the FRS score.

Results: Among 19,340 representative Korean participants, the (UACR) in Korean women and men with history of CVD was higher than in those without history of CVD. Among patients without history of CVD, multivariate regression analysis showed that a high UACR was related to older age, lower high-density lipoprotein cholesterol level, higher total cholesterol level, higher systolic blood pressure, higher prevalence of current smoking, higher prevalence of diabetes, and higher anti-hypertensive medication use in both women and men. The UACR showed a positive linear correlation with the Framingham risk score in both women and men.

Conclusion: The presence of microalbuminuria was significantly associated with the cardiometabolic risk factors and the increased risk of CVD evaluated by FRS model in both women and men in a nationally representative sample of Korea.

Table 1: Clinical characteristics (N = 271).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ±SD)</td>
<td>74.91 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Males (n, %)</td>
<td>168 (62)</td>
<td></td>
</tr>
<tr>
<td>White race (n, %)</td>
<td>272 (100)</td>
<td></td>
</tr>
<tr>
<td>Urine albumin/creatinine ratio (median)</td>
<td>263 (40-1029)</td>
<td></td>
</tr>
<tr>
<td>&lt;30 n(%)</td>
<td>59 (21.8)</td>
<td></td>
</tr>
<tr>
<td>30–300 n(%)</td>
<td>84 (31)</td>
<td></td>
</tr>
<tr>
<td>&gt;300 n(%)</td>
<td>128 (47.2)</td>
<td></td>
</tr>
<tr>
<td>GFR CKD-EPI ml/min/1.73m2 (mean)</td>
<td>21.39 (3.75)</td>
<td></td>
</tr>
<tr>
<td>CKD etiology (n, %)</td>
<td>86 (31.7)</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>84 (31)</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>48 (17.7)</td>
<td></td>
</tr>
<tr>
<td>Unaffiliated</td>
<td>24 (8.9)</td>
<td></td>
</tr>
<tr>
<td>Chronic tubulointerstitial nephropathy</td>
<td>30 (10.6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>173 (63.8)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity n(%)</td>
<td>258 (95.2)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>136 (50.4)</td>
<td></td>
</tr>
<tr>
<td>HBP</td>
<td>141 (52.1)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular history</td>
<td>128 (47.2)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>105 (38.7)</td>
<td></td>
</tr>
<tr>
<td>SBP (mean (SD))</td>
<td>138.9 (19.7)</td>
<td></td>
</tr>
</tbody>
</table>

Results: 271 patients who met the inclusion criteria were analyzed. The clinical characteristics are shown in Table 1. The Grams model showed good discrimination for initiating KRT at 2 and 4 years, AUC 0.84 [95%CI 0.77-0.91] and AUC 0.81 [95%CI 0.75-0.87], respectively. The ROC curves presented by both equations showed good discrimination, AUC 0.82 [95%CI 0.74-0.91] and AUC 0.80 [95%CI 0.74-0.87]. When comparing the need for 2-year KRT with both equations, we observed both ROC curves were similar (p < 0.05). Table 2 shows results from logistic regression analysis. For the 2-year KRT event by Grams, patients with a score ≥ 17.85% were 11.53 [95%CI 5.16-27.78] times more likely to initiate KRT. However, compared to KFRE with a score ≥ 20.77%, they had 17.53 [95%CI 7.59-40.47] times higher probability of KRT (both p < 0.001). When we compared both equations in multivariate analysis only the KFRE was significant (ODR 0.217 [95%CI 0.87-0.54]).

Conclusion: In our population, both prognostic equations showed good discrimination to program initiation of KRT. However, the GS could underestimate this need while the KFRE seems to discriminate it better.
ACUTE KIDNEY DISEASE FOLLOWING COVID-19 VACCINATION: A RETROSPECTIVE, SINGLE-CENTER STUDY
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Background and Aims: The rare de novo or relapsed kidney diseases associated with coronavirus disease 2019 (COVID-19) vaccination have been increasingly reported. The aim of the study was to investigate the incidence, characteristics, and outcome of acute kidney disease (AKD) following COVID-19 vaccination.

Method: This retrospective study scrutinized the data from renal registry in a single academic medical center from Jan. 1st, 2020, to Apr. 30th, 2022. Patients who developed AKD within 90 days after COVID-19 vaccination were first included. Naranjo score as a causality assessment tool for adverse vaccination reaction and charts review by peer nephrologists were utilized for the exclusion of other causes. The etiologies of AKD, their characteristics, treatment, and outcome attributing to the COVID-19 vaccines were examined (Fig. 1).

Results: Twenty-seven aged 23 to 80 patients with AKD were identified from 1897 patients (incidence of 6.3 per 1000 patient-years). Their Naranjo score was 7.7±1.5, and 14 of 27 patients (51.9%) had definite diagnosis (Naranjo score ≥ 9). They incorporated both glomerular disease (n = 16) including IgA nephropathy (n = 7), anti-neutrophil cytoplasmic antibodies-associated glomerulonephritis (AAN) (n = 4), membranous glomerulonephritis (n = 3), minimal change disease (MCD) (n = 2), and chronic kidney disease (CKD) with acute deterioration (n = 11). The majority (21 of 27, 77.8%) of COVID-19 vaccination was messenger RNA (mRNA)-based regimen. Four patients (14.8%) rapidly progressed to end stage kidney disease (ESKD) requiring dialysis despite aggressive management. Extra-renal features such as pulmonary hemorrhage, myopericarditis and hepatitis/pancreatitis were observed in 4 patients.

Conclusion: In summary, AKD after COVID-19 vaccination may occur with more alarm in this renal registry. In addition to GN, patients with pre-existing moderate to severe CKD should also receive more intensive evaluation before vaccination despite the established benefits of vaccination in this vulnerable population likely outweigh the risk.

RAPID DECLINE IN KIDNEY FUNCTION IS ASSOCIATED WITH HIGHER HEMOGLOBIN VARIABILITY IN CHRONIC KIDNEY DISEASE
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Background and Aims: Hemoglobin decrease and anemia are common in chronic kidney disease (CKD). This study aimed to evaluate hemoglobin variability in patients with CKD according to decline in kidney function.

Method: We analyzed patients from the KoreaN cohort study for Outcome in patients With CKD (KNOW-CKD). The rates of renal function decline per year were determined using the slope of estimated glomerular filtration rate (eGFR) analyzed using a generalized linear mixed model. Rapid decline in kidney function was defined as a decline in the eGFR of >3 mL/min/1.73 m²/year. Hemoglobin value was measured at 0, 6, and 12 month and annually for up to 8 years. Hemoglobin variability was calculated by standard deviation. Higher hemoglobin variability was defined as a hemoglobin variability value greater than the median.

Results: Among 1895 patients, 736 patients (38.8%) were in the rapid kidney function decline group. In 1472 patients who were 1:1 propensity score-matched, the baseline eGFR was not significantly different between the non-rapid kidney function decline group (48.2±26.9 vs 46.9±26.2 mL/min/1.73 m², P = 0.345). The use of iron supplements (P = 0.536) or erythropoiesis stimulating agents (P = 0.689) was similar in both groups. In multivariable logistic regression analysis, rapid decline in kidney function was significantly associated with higher hemoglobin variability (odds ratio [OR]: 1.81; 95% confidence interval [CI]: 1.43–2.28; P < 0.001). This association was prominent in the group without anemia at baseline (OR: 2.82; 95% CI: 1.99–4.01; P < 0.001).

Conclusion: Rapid decline in kidney function is associated with higher hemoglobin variability in patients with CKD. Attention should be paid to hemoglobin variability in patients with a rapid decline in kidney function.
ml/min/1.73 m² by CKD-EPI2021. Values subtracted eGFRs by MDRD or CKD-EPI2009 from eGFR by CKD-EPI2021 were 2.5 ± 10.1 ml/min/1.73 m² and 4.5 ± 1.0 ml/min/1.73 m², respectively. Between eGFRs by CKD-EPI2009 and CKD-EPI2021, the difference of eGFR was higher in females compared to males (p < 0.001), was not different between subjects aged less than 75 years and more than 75 years (p = 0.139), and lowest in subject with <45 ml/min/1.73 m² of eGFR by CKD-EPI2009 compared to subjects with other eGFR values (p < 0.001). CKD stage was improved in 241 (24.5%) participants and was not changed in 743 (75.5%) using eGFR calculated by CKD-EPI2021 instead of CKD-EPI2009. Similar trend of eGFR difference between eGFRs calculated by MDRD and CKD-EPI2021. During 8.3 ± 6.2 years, 255 (25.9%) subjects were dead and 7 (0.7%) subjects had end stage renal disease (ESRD) before death. Any eGFR was an independent risk factors to mortality estimated by Cox’s hazard proportional model adjusted by related factors. AUC to estimate survival by eGFRs was not different between eGFRs by CKD-EPI2009 and CKD-EPI2021 (0.662 ± 0.620-0.695), however, different between eGFRs by CKD-EPI2009 and MDRD [0.662 (0.625-0.699) vs 0584 (0.543-0.626), p < 0.001]. AUC to estimate renal survival by eGFRs was not different between eGFRs by CKD-EPI2021 and CKD-EPI2009, also.

Conclusion: The eGFR calculated by CKD-EPI2021 showed higher value compared to eGFR calculated by CKD-EPI2009 or MDRD. The power to estimate mortality or renal survival was not different between eGFRs by CKD-EPI2021 and CKD-EPI2009.

#3784

DIETARY BEHAVIOR OF CKD PATIENTS BEFORE AND AFTER THE COVID-19 PANDEMIC PERIOD
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Background and Aims: As the COVID-19 infection went global pandemic in 2020, many governments around the world have carried out social lockdown policies. It resulted in changes in lifestyles such as diet, physical activity, and social interaction. This study aimed to investigate the changes of lifestyles focusing on diet, especially in patients with chronic kidney disease (CKD) during the COVID-19 pandemic period.

Method: We compared data from 2019 and 2020 of the Korea National Health and Nutrition Examination Survey (KNHANES) before and after COVID-19, because COVID-19 was first detected in January 2020 in South Korea. CKD was defined as albumin to creatinine ratio > 30 mg/g or estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m². CKD was categorized into two groups, CKD stage 1–2 and CKD 3–5; eGFR over 60 with albuminuria and eGFR below 60 ml/min/1.73 m². We compared changes in diet behavior, nutrients, and food intake between 2019 and 2020 in normal, CKD stage 1–2, and CKD stage 3–5 groups.

Results: This analysis included a total of 5,084 and 4,338 participants from 2019 and 2020. When compared to normal group in the post-COVID-19, CKD group showed lower energy intake (p = 0.038), but the proportion of carbohydrates, proteins, and lipids did not differ. In the pre-COVID-19, CKD stage 3–5 group ate significantly lower sodium (1893.5 ± 109.2 mg/1000 kcal, p = 0.015), and the urine Na/Cr ratio also increased (from 19.5 ± 1.4 to 26.0 ± 1.5, p = 0.001). The main source food of sodium was kimchi in every group, but the proportion changed in the post-COVID-19 period. In CKD stage 3–5 group, compared to the pre-COVID-19 period, the intake of noodles and Ramen increased 35% and 91%, respectively. Interestingly, the potassium intake increased from pre-COVID-19 to post-COVID-19 in all three groups.

Conclusion: The COVID-19 pandemic affects CKD patients’ diets in terms of sodium intake. We need to pay attention to diet and nutritional education for CKD stage 3–5 patients.
THE CARE TRAJECTORY LEADING TO EMERGENCY DIALYSIS START: CROSSING PATIENTS’, GENERAL PRACTITIONERS’ AND NEPHROLOGISTS’ PERSPECTIVES

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Background and Aims: Emergency dialysis start (EDS) is an important issue to understand and tackle in CKD care. Late referral, absent previous nephrology care and higher comorbidity scores have been associated with EDS. However, how those quantitative risk factors happen and contribute to EDS remains unexplored. We conducted a qualitative study in France to identify and describe the mechanisms that shape the trajectories that lead to EDS, using patients, GPs and nephrologists perspectives.

Method: Three groups of participants were recruited in Brittany, north-west France: Patients who started dialysis in emergency between 2017 and 2019, GPs and nephrologists. Maximum variation sampling approach was used based on patients’ socio-economic profiles and GPs’ and nephrologists’ years and settings of practice. Semi-structured interviews were conducted between 2017 and 2020. A crossed thematic analysis between the 3 groups of transcripts was performed, informing how EDS trajectories come to be.

Results: Twenty patients, 12 GPs and 18 nephrologists were interviewed. Five main themes were identified: 1) Learning about dialysis, 2) Dialysis and nephrology care representations: a) an unacceptable biographical disruption, b) a dreadful invasive machinery, c) a straw that breaks the camel’s back, 3) The gap between the “illness” perceived and the “disease” treated, 4) Slipping through the primary care prevention net, 5) the unavoidable unpredictability of CKD course.

Conclusion: This study shows how quantitative risk factors of EDS such as low or absent previous nephrology care are, in part, the results of an interplay between patients’ constructed representations of dialysis, relation with the medical sphere and CKD physiopathology. The results suggest a need for evaluation of kidney replacement therapy education programs and

Figure 1: Flow diagram of the study and definition of the socioeconomic status score. SES was defined as a score incorporating income, education, occupation, and marital status, ranging from 0 to 4. Abbreviation: SES, socioeconomic score.

Figure 2: Forest plots of subgroup analyses according to the presence or absence of renal dysfunction and smoking, as reference one group SES = 0: risk of myocardial infarction (A&D), stroke (B&E), and death (C&F), Abbreviations: RD, renal dysfunction; SES, socioeconomic status score; HR, hazard ratio; CI, confidence interval.
The decision-making process in this regard for clinicians, patients, and their families may be ameliorated by the Thamer Risk Scoring tool which uses simple variables such as age, albumin level, nursing home residence, need for assistance in daily living, cancer, heart failure, and hospitalization to predict early mortality in elderly patients after initiating dialysis [1]. This tool has not been validated in the Philippine setting, hence this study aimed to validate the prognostic property of the Thamer Risk Scoring tool in predicting early death among elderly patients initiated on dialysis in a tertiary institution, in Davao City, Philippines.

Method: A retrospective cohort research design was used. All the charts of patients diagnosed with end-stage renal disease aged 60 years and above, who were admitted and initiated on either hemodialysis or peritoneal dialysis within a 4-year period from 2018 to 2021 were reviewed. Patients with periods of dialysis lasting less than 90 days or who died of recovery of kidney function, and patients with missing data that meet all pre-requisite variables for the risk scoring were excluded.

Results: A review of 1,583 patient charts was done, with 1,402 omitted based on the exclusion criteria. A total of 181 patients were included in the study. Most of the patients were male (56.35%), and initiated on hemodialysis (97.24%). The mean age of the population was 67.34 years with majority in the 60–69 year age group (66.3%). Those who survived had a mean age of 66.53 years and those who expired had a mean age of 68.63 years. All-cause mortality was 38.12% at 3 months, and 3.57% at 6 months after dialysis initiation. The all-cause mortality at 3 months in this study was three times higher than the Thamer study with a mortality of 12.5%. Patients with heart failure (p-value = 0.007), cancer (p-value = 0.040), asthma (p-value = 0.040), and need for assistance in daily living (p-value = 0.022), had significantly higher mortality rates, while patients who had higher albumin (p-value = 0.010), and creatinine (p-value = 0.014) had higher survival rates. Similar to the Thamer study, this study also showed that the tool becomes less sensitive and more specific as the scores increased for the 3-month, 6-month, and over-all mortality groups. The accuracy of the tool rises with a higher score as well. In the Thamer study, their validation cohort had an area under the receiver operating characteristic curve (AUROC) = 0.691 for their risk scoring tool while this study showed an AUROC = 0.6245, 0.2847, and 0.5993 in the 3-month, 6-month, and over-all mortality groups respectively which does not show statistical strength.

Conclusion: Patients with older age, comorbidities such as heart failure, cancer, asthma, and those who need assistance in daily living had higher mortality rates. Despite the poor performance of the Thamer risk scoring tool in predicting mortality in terms of AUROC in this study, the sensitivity, and specificity had a similar performance in the Thamer study. Furthermore, the consistent trend of accuracy of predicting mortality in these groups reflect that a higher score portends to a higher accuracy in predicting mortality.

REFERENCE

Figure 1: Contrast injected into the right renal pelvis moved to duodenum during nephrostomy tube placement, confirming a fistulous connection.

Figure 2: Macroscopic evidence of the pyelo-duodenal fistula after nephrectomy, with necrotic area surrounding the hiatus (arrows). Evidence of fibrotic renal parenchyma.
#3546

**“SURPRISE QUESTION”: IS IT A USEFUL TOOL IN CKD STAGES 4 TO 5?**

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**Background and Aims:** The “Surprise Question” (SQ) (“would you be surprised if this patient died in 6 months/year?”) has proven to be an interesting prognostication tool in a range of settings. However, its reliability in non-dialysis-dependent CKD is still unclear. Our aim was to study the applicability of the SQ to an outpatient CKD-EPI stages 4 to 5 and correlate it with mortality.

**Method:** Observational, prospective and single center study. Baseline comorbid conditions, cause of CKD, degree of autonomy, literacy, social support and baseline laboratory values (i.e., serum creatinine/estimated glomerular filtration rate, serum albumin and hemoglobin) were collected.

**Results:** A total of 269 patients completed the study; mean age 65 years old; 256 patients (85.3%) had hypertension and 124 (41.3%) had diabetes. The main causes of renal disease were diabetic kidney disease (n = 53; 17.7%), hypertension (n = 15; 5%) and IgA nephropathy (n = 11; 3.7%). The etiology of kidney disease was undetermined for 24 patients (8.0%). Average CKD-EPI was 15.5 ± 7.4 mL/min/1.73 m². A total of 188 patients (63%) were independent for daily living activities and 68 (23%) were professionally active and 45 (16%) were accompanied by family members or caregivers in outpatient consultation to discuss and define the care of plan regarding end stage renal disease. Mean follow up time of the study was 365 ± 254 days, and 27 (9%) patients died during this time period. Using the SQ, providers responded Yes and No for 162 (54%) and 92 (31%) patients, respectively. There were no differences in CKD-EPI stage, arterial hypertension, cerebrovascular disease and dyslipidemia. The No group was older (73 ± 16 vs. 63 ± 16, p = 0.001) and had more diabetes (n = 46, 55%, p = 0.015). About 8 (30%) and 18 (67%) of Yes and No patients died, respectively (P > 0.001). In the Cox-proportional hazard model adjusted to diabetes, the risk of all-cause mortality was significantly increased by around 55%, p = 0.001. Among patients on chronic dialysis therapy (KRT), cardiovascular events, risk of requiring kidney replacement therapy (KRT), cardiovascular events and death. Our aims was validation of the Grams score as a prognostic tool in patients with CKD G4 aged over 65 years old in our hospital area.

**Conclusion:** SQ proved to be a support tool in order to identify patients at high risk of death, who might not have a full benefit of starting dialysis. The choice around kidney replacement therapy is a shared decision-making process, in which competing risks and benefits must be considered. It is essential and urgent to identify means of support for patients, caregivers and health providers to provide and discuss personalized prognostic information.

Figure 1: Cox Regression showing the cumulative survival outcome, according to the “Surprise question” answer at baseline.

#3348


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**Background and Aims:** Little is known about the prevalence of chronic kidney disease (CKD) during the coronavirus disease 2019 (COVID-19) pandemic, as well as the pandemics’ impact on CKD diagnosis. We aimed to investigate the long-term trends in CKD prevalence throughout the pre- and early pandemic periods in adults using a nationwide serial survey from South Korea.

**Method:** We used data from 108,152 Korean adults from 2007 to 2020 obtained from a representative longitudinal serial study. We defined CKD as a condition when the participant's estimated glomerular filtration rate was < 60 mL/min/1.73 m², one-time point proteinuria was ≥ 1+ on a urinary dipstick test according to recent guidelines, or previous diagnosis of CKD. We examined the overall trends in the prevalence of CKD during the study period and the impact of the early pandemic on the prevalence of CKD.

**Results:** Among the included adults (n = 80,010), the overall national prevalence of CKD was 6.2%. The trend slope gradually increased from 2007 to 2019, however, there was a sudden decrease in 2020 (2007–2010, 5.1%; 95% confidence interval (CI), 4.7–5.5%; 2017–2019, 7.1% [95% CI, 6.6–7.6]; pandemic period, 6.5% [95% CI, 5.7–7.3]; and βdiff, -0.19; 95% CI, -0.24–0.13). The prevalence of CKD among younger adults and those with poor medical utilization significantly decreased during the early pandemic.

**Conclusion:** This study was the first large-scale study to investigate the longitudinal prevalence of CKD from 2007 to 2020. Our results improve the understanding of outpatient health service utilization during the COVID-19 pandemic and suggest the need for governmental support to prevent the aggravation of CKD in society. Consequently, the nephrology community has a potential role in pertinent policies to reduce the public health burden of CKD by properly allocating limited medical resources.

#4031

**VALIDATION OF THE GRAMS MODEL AS A PROGNOSTIC TOOL IN ADVANCED CHRONIC KIDNEY DISEASE (ACKD)**

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Spain

**Background and Aims:** Elderly patients with Advanced Chronic Kidney Disease (ACKD) present high cardiovascular comorbidity and increased mortality risk. The CKD-G4+ risk calculator was developed by Grams specifically for the population with CKD-G4 and analyzes the risk of requiring kidney replacement therapy (KRT), cardiovascular events and death. Our aims was validation of the Grams score as a prognostic tool in patients with CKD G4 aged over 65 years old in our hospital area.

**Method:** Descriptive and retrospective non-randomized study of a cohort of patients older than 65 years with CKD G4 attending for the first time for consultation during 2016 and 2017. Follow-up for 4 years or first clinical event defined as need for KRT, eGFR < 8 mL/min/1.72 m² or death. Demographic and clinical data were collected for Grams model risk calculation (age, sex, CKD-EPI eGFR, urine albumin/creatinine ratio (CAC), systolic blood pressure (SBP), diabetes, smoking, cardiovascular history, non-fatal cardiovascular event (CHF, AMI, stroke) and death). SPSS statistical analysis.

**Results:** Of 663 patients who started follow-up in ACKD consultations in our hospital area between 2016 and 2017, 303 patients who met inclusion criteria were analyzed, 31 were excluded due to loss to follow-up. The clinical characteristics of the studied population are collected in Table 1. The results are collected in Table 2, they include predicted and observed incidences of death, KRT onset and cardiovascular events in 2 and 4 years from the first visit. Predictors used in this study included Grams calculator risk scores at 2 and 4 years (Grams-2 and Grams-4, respectively) for any KRT, cardiovascular events, and death.

**Conclusion:** In our cohort of patients with G4 ACKD older than 65 years old, the Grams score provides good discrimination to significantly predict the onset of KRT and cardiovascular events. The risk of death was moderately accurate and should be taken into account for care planning. Further external validation studies are required.
Erectile dysfunction is a frequent problem and is associated with an increase in arterial stiffness and an increase in the incidence of erectile dysfunction. Moreover, erectile dysfunction was more common in patients with increased PWV.

Table 2: Predicted and observed 2-year and 4-year KRT, death and cardiovascular (CV) events.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Median(IQR)</th>
<th>Value p</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRT/No KRT</td>
<td>31.5(23.4-32.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Death/No death</td>
<td>31.5(16.77-30.32)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CV Events/No CV Events</td>
<td>28.9(20.45-37.65)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
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#4112 PULSE WAVE VELOCITY AND ERECTILE DYSPNFUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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**Background and Aims:** Erectile dysfunction is a frequent problem and adversely affects quality of life. In recent years, it has been shown to be an early indicator of cardiovascular disease and endothelial damage. For patients with chronic kidney disease, the incidence of cardiovascular events is increased, and erectile dysfunction is also more frequent. In this study, we evaluated patients with chronic kidney disease and the incidence and the association of erectile dysfunction with pulse wave velocity (PWV) and reflection wave parameters.

**Method:** The incidence of erectile dysfunction was examined with the use of IIEF (5) Sexual Health Questionnaire in adult male patients aged less than 65 years with chronic kidney disease stage I-V or a history of kidney transplantation that were actively monitored or treated as outpatients. Peripheral blood pressure, central blood pressure, PWV and reflection wave parameters (augmentation pressure and augmentation index) were evaluated using the Mobil-o-graph device in office measurements.

**Results:** Overall, 69 men with a mean age of 46.5 ± 11.79 years were included in the study. Chronic kidney disease (CKD) classification according to baseline eGFR calculation was as follows: 12 patients with CKD-I, 27 with CKD-II, 12 with CKD-III, 6 with CKD-IV and 12 with CKD-V on maintenance hemodialysis. Erectile dysfunction of all degrees (mild to severe) was detected in 52% of patients. From the correlation of the various parameters assessed with the degree of erectile function, as calculated by the IIEF questionnaires, it was found that the renal function as estimated by eGFR showed a positive correlation (r = 0.24, p = 0.047), while age and PWV showed a negative correlation (r = -0.384, p = 0.002 and r = -0.474, p < 0.001 respectively). Moreover, pulse wave velocity was the only parameter which could predict erectile dysfunction (β = -0.995, 95% CI -0.465 to -10.074, p = 0.032).

**Conclusion:** The results of the study showed that worsening kidney function is associated with an increase in arterial stiffness and an increase in the incidence of erectile dysfunction. Moreover, erectile dysfunction was more common in patients with increased PWV.

#5340 ASSOCIATION BETWEEN PARABEN EXPOSURE AND INDEX OF CHRONIC KIDNEY DISEASE (CKD) AMONG THE GENERAL TAIWANESE POPULATION

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Background and Aims: Exposure to consumer chemicals has been associated with chronic kidney disease (CKD) among humans, but their associations with estimated glomerular filtration rate (eGFR) are inconsistent. We aimed to assess the relationship between paraben exposure and renal function including the serum level of blood urea nitrogen (BUN), and the urinary levels of microalbumin, albumin, protein, and creatinine from a population-based study.

Method: We enrolled 310 participants (≥18 y, N = 240; <18 y, N = 70) who provided questionnaire information as well as blood and urine samples from a nationally representative study. Urinary parabens including methylparaben (MeP), ethylparaben (EtP), propylparaben (PrP), and butylparaben (BuP) are measured by liquid chromatography/tandem mass spectrometry. From the renal function index, we measured the serum level of blood urea nitrogen (BUN), and the urinary levels of microalbumin, albumin, protein, and creatinine. We used multiple logistic regressions to evaluate the relationship between paraben exposure and renal function in our participants.

Results: Median levels of urinary MeP; EtP; PrP and BuP in adults were 399 [interquartile range (IQR) = 257–611], 38.3 (IQR = 25.9–62.2), 115 (IQR = 74.6–160) and 6.60 (IQR = 4.42–9.42) ng/mL, respectively, which were significantly lower than those in children/adolescents (MeP: 186 (IQR = 6.92–453); EtP: 13.0 (IQR = 0.05–38.1); 60.3 (IQR = 0.62–101); 2.65 (IQR = 0.73–7.84) ng/mL (all P <0.001). Multivariate regression models adjusted for the same confounding factors confirmed the association of BUN and eGFR with urinary EtP with a log-linear relationship (β: 0.137; 95% CI = 0.003 to 0.272; β: -0.101; 95% CI = -0.202 to -0.001), which means BUN increased by 0.137 × 10^-2 mg/dL and eGFR decreased by 0.0 × 10^-2 mL/min/1.73 m^2 with a 1% increase in urinary EtP level, respectively. The multiple logistic regression showed that the adjusted odds ratio of the higher EtP and PrP level (median) in participants ≥18 y for lower eGFR (eGFR <90 mL/min/1.73 m^2) was 1.86 and 1.87 times (95% CI = 1.03–3.34 and 1.04–3.37) than the lower group, respectively.

Conclusion: Our findings suggested that daily exposure to EtP were significantly positively associated with an increased risk of higher BUN and lower eGFR in Taiwanese ≥18 y. Comprehensive or mechanistic studies are required to elucidate these associations.

#3922 CLINICOPATHOLOGICAL CHARACTERISTICS OF LIGHT AND HEAVY CHAIN DEPOSITION DISEASE: A CASE SERIES FROM A SINGLE CENTER

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Background and Aims: Light and heavy chain deposition disease (LHCDD) is the rarest form of monoclonal immunoglobulin deposition disease (MIDD) characterized by the deposition of the monoclonal light chain and heavy chain. At present, the large-scale clinical research data of LHCDD is limited. We explore the clinicopathological characteristics and outcome of LHCDD in a single center of China, to obtain a better understanding of this disease.

Method: We reviewed 65291 native kidney biopsies from January 2008 to December 2022. Ten patients with biopsy-proven LHCDD diagnosed were studied retrospectively.

Results: 4 males and 6 females, with an average age of 52.5 ± 8.9 years were enrolled. The patients were presented with hypertension (80%), anemia (90%), elevated serum creatinine (70%), proteinuria (100%), nephrotic syndrome (30%) and microscopic hematuria (90%). Serum immunofixation electrophoresis showed that 8 (80%) patients were positive for monoclonal immunoglobulin (IgG-κ/IgG-λ/IgA-κ/IgA-λ: 3/2/3). Serum free light chain (FLC) ratio was abnormal in 9 (90%) patients. Among them, 5 patients had an Elevated FLC ratio (κ:χ > 1.65), and an FLC ratio χ<0.20 was observed in 1 patient. Two patients were diagnosed with multiple myeloma. Histologically, nodular mesangial sclerosis was identified in 9 (90%) patients. Immunofluorescence showed that 6 patients had deposits of heavy chain IgG (γ-κ/κ-γ/κ-λ/κ-κ/λ-κ/λ-κ: 2/1/1/1/1/1), and 4 patients of heavy chain IgA (κ-κ/κ-κ/κ-κ/κ-κ/κ-κ: 2/1/1/1/1/1). During a median of 28 months of follow-up (range, 6–104 months) in 9 patients, 8 patients received chemotherapy. Three (33%) patients had complete hematologic remission (CR), 2 (22%) had very good partial hematologic response (VGPR) or partial hematologic response (PR), and 4 (44%) had no response (NR). One (11%) had stable/improved renal function, 6 (67%) had worsening renal function, and 3 (33%) progressed to ESRD. All 9 patients survived.

Conclusion: In this case series of LHCDD in a single center in China, light and heavy chain deposition in renal tissues was most frequent with IgG-κ, followed by IgA-κ, IgG-λ and IgA-κ. More than half patients had hematologic response but poor renal prognosis.

#5932 BALKAN ENDEMIC NEPHROPATHY AND MALIGNANT TUMOR OF THE UPPER TRACT UROTELIUM: AFTER 45 YEARS

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Background and Aims: Balkan endemic nephropathy (DEN) is a chronic progressive tubulo-interstitial kidney disease of unknown etiopathogenesis described more than 65 years ago. One of the general importance of the disease is the association with malignant tumors of the upper urothelium (MUUT). Epidemiological monitoring of BEN and MUUT plays a particularly important role. In the works published so far, there is a large discrepancy in the results of epidemiological works in relation to the researchers, the period and the region of observation. The aim of this paper was to examine the occurrence of MUUT in endemic settlements for BEN and the ratio of tumor frequency in endemic and non-endemic settlements of the Jablanica district.

Method: The observed research period is from 1978 to 2022. During the study of the frequency of MUUT (malignant tumors of the upper urothelium), the operative material of the urological service of the Leskovac General Hospital was used. The patients were divided according to their place of residence from individual settlements in the Jablanica district, and data from the Nephrology Clinic of the Urgent Clinical Center of Nis were used to classify the settlements: A: endemic settlements of patients with BEN (Balkan endemic nephropathy); B: hypoendemic settlements; C: non-endemic urban and D: non-endemic rural settlements. Some of the analyzes in this work were carried out so that groups A, B are unique endemic and C, D are non-endemic settlements. Data on the total number of inhabitants of the Jablanica district were obtained based on official data from the population census in 1981, 1991, 2002, 2011 and 2022. The incidence rate was calculated per 100,000 inhabitants. For practical reasons, the observed period is divided into the first (1978-2002) and the second (2003-2022).

Results: In the period from 1978 to 2022, 106 MUUT (55 men and 51 women) were registered in the Jablanica district, and the PGSI was 0.924. In endemic settlements (A) there were 14, hypoendemic (B) 10, non-endemic urban (C) 25 and in non-endemic rural (D) 57 MUUT. In the first observation period, the PGSI in Jablanica district was 1.3, and in the second, 0.93. In endemic settlements (A) in the first period, the frequency of MUUT was 9.1 times higher than in the second (17.56/1.93), while in hypoendemic ones (B) the frequency was 3.2 times higher in the first compared to the second observation period (5.06/1.58). In the last five years of observation (2018-2022), not a single MUUT was registered in the Jablanica district, and in the endemic settlements (A,B) only three tumors were registered in the last 25 years. In the observed period, the linear trend in endemic settlements (A) was in a statistically significant decline (y = -0.0276+55.691; r2 = 0.2128), while in the first period (1978-2002) it was in a statistically weak decline (y = -0.0054+0.59; r2 = 0.0031) and in the second period (2003-2022) it is not valid because only one tumor was registered. In the observed period, the linear trend of BEN incidence was in a statistically significant decrease (y = -0.164×+6.0669; r2 = 0.5788).

Conclusion: The high frequency of MUUT in endemic settlements for BEN in the first period of observation, perhaps indicates a common nephropathogenic and carcinogenic etiological factor, and therefore the more correct name of the disease may be Balkan nephroprourophy. In the observed period, we have a large discrepancy in results compared to the observation periods, and one of the main reasons is the drastic decrease of patients with BEN in endemic settlements, and the reasons should be sought in the lower toxicity of the causative agent, better water supply, better health awareness of patients, health and construction prevention and not having marriage between-at-risk patients. Is BEN disappearing?
"PRIMUM NON NOCERE": DIGITAL TOOLS AND MENTAL LOAD IN CLINICIANS AND PATIENTS: THE "E3 TASK FORCE" PROJECT
Corinne Isnard Bagnis1,2

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Background and Aims: The Covid 19 pandemia has been an extremely potent enhancer of digital health solutions spreading. Telemedicine was already available in France before SARS-COV2, but not used as a standard of care. It seems like when sticking to the expressed needs and objectives, the implementation of digital solutions became a reality with a high level of acceptability. Since e-health is spreading and the commercial offer of digital solutions dramatically increasing, it seems critical to predict the impact of those new tools on mental load of users in order to make sure digital solutions really bring better quality of care together with quality of life (patients) or professional life (health care professionals).

Method: Assistance publique - Hôpitaux de Paris launched in 2022 an ambitious project focusing on digital innovation at Hotel Dieu, making the largest hospital in Europe also an active promotor of digital health. This project includes an Innovation Hub, a large incubator for Start-ups, and (among others) the Digital Medical Hub (DMH). DMH is combining an academic platform dedicated to promoting scientific research on E-health and an open innovation structure promoting transformation strategies for e-health projects. Academic DMH initiated (March 2022) an innovative project aiming at defining what are the critical parameters involved into the lived experience of e-health users (clinicians and patients) with regard to mental load. This project included 3 steps: 1) a "consensus of experts" strategy conducted through meetings allowing the group to provide a list of the main dimensions impacting the (positive or negative) changes observed on daily life and mental load. The group includes neurosciences experts, clinicians (nephrologist, cardiologist, psychiatrist), e-health and digital solution experts, neuroergonomics and ergonomics experts, work psychologists, health economy specialist, market access experts). The following task of the group is to identify among those dimensions, those that are measurable or propose a way to evaluate them. 2) In parallel, a large opinion barometer is spread among health care professionals (HCP), digital entrepreneurs, and stakeholders in the field of health in order to collect over 500 answers allowing to describe expectations, fears and representations about e-Health implementation in France. 3) The last step of our research project is experimental with semi structured interviewing of health care professionals in two different hospitals to explore the experience of actors exposed to digital solutions usage daily. The expert group conducting this research has turned into a Task Force to build the research plan for the next steps, after publishing the first conclusions of this work in the form of a "white book".

Results: A white paper is under review describing the dimensions identified by the consensus of experts group as impacting mental load of HCP and, when available, the tools for quantitative assessment of impact. The result of the opinion barometers will be available in June and the qualitative study if ongoing.

Conclusion: Sharing this experience is shedding light on the importance for the Nephrology community to think about how to take part to the digital revolution in the field of Nephrology. There is incredible need for training and teaching to develop a commun culture about digital health. Patients and professionals should explore and express needs for digital tools in order to act as promoters of the digital transformation of health system.
in unadjusted (HR 2.35; CI 95% 0.61–9.15) and adjusted (HR 1.29; CI 95% 0.30–5.56) Cox proportional hazard models. As a continuous variable, each mL·kg\(^{-1} \cdot \text{min}^{-1}\) increase in VO\(_2\text{peak}\) was not associated with mortality risk (HR 0.94; CI 95% 0.79–1.11). Univariate Kaplan-Meier analysis showed that severe CRF patients did not have significantly worse survival rates than those with mild-moderate CRF (p = 0.186).

**Conclusion:** Our findings indicated that severe CRF was not associated with all-cause mortality in patients receiving HD. Despite severe CRF being prevalent, larger cohort studies are needed to establish strong conclusions on its association with all-cause mortality.

#4028

INSIDE CKD: PROJECTING THE POPULATION LEVEL CLINICAL BURDEN OF CHRONIC KIDNEY DISEASE ACCORDING TO URINE ALBUMIN-TO-CREATININE RATIO CATEGORIES

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**Background and Aims:** Chronic kidney disease (CKD) and its associated complications constitute a major challenge for healthcare systems worldwide. Albuminuria, measured as albumin-to-creatinine ratio (uACR), is a critical marker of glomerular injury and endothelial dysfunction. Elevated uACR is an independent predictor of CKD progression and cardio-renal mortality [1,2]. However, there is a paucity of data translating the burden of CKD at the population level according to uACR categories, in order to promote evidence-based policies. This study aims to assess the future epidemiological and financial burden of CKD using the Inside CKD microsimulation [3]. Specifically, we report CKD population level projections for cardio-renal complications, progression to end stage kidney disease (ESKD), and death due to any cause according to uACR categories.

**Method:** The Inside CKD microsimulation was used to simulate virtual individuals from 28 countries and regions. Individuals were assigned baseline characteristics such as age or sex based on national statistics, and estimated glomerular filtration rate (eGFR), uACR, CKD stage, and cardio-renal complications based on data from national health surveys or epidemiological studies. The following cardio-renal complications were projected between 2022 and 2027 according to uACR categories (normo-, micro-, macro-albuminuria): myocardial infarction (MI), stroke, heart failure (HF), CKD transition from stage 3 to 4 and from 4 to 5 (defined as a change in either eGFR or uACR category), and death due to any cause.

**Results:** Projected estimates for the total CKD population (all stages) with macro-albuminuria varied by country and region for 2023 (mean = 9.8%, range = 1.6% – 40.2%). The lowest percentages of macro-albuminuria (< 5%) were in Romania, Belgium, and the UK, compared to the highest (≥ 27%) in Brazil, Philippines and Mexico. Macro-albuminuria is associated with a higher relative risk of cardio-renal outcomes on a per person basis, but according to these estimates only a small proportion of the population have macro-albuminuria. Hence, the predominant CKD population with normo- or micro-albuminuria would be expected to account for most of the clinical burden. Accordingly, most of the cardio-renal incident events projected to occur by 2027 will be in the population with normo- or micro-albuminuria in all countries and regions (Figure 1): MI (97.9%), stroke (96.5%), HF (98.0%), the transition from CKD stage 3 to 4 (94.9%) and from stage 4 to 5 (97.5%), and death due to any cause (95.6%) (percentages represent mean and included the combined normo- and micro-albuminuria populations).

**Conclusion:** Although, macro-albuminuria is associated with a higher relative risk of cardio-renal outcomes on a per patient basis, the total CKD population should be considered with regards to the clinical burden in absolute terms. The Inside CKD microsimulation supports early intervention in the total CKD population, including individuals with normo- or micro-albuminuria, to reduce cardio-renal outcomes, delay progression to ESKD, and therefore the requirement for costly interventions, including heart related hospitalisations, transplantation and dialysis.
REFERENCES


#4875
MANAGEMENT OF TUBULOINTERSTITIAL DISEASE IN PREGNANCY: TEN-YEARS EXPERIENCE OF A NEPHRO-OBSTETRIC CLINIC
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Equal contribution: Estela Nogueira and Nadiesda Peres

Background and Aims: Tubular renal acidosis and salt losing nephropathies are rare conditions but their management during pregnancy that can be challenging due to the physiological adaptation of kidney function. Herein, the authors report the management and outcomes of 7 gestations in patients with Gitelman disease (GS) and renal tubular acidosis (RTA).

Method: Retrospective analysis of maternal, obstetric and perinatal outcomes of pregnant women with tubulo-interstitial diseases surveilled at our Nephro-Obstetric clinic from 2011 to 2021.

Results: We evaluated 7 pregnancies in 5 women. Mean age was 29 years [21-36]. They were all caucasian. Genetic diagnosis was performed during pregnancy in only one patient. Tubular disorder was caused by Gitelman disease in 3 patients and by renal tubular acidosis in 2 patients (ATP6VA4 and REN genes mutations). There were 4/1 patients in CKD G1/G3a, respectively, and none developed renal function deterioration. Only one patient developed transient proteinuria during both gestations and all patients had a low blood pressure profile. Management during the first trimester was especially challenging in GS patients, due to nausea, vomiting and hyperemesis gravidarum, which required hospital admission for intravenous potassium chloride therapy in all GS patients during the first trimester. Potassium levels in GS patients were generally below normal levels throughout pregnancy (mean 3 meq/L, 2.2-3.4 meq/L), even with progressive increase in therapy. Pre-pregnancy potassium chloride replacement increased from 4–10 tablets of 600 mg/day to a maximum of 9–21 tablets/day. One patient was also treated with spironolactone. The need for oral magnesium slightly increased from 2–3 ampoules of 1500mg/day to 2–4 ampoules/day. GS patients frequently developed transient proteinuria during both gestations and all patients had a low blood pressure profile. Management during the first gestation was especially challenging in GS patients, due to nausea, vomiting and hyperemesis gravidarum, which required hospital admission for intravenous potassium chloride therapy in all GS patients during the first trimester. Potassium levels in GS patients were generally below normal levels throughout pregnancy (mean 3 meq/L, 2.2-3.4 meq/L), even with progressive increase in therapy. Pre-pregnancy potassium chloride replacement increased from 4–10 tablets of 600 mg/day to a maximum of 9–21 tablets/day. One patient was also treated with spironolactone. The need for oral magnesium slightly increased from 2–3 ampoules of 1500mg/day to 2–4 ampoules/day. GS patients frequently complained of astenia and cramps. Regarding RTA patients, there was also a need to increase sodium bicarbonate dosage from 3–4.5g/day to a maximum of 2–3g/day. Regarding obstetric and perinatal outcomes, none of the patients developed preclampsia, mean gestational age at delivery was 40 weeks (38-41), mean birth weight was 3233g (2775-3825) and mean Apgar score was 10/10/10 at 1st, 5th and 10th minutes respectively.

Conclusion: In GS patients, management in the first trimester of pregnancy can be challenging due to nausea and vomiting, generally requiring admission for therapy with iv potassium. In spite of increasing doses in oral supplementation, ionic and acid base homeostasis during pregnancy is difficult to achieve. In our small series, maternal, obstetric and perinatal outcomes do not seem to be affected by this unbalance.
Table 1: CKD-EPI Equations to estimate 24h urine creatinine, Na, K and protein.

<table>
<thead>
<tr>
<th>Equation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine - CKD-EPI</td>
<td>Estimated 24h-urine creatinine (mg/24h) ( (\text{eCr}_{24h}(\text{CKD-EPI})) = 879.89 + 12.51 \times \text{weight (kg)} - 6.19 \times \text{age} + (34.51 \times \text{if black}) - (379.42 \times \text{if women}). )</td>
</tr>
<tr>
<td>Na - CKD-EPI</td>
<td>Estimated 24h-urine Na (mEq/24h) ( (\text{Na}<em>{24h}(\text{CKD-EPI})) = N</em>{\text{calc}} \times e\text{Cr}<em>{24h}(\text{CKD-EPI}) / C</em>{\text{Cr}}/10 )</td>
</tr>
<tr>
<td>K - CKD-EPI</td>
<td>Estimated 24h-urine K (mEq/24h) ( (\text{K}<em>{24h}(\text{CKD-EPI})) = K</em>{\text{calc}} \times e\text{Cr}<em>{24h}(\text{CKD-EPI}) / C</em>{\text{Cr}}/10 )</td>
</tr>
<tr>
<td>Protein – CKD-EPI</td>
<td>24h-urine protein (mg/24h) ( (\text{Protein}<em>{24h}(\text{CKD-EPI})) = \text{Protein}</em>{\text{calc}} \times e\text{Cr}<em>{24h}(\text{CKD-EPI}) / C</em>{\text{Cr}}/100 )</td>
</tr>
</tbody>
</table>

C4 - CO-MORBIDITIES (ANAEMIA, CARDIOVASCULAR, CKD-MBD, ETC.)

#2962

Efficacy and Safety of Roxadustat in Non-Dialysis-Dependent CKD Patients With or Without Inflammation: A Pooled Analysis of Four Phase 3 Studies

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Background and Aims: Chronic kidney disease (CKD)-associated anemia is commonly treated with erythropoiesis-stimulating agents (ESAs); however, some patients respond inadequately to ESAs. Inflammation may be a cause of ESA hyporesponsiveness. Roxadustat, an oral medication, is a hypoxia-inducible factor prolyl hydroxylase inhibitor that has shown efficacy in patients with anemia of CKD. This pooled analysis examined the efficacy and safety of roxadustat in correcting hemoglobin (Hb) levels in subgroups of patients with anemia of CKD regardless of inflammation status.

Method: Data from four phase 3, randomized, placebo-controlled (OLYMPUS [NCT02174627], ALPS [NCT01887600], ANDES [NCT01750190]) or erythropoiesis-stimulating agent–controlled (ESA; DOLOMITES [NCT02021381]) studies in patients with NDD CKD were pooled for this analysis. Mean Hb change from baseline to Weeks 28–52 was greater with roxadustat than with placebo, and comparable between roxadustat and ESA, regardless of inflammation at baseline (Fig. 1). At Week 24, roxadustat dose was not increased in patients across hsCRP quintiles (hsCRP quintiles 1–5: 3.3, 3.0, 2.7, 3.1, 3.1 mg/kg, respectively). Roxadustat dose was not significantly higher at Week 24 for patients with moderate-to-high baseline hsCRP levels (quintile 4, >3.48 to ≤5.17 mg/L; least squares mean [LSM], 3.05; 95% CI, 2.83–3.36) compared with patients with low baseline hsCRP levels (quintile 1, <0.71 mg/L; LSM, 3.04–3.56; treatment comparison between quintile 1 and quintile 4: LSM difference, 0.25; 95% CI, −0.11 to 0.61; treatment comparison between quintile 1 and quintile 5: LSM difference, 0.20; 95% CI, −0.17 to 0.57; Fig. 2), indicating that patients with increased inflammation at baseline did not consistently require a higher roxadustat dose. The overall percentages of patients responding inadequately to ESAs (≥1.5 g/dL for roxadustat (hsCRP quintiles 1–5: 9.17 [0.82], 9.26 [0.68], 9.18 [0.75], 9.15 [0.74], 9.08 [0.82]), placebo (hsCRP quintiles 1–5: 9.09 [0.74], 9.20 [0.71], 9.15 [0.69], 9.09 [0.71], 9.01 [0.76]), and ESA (hsCRP quintiles 1–5: 9.53 [0.69], 9.53 [0.64], 9.54 [0.73], 9.60 [0.66], 9.53 [0.71]) were similar across hsCRP quintiles. The mean Hb change from baseline to Weeks 28–52 was greater with roxadustat than with placebo, and comparable between roxadustat and ESA, regardless of inflammation at baseline (Fig. 1). At Week 24, roxadustat dose was not increased in patients across hsCRP quintiles (hsCRP quintiles 1–5: 3.3, 3.0, 2.7, 3.1, 3.1 mg/kg, respectively). Roxadustat dose was not significantly higher at Week 24 for patients with moderate-to-high baseline hsCRP levels (quintile 4, >3.48 to ≤5.17 mg/L; least squares mean [LSM], 3.05; 95% CI, 2.83–3.36) compared with patients with low baseline hsCRP levels (quintile 1, <0.71 mg/L; LSM, 3.04–3.56; treatment comparison between quintile 1 and quintile 4: LSM difference, 0.25; 95% CI, −0.11 to 0.61; treatment comparison between quintile 1 and quintile 5: LSM difference, 0.20; 95% CI, −0.17 to 0.57; Fig. 2), indicating that patients with increased inflammation at baseline did not consistently require a higher roxadustat dose. The overall percentages of patients with at least one treatment-emergent adverse event were similar across hsCRP quintiles for patients treated with roxadustat (hsCRP quintiles 1–5: 88.5, 87.9, 87.5, 87.7, 87.9, and ESA (hsCRP quintiles 1–5: 90.9, 91.4, 91.7, 91.9, 91.7). The most common treatment-emergent adverse events were hypertension (hsCRP quintiles 1–5 [%]; roxadustat: 16.8, 16.5, 17.4, 22.2, 18.9; placebo: 7.9, 9.5, 11.8, 9.3, 8.5; ESA: 45.7, 36.4, 39.7, 22.1, 31.2), end-stage renal disease (hsCRP quintiles 1–5 [%]; roxadustat: 21.3, 22.7, 21.1, 24.6, 23.1; placebo: 13.8, 15.9, 15.3, 18.1, 16.5; ESA: 32.6, 36.4, 34.5, 39.7, 36.4), and decreased glomerular filtration rate (hsCRP quintiles 1–5 [%]; roxadustat: 4.6, 5.0, 4.3, 5.3, 5.1; placebo: 2.0, 2.0, 2.4, 1.3, 3.1; ESA: 13.0, 22.7, 19.0, 13.2, 16.9).

Conclusion: Independent of baseline inflammation status, roxadustat increased Hb levels greater than placebo and comparable to ESA with a similar safety profile. Patients with high baseline hsCRP did not require increased roxadustat doses to maintain Hb levels up to Week 24. These data suggest that roxadustat is effective in patients with anemia of NDD CKD regardless of inflammation status.
PREVALENCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background and Aims: The presence of electrocardiogram (ECG) abnormalities is high in patients with end-stage kidney disease, but no studies have examined the prevalence of ECG abnormalities according to different strata of estimated glomerular filtration rate (eGFR) in a population-based setting.

Method: This was a retrospective cross-sectional study including 310,060 individuals from the Copenhagen General Practitioners’ Laboratory who had an available digital ECG recorded between 2001 and 2015 and a creatinine measurement within 7 days of the ECG. eGFR was calculated using the The Chronic Kidney Disease Epidemiology Collaboration equation. ECG abnormalities were categorized as no, minor or major, as done previously [1]. Patients with both minor and major ECG abnormalities were assigned as major ECG abnormalities. The prevalence of ECG abnormalities was examined according to different strata of renal function [eGFR (ml/min/1.73 m²) >90, 61–90, 46–60, 31–45, 30-16 and ≤15]. Ordinal logistic regression was used to illustrate the probability of ECG abnormalities as a function of eGFR.

Results: The median age was 55 [IQR, 41-69] years and 46% were male. A total of 47,249 (17.9%) of the included patients had an eGFR <60. The prevalence of major ECG abnormalities increased with declining eGFR: >90 (16.5%), 61–90 (21.6%), 46–60 (36.5%) 31–45 (52.1%), 30-16 (57.9%) and ≤15 (60.1%). Ordinal logistic regression, the risk of having major ECG abnormalities compared to minor/no abnormalities significantly decreased pr. 5 ml/min increase in eGFR, OR 0.90 (95% CI, 0.85-0.90), Fig. 1. The most common major ECG abnormalities were left ventricular hypertrophy and ST-T deviations. The prevalence of all ECG abnormalities is shown in Table 1.

Conclusion: ECG abnormalities are common in patients with chronic kidney disease, and the probability of major ECG abnormalities increases with declining eGFR.

Figure 1: Predicted probability of ECG abnormalities according to eGFR.
Table 1: Prevalence of ECG abnormalities.

<table>
<thead>
<tr>
<th>Minor ECG abnormality</th>
<th>Major ECG abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (median, iqr)</td>
<td>eGFR (ml/min/1.73 m²)</td>
</tr>
<tr>
<td>n = 105,105</td>
<td>n = 153,984</td>
</tr>
<tr>
<td>&gt;90</td>
<td>61-90</td>
</tr>
<tr>
<td>Males</td>
<td>53,221 (50.6)</td>
</tr>
<tr>
<td>Heart rate, bpm (median, iqr)</td>
<td>69 (61-78)</td>
</tr>
<tr>
<td>No ECG abnormality</td>
<td>82,968 (78.9)</td>
</tr>
<tr>
<td>Minor ECG abnormality</td>
<td>4782 (4.5)</td>
</tr>
<tr>
<td>First-degree atrioventricular block</td>
<td>1736 (1.7)</td>
</tr>
<tr>
<td>Incomplete bundle branch block</td>
<td>2420 (2.3)</td>
</tr>
<tr>
<td>Left fascicular block</td>
<td>1212 (1.2)</td>
</tr>
<tr>
<td>QTcF prolongation</td>
<td>1854 (1.8)</td>
</tr>
<tr>
<td>Major ECG abnormality</td>
<td>17,355 (16.5)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>9822 (9.3)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>663 (0.6)</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>1160 (1.1)</td>
</tr>
<tr>
<td>Intraventricular conduction disorder</td>
<td>725 (0.7)</td>
</tr>
<tr>
<td>Q waves</td>
<td>3560 (3.4)</td>
</tr>
<tr>
<td>ST-T deviations</td>
<td>2802 (2.7)</td>
</tr>
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REFERENCE


#2700

RENAI OSTEODYSTROPHY AND CLINICAL OUTCOMES: RESULTS FROM THE BRAZILIAN REGISTRY OF BONE BIOPSY

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Background and Aims: Mineral and bone disorders caused by chronic kidney disease (CKD-MBD) encompass biochemical/hormonal abnormalities, soft tissue calcifications and bone morphological changes known as renal osteodystrophy (ROD). Data from prior studies have consistently shown that patients with CKD-MBD are susceptible to an increased risk of mortality, bone fractures and major cardiovascular outcomes. This study is a sub-analysis of the Brazilian Registry of Bone Biopsy (REBRABO), a prospective, national multicenter cohort of patients with CKD who underwent bone biopsy, aimed at addressing the relationship between ROD type and the occurrence of bone fractures, hospitalizations, cardiovascular events, and a composite of all-cause mortality.

Method: During the period from August 2015 to December 2021, 511 patients with CKD who underwent bone biopsy and with diagnosis of ROD were included in REBRABO. Bone biopsy was indicated by medical reasons or research protocol. Were excluded from this analysis patients who lost their follow-up (N = 111), had no bone biopsy report (N = 40), had an estimated glomerular filtration rate > 90 mL/min (N = 28), not signed their consent (N = 24), had bone fragments inadequate for diagnosis (N = 23), had a bone biopsy indicated by a specialty other than nephrology (N = 6), or were < 18 years old (N = 4). Baseline was defined as the time when the patient underwent bone biopsy. The prospective analysis included data from patients who completed at least 12 months of follow-up. The mean follow-up was 1242 (693-1508) days. The following events were adjudicated: bone fractures, hospitalization, major cardiovascular events - MACES (unstable angina, nonfatal acute myocardial infarction, elective or emergency coronary revascularization, transient ischemic attack, stroke, and cardiovascular death), and death. Bone fragments were obtained via transiliac bone biopsies using an electrical trephine after prelabeling with tetracycline (3 days) administered over two separate periods. The samples were classified as osteitis fibrosa (OF), mixed uremic osteodystrophy (MUO), adynamic bone disease (ABD), osteomalacia (OM) and normal/minor alterations, according to TMV system. Cox regression analysis was performed to detect independent determinants of clinical outcomes.

Figure 1: Effects of bone turnover, mineralization, and volume on death outcome.

Cox regression analysis survival curves for death outcome. Variables tested in the models: age, previous cardiovascular disease, previous parathyroidectomy, proportion of patients out of the normal range for serum phosphate levels, plus: bone turnover (reference: high bone turnover) in (A), or bone mineralization (reference: abnormal bone mineralization) in (B), or bone volume (reference: low bone volume) in (C). Overall p = 0.0001.
Results: A total of 275 patients were included. This was a population with a mean age of 52 (42–60) years, 143 (52%) were men, 39 (14%) had diabetes, and 248 (90%) were on dialysis. During follow-up, a total of 28 bone fractures, 97 hospitalization events, 44 MACEs, and 70 deaths were reported, with incidence of 15.1% (4.4%/year), 49.5% (14.6%/year), 23.3% (6.85%/year) and 25.5% (7.5%/year), respectively. Patients who presented MACEs had lower serum hemoglobin levels [11.1 (9.6-12.6) vs. 12 (10.8-13.5; p = 0.026), higher prevalence of diabetes mellitus [11 (25%) vs. 15 (10%); p = 0.013] and previous cardiovascular disease [8 (18%) vs. 8 (5%); p = 0.008]. Age, previous cardiovascular disease, and proportion of serum phosphate levels out of the normal range were independent predictors for death [OR 1.046 (CI: 1.024-1.069), p = 0.0001; OR 1.856 (CI: 1.009-3.413), p = 0.04; OR 1.942 (CI: 1.116-3.379), p = 0.019; respectively]. Participants were grouped according to the ROD subtype as: OF (n = 113; 41%), ABD (n = 79; 29%), MUO (n = 59; 21%), OM (n = 12; 4%), and normal/Minor alterations (n = 12; 4%). ROD subtypes were not related to incident outcomes.

Conclusion: The incidence of bone fractures, hospitalizations, cardiovascular events, and of a composite of all-cause mortality did not differ between the types of ROD.

#5603
HYPERKALAEMIA MAY LIMIT POTENTIAL PARENTERAL INTERVENTIONS IN PATIENTS WITH LOW GFR AND SIGNIFICANT PROTEINURIA
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Background and Aims: Evidence-based therapies including ACE inhibitors, ARBs and mineralocorticoid receptor antagonists (MRA) can significantly delay progression of CKD, yet their use is potentially limited by hyperkalaemia risk. In this study, we describe hyperkalaemia events among CKD patients to provide a better understanding of the current unmet need.

Method: This was a retrospective secondary data analysis from electronic medical records (EMR) in the US TriNeXa analytics data CKD subset from Jan 2015-Dec 2019. Patients with ≥1 uACR measure were included, whereby the first date of the uACR measure was considered the index date. The study cohort included patients aged > 18 years with a) two consecutive estimated glomerular filtration rate (eGFR) values between 20 and 90 mL/min/1.73m² recorded 91–730 days apart prior to the index date, or b) at least one CKD diagnosis code before the index date. Patient demographics, ACE/ARB, MRA and SGLT2i treatments on index were described. The frequency of HK (defined as serum potassium > 5.5 mmol/L or a diagnosis code) during a 1-year baseline period and 1-year follow-up period was described by uACR (<700mg/g, 300–700mg/g, <300mg/g) and eGFR (<20mL/min/1.73m², 20–45mL/min/1.73m², 45–60mL/min/1.73m², 60–90mL/min/1.73m² and >90mL/min/1.73m²) categories.

Results: Baseline characteristics of the included patients are described in the table below. During the 1-year follow-up period, HK events were more frequently recorded for patients with uACR>700mg/g (15.3%), eGFR<60mL/min/1.73m² (9.3%) and combined uACR>700mg/g and eGFR<60mL/min/1.73m² (18.3%).

Conclusion: The preliminary results of this analysis shows that HK occurs more frequently among patients with low eGFR and/or high uACR. Despite guidelines, uACR testing is not done frequently in clinical practice and likely performed more frequently among patients with high uACR. Further analyses and more conservative study definitions will be applied to more comprehensively clarify the unmet need among patients at risk of HK. Of particular interest are the patients who discontinued RAASi treatment after a hyperkalaemia event during baseline and were not on renoprotective treatment, yet who had recurrent hyperkalaemia. Adequate treatment options for these patients are currently limited, and there is a need for more renoprotective treatments with limited hyperkalaemia risk.

Table 1: Baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>uACR &lt; 300 mg/g</th>
<th>uACR 300 - 700 mg/g</th>
<th>uACR &gt; 700 mg/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>185,458</td>
<td>163,674 (88%)</td>
<td>9,331 (5%)</td>
<td>12,453 (7%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>97,082 (52%)</td>
<td>87,317 (53%)</td>
<td>4,185 (45%)</td>
<td>5,580 (45%)</td>
</tr>
<tr>
<td>Female</td>
<td>88,376 (48%)</td>
<td>76,357 (47%)</td>
<td>5,146 (55%)</td>
<td>6,873 (55%)</td>
</tr>
<tr>
<td>Age at index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>65.6</td>
<td>65.7</td>
<td>66.0</td>
<td>63.4</td>
</tr>
<tr>
<td>Median</td>
<td>67</td>
<td>67</td>
<td>68</td>
<td>65</td>
</tr>
<tr>
<td>eGFR (in mL/min/1.73 m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR&lt;20</td>
<td>6,151 (3%)</td>
<td>3,234 (2%)</td>
<td>811 (9%)</td>
<td>2,106 (17%)</td>
</tr>
<tr>
<td>20 &lt;= eGFR&lt;45</td>
<td>38,542 (21%)</td>
<td>29,737 (18%)</td>
<td>3,388 (36%)</td>
<td>5,417 (44%)</td>
</tr>
<tr>
<td>45 &lt;= eGFR&lt;60</td>
<td>44,506 (24%)</td>
<td>39,958 (24%)</td>
<td>2,212 (19%)</td>
<td>2,336 (19%)</td>
</tr>
<tr>
<td>60 &lt;= eGFR&lt;90</td>
<td>90,716 (49%)</td>
<td>85,652 (52%)</td>
<td>2,700 (29%)</td>
<td>2,364 (19%)</td>
</tr>
<tr>
<td>90 &lt;= eGFR</td>
<td>3,452 (2%)</td>
<td>3,257 (2%)</td>
<td>105 (1%)</td>
<td>90 (1%)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>2,091 (1%)</td>
<td>1,836 (1%)</td>
<td>115 (1%)</td>
<td>140 (1%)</td>
</tr>
<tr>
<td>Co-morbidities (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>10,037 (5%)</td>
<td>7,158 (4%)</td>
<td>971 (10%)</td>
<td>1,908 (15%)</td>
</tr>
<tr>
<td>Type II diabetes mellitus</td>
<td>129,989 (70%)</td>
<td>113,319 (69%)</td>
<td>7,096 (76%)</td>
<td>9,574 (77%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>143,328 (77%)</td>
<td>125,311 (77%)</td>
<td>7,679 (82%)</td>
<td>10,338 (83%)</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>28,507 (15%)</td>
<td>23,940 (15%)</td>
<td>1,979 (21%)</td>
<td>2,588 (21%)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>19,296 (10%)</td>
<td>15,164 (9%)</td>
<td>1,648 (18%)</td>
<td>2,484 (20%)</td>
</tr>
<tr>
<td>Co-medication (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renin angiotensin aldosterone system inhibitor (RAASI)</td>
<td>45,586 (28%)</td>
<td>3,067 (33%)</td>
<td>4,247 (34%)</td>
<td>52,900 (28.5%)</td>
</tr>
<tr>
<td>SGLT2 inhibitors</td>
<td>3,188 (2%)</td>
<td>159 (2%)</td>
<td>178 (1%)</td>
<td>3,525 (2%)</td>
</tr>
<tr>
<td>Mineralocorticoid Receptor Antagonists</td>
<td>6,248 (4%)</td>
<td>534 (6%)</td>
<td>801 (6%)</td>
<td>7,583 (4%)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>56,751 (35%)</td>
<td>3,966 (43%)</td>
<td>5,954 (48%)</td>
<td>66,671 (36%)</td>
</tr>
<tr>
<td>Angiotensin-converting-enzyme (ACE) inhibitors</td>
<td>46,878 (29%)</td>
<td>3,152 (34%)</td>
<td>4,380 (35%)</td>
<td>54,410 (29%)</td>
</tr>
<tr>
<td>Angiotensin receptor blockers (ARBs)</td>
<td>33,582 (18%)</td>
<td>28,922 (18%)</td>
<td>1,882 (20%)</td>
<td>2,778 (22%)</td>
</tr>
</tbody>
</table>
ALBUMINURIA IN PATIENTS ADMITTED WITH HEART FAILURE IS ASSOCIATED WITH MORE SYSTEMIC CONGESTION ASSESSED BY ULTRASOUND

Natalia Kontareva, Yulia Khruuleva, Robinson Tsimine Andriamanohery, Irina Misan, Rena Aslan, Marina Efremovtsve, Svyatoslav Galochkin and Zhanna Kobalava

Russia

Background and Aims: Albuminuria is frequently observed in patients with heart failure (HF) and is associated with worse outcomes. New instrumental methods of congestion assessment in HF are superior in accuracy to physical examination and, therefore, are becoming the new standards for congestion registration. The relationship of albuminuria with congestion assessed by ultrasound in HF population is unclear. We aimed to investigate the relationship between albuminuria level and congestion measured by lung ultrasound (LUS) and Venous Excess Ultrasound (VExUS) at admission in patients with ADHF.

Method: In this prospective study we included 58 patients which were admitted with ADHF (typical signs and symptoms with NT-proBNP > 300 pg/ml). Patients with end-stage chronic kidney disease (CKD), malignancy were excluded. Routine clinical examination and laboratory tests, echocardiography, eight-zone LUS, and VExUS assessment of veins: caval inferior, hepatic, portal, and renal were performed. Patients were divided into two groups according to albumin/creatinine ratio at hospitalization: without albuminuria (uACR<30 mg/gCr) and with albuminuria (uACR>30 mg/gCr).

Results: 72% were male, mean age was 72 (55;79) (Me (IQR) years, 52% (n = 30) had reduced ejection fraction (EF), 77% - hypertension (HTN), 66% - atrial fibrillation (AF), 37% - diabetes mellitus (DM), 58% - coronary artery disease (CAD), 17% (n = 10) - previously known CKD. On physical examination at admission 67% (n = 39) patients had orthopnea,69% (n = 40) - exertional dyspnea, 53.4% (n = 31) - elevated jugular venous pressure, 91.4% (n = 53) - ankle edema, 50% (n = 29) - hepatomegaly and 82.8% (n = 48) pulmonary crepitations. Mean NT-proBNP was 2062 (13443246) (Me (IQR) pg/ml 49 (84%) had pulmonary congestion assessed by LUS (mean number of B-lines 34 (25;48)), 86% (n = 50) - congestion by VExUS, from which the majority of patients had the most severe, 3rd grade (1< - 32%, 2nd - 16%, 3rd - 52%). The prevalence of albuminuria was 65.5% (n = 38): 92% (n = 35/38) patients had albuminuria categories A2 and 8% (n = 3/38) had A3 category. Groups with and without albuminuria were similar in gender, age, prevalence of EF<40%, comorbidities, exertional dyspnea, orthopnea, elevated jugular venous pressure, hepatomegaly, pulmonary crepitations, levels of NT-proBNP and serum creatinine. Differences between groups with and without albuminuria were detected in the frequency of ankle swelling (100% (n =38/38) vs 75% (n = 15/20), p = 0.003). Patients with albuminuria had a trend to more frequently having pulmonary congestion than without albuminuria (89% (n = 34/38) and 75% (n = 15/20), p = 0.15 respectively). The prevalence of congestion assessed by VExUS was higher in patients with albuminuria (95% (n = 36/38) and 70% (n = 14/20), p = 0.090 respectively).

Conclusion: In patients hospitalized with ADHF albuminuria is associated with systemic congestion assessed by VExUS. The relationship between pulmonary congestion by LUS and albuminuria should be a matter of future studies.

RESULTS

ALBUMINURIA VS. SYSTEMIC CONGESTION ASSESSED BY LUS AND VEXUS

Comparison of patients with and without albuminuria and their congestive scores assessed by LUS and VExUS are shown in Table 1.

### Table 1: Comparison of Patients with and without Albuminuria and Their Congestive Scores

<table>
<thead>
<tr>
<th>Category</th>
<th>Albuminuria (n = 38)</th>
<th>Without Albuminuria (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF &lt; 40%</td>
<td>92% (35/38)</td>
<td>75% (15/20)</td>
<td>0.15</td>
</tr>
<tr>
<td>Pulmonary Congestion</td>
<td>86% (50/58)</td>
<td>70% (14/20)</td>
<td>0.090</td>
</tr>
<tr>
<td>LUS congestion</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Discussion

The results of this study suggest a significant association between albuminuria and systemic congestion assessed by LUS and VExUS. This association is independent of conventional clinical variables such as age, sex, and EF. The higher prevalence of pulmonary congestion and lower EF in patients with albuminuria is consistent with previous findings [1, 2]. The higher prevalence of pulmonary edema in patients with albuminuria may be due to increased capillary permeability or decreased clearance of albumin. These findings support the hypothesis that albuminuria is a marker of increased capillary permeability and decreased clearance of albumin, which may contribute to the development of pulmonary congestion in patients with ADHF.

ACKNOWLEDGMENTS

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REFERENCES


#3777

ACTIVATION OF HYPOXIA-INDUCIBLE FACTORS IN ERYTHROID PROGENITOR CELLS RESULTS IN DEFECTIVE ERYTHROPOIESIS

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Background and Aims: Hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) activates HIF in renal pericytes and fibroblasts to promote erythropoietin production and erythropoiesis. However, the effects of HIF stabilization in the erythroid lineage are not clear. We aim to study the effects of erythroid lineage-specific stabilization of HIF on erythropoiesis by preclinical models.

Method: EpoGFP-Cre/+;VhIF/F mice were used to achieve erythroid lineage-specific stabilization of HIF. Surface expression of TER-119, CD44, and forward scatter (FSC) were used to define erythroblast, reticulocyte, and red blood cell in the bone marrow. Expression of propidium iodide and surface annexin V were used to define apoptosis. Stress erythropoiesis was induced by subcutaneous administration of phenylhydrazine.

RESULTS

Compared with littermate VhIF/F mice, EpoGFP-Cre/+;VhIF/F mice had decreased hematocrit, decreased percentage of erythroblasts in the bone marrow, and increased apoptosis of erythroblasts in the bone marrow under steady state. These phenotypes of defective erythropoiesis were normalized in mice harboring concomitant Vhl, Hif1a, and Hif2a deletion (EpoGFP-Cre/+; VhIF/F;Hif1a-/-;Hif2a-/- mice). Although macrophages in the bone marrow also express Epor, macrophage-specific Vh deletion in either Tg(Cay1r-CreERSt1);VhIF/F or Lyz2Cre-/-;VhIF/F mice did not result in defective erythropoiesis. During stress erythropoiesis, compared with littermate VhIF/F mice, EpoGFP-Cre/+;VhIF/F mice had similar hematocrit, lower percentage of erythroblast in the bone marrow, and increased percentage of erythroblast in the spleen.

Conclusion: Vh deletion in erythroid progenitor cells impairs erythropoiesis in murine bone marrow in the steady state. The phenotypes of defective erythropoiesis were partially reversed during stress erythropoiesis.
Conclusion: The results indicate the high P exposure could lead to an impairment of vascular health by causing decrease in miR-145 levels with the α-tocopherol supplementation. The results indicate the high P exposure could lead to an impairment of vascular health by causing decrease in miR-145 levels with the α-tocopherol supplementation.

#5864

EFFECT OF IV FERRIC CARBOXYMALTOSE ON PHYSICAL PERFORMANCE AND QOL IN PATIENTS WITH CKD NOT ON DIALYSIS, MILD ANEMIA AND IRON DEFICIENCY

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Background and Aims: Iron deficiency (ID) in patients with chronic kidney disease (CKD) is highly prevalent and contributes to a poorer quality of life. According to current guidelines, treatment with intravenous (IV) iron is limited to CKD patients with ID and anemia to avoid/delay the use of erythropoiesis-stimulating agents (ESAs) or the reduce the doses of ESA in patients treated with these drugs. Considering the effects of the correction of ID in other settings, we hypothetized that treatment with IV iron in patients with ID and borderline anemia can improve physical performance and their quality of life, independent of the effects on hemoglobin.

Method: Prospective, uncenteric, single-arm study in CKD patients with ID, mild anemia and with-out heart failure. The inclusion criteria were: age ≥ 18 years, CKD patients stages 3–5 not on dialysis, iron deficiency (ferritin <100 ng/ml or ferritin <200 ng/ml if TSAT <20%), mild anemia (Hb 10.5–11.5 g/dL). At the baseline visit, after all the studies were performed, IV ferric carboxymaltose was administered in a single dose, according to the degree of ID calculated by the Ganzoni’s formula. The co-primary outcome was the change in physical performance, evaluated through the 6 minute-walk test (6MWT) at one week and at four weeks. Secondary end-points: Patient’s global assessment (PGA) and quality of life (EQ-5D), Piper’s fatigue test, serum phosphorous at four week. Laboratory data, PGA, EQ-5D and Piper test questionnaires were evaluated at baseline, and at weeks 1 and 4 after receiving IV ferric carboxymaltose.

Results: 41 patients completed the study. Primary end-point: the 6MWT increased significantly from 296 ± 101 m to 314 ± 106 m at week 1 (p < 0.01), and to 325 ± 111 meters at week 4 (p < 0.01), at week 6 (p = 0.083). A significant improvement in the PGA test values was detected when compared baseline vs 4 weeks (adjusted p value = 0.031). No significant differences were found between the baseline and week 1 (adjusted p value = 0.083), and week 1 and week 4 visits (adjusted p value = 0.086). No significant differences were found between the initial, 1-week, and 4-week visits in the EQ-5D quality of life questionnaire nor Piper’s fatigue test. Phosphorus levels decreased significantly at week 1 from baseline (3.16 ± 0.7 vs 3.72 ± 0.6) (adjusted p <0.01), with a partial recovery of serum levels in week 4 (3.57 ± 0.7 mg/dL). There were no significant increases in hemoglobin concentration between the different time periods.

Conclusion: IV ferric carboxymaltose administration significantly improved the functional capacity of CKD patients with ID in short term. PGA also improved slightly but significantly. Effects that were independent of the functional capacity of CKD patients with ID in short term. PGA

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substantial variation across countries, from 7.3 in the UK to 45.6 in Thailand. For HD, the RBCT rate was 23.9 (95% CI: 23.3, 24.5), also higher than in ND-CKD, with international variation observed. In the HD cohort, RBCT rates were lower in China (6.3) compared to the US (8.9), Canada (17.4), and the Gulf Cooperation Council region (21.6). Within HD-Europe, RBCT rates were highest in Belgium (48.1) and Sweden (40.4), and lowest in Germany (15.4), France (19.0), and Italy (20.4).

As expected, however, rates of VAT were higher in IDD patients than PDD patients. Mean ages of the IDD and PDD cohorts were 70.3 and 63.3 years, respectively. Compared with the PDD cohort, patients in the IDD cohort were more likely be female (48.2% vs 45.7%), of non-Hispanic White race (61.6% vs 40.4%), less likely be of lower-income status (33.0% vs 47.4% for Medicare/Medicaid dual enrollment and 38.6% vs 57.0% for Part D low-income subsidy) and with higher proportion of comorbidities. First event rates are shown in the Table for the IDD and PDD cohorts. Compared with the PDD cohort, patients in the IDD cohort had higher rates of all-cause mortality (17.3 vs 16.8 per 100 patient-years), stroke (1.8 vs 1.4), VAT (109.4 vs 67.2 per 100 patient-years), and MACE (20.9 vs 20.3); however, they had lower rates of MI (3.1 vs 3.5), HF (7.1 vs 8.9), DVT (3.2 vs 4.0), and MACE+HF (25.6 vs 26.9). For non-CV events, patients in the IDD cohort had lower event rates for nearly all events except malignancies.

Conclusion: ESA-treated IDD patients had higher event rates for some CV events but lower rates for most non-CV events compared with PDD patients. As expected, however, rates of VAT were higher in IDD patients than PDD patients. These background event rates in real-world populations with wide ESA use provide context when considering potential alternative treatments for anemia. Limitation of this descriptive study includes the reporting of crude (unadjusted) rates, and therefore should be interpreted with caution. Funding: GSK (study 217316).

REFERENCES


ASSOCIATION BETWEEN CKD-MBD AND SYMPTOM BURDEN IN OLDER PATIENTS WITH ADVANCED CKD – RESULTS FROM THE EQUAL STUDY

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Background and Aims: Patients with advanced chronic kidney disease (CKD) typically develop a constellation of various non-specific symptoms known as the uremic syndrome. This symptom burden affects patients’ quality of life and is one of the most relevant reasons for initiating dialysis. Several factors are thought to be involved in symptoms development, including mineral bone disorder (CKD-MBD). However, evidence linking deranged mineral biomarkers and CKD symptoms is mostly limited to few symptoms in dialysis patients. We studied the association between PTH, phosphate and calcium and the overall symptom burden in a cohort of elderly non-dialysis patients with advanced CKD, during 5 years of follow up. Secondly, we investigated whether these biomarkers are specifically associated with a wide spectrum of CKD-related signs and symptoms.

Method: We used data from the EQUAL study, which included patients aged ≥65 with eGFR ≤20 ml/min/1.73m² from six European countries. Symptoms were repeatedly assessed at 6-month intervals through a questionnaire on 33 CKD-related signs and symptoms. Generalized linear mixed models were used to study the association between mineral biomarkers and the overall symptom number (range 0–33), the overall symptom severity (range 0–165, with higher scores indicating higher severity), the probability of having each symptom and its severity (range 1–5). Models were adjusted for age, sex, Charlson Comorbidity Index, kidney function, albumin, hemoglobin and CKD-MBD medications.

Results: At baseline, the 1396 patients included in the study had a mean (SD) of 12.6 (±6.4) symptoms and a median symptom severity score of 32 (19–50), with the most prevalent symptoms being fatigue, loss of strength, muscle cramps, bone pain, swelling in legs, dry skin, and sexual disorders. Among the mineral biomarkers, only PTH had a significant association with the overall symptom number and severity. Furthermore, a doubling in PTH was associated with an increased probability of reporting shortness of breath (OR 1.13 [1.01, 1.27], p 0.03) and decreased probability of loss of strength (OR 0.90 [0.81, 1.00], p 0.05). Both PTH and phosphate had significant U-shaped associations with gastrointestinal symptoms (decreased appetite, nausea, and vomiting). A doubling in phosphate level was linearly associated to the severity of muscle cramps (β 0.20 [0.06, 0.36], p 0.007) and bone pain (β 0.24 [0.09, 0.39], p 0.002), in patients who experienced these symptoms. Phosphate was also non-linearly associated with the probability of having trouble falling asleep. One mmol/L increase in calcium was associated with both a decreased probability of having muscle cramps (OR 0.50 [0.25, 0.98], p 0.04) and its severity (β -0.43 [-0.69, -0.17], p 0.001).

Conclusion: Serum levels of PTH are associated with the overall symptom burden in older non-dialysis patients with advanced CKD, and PTH, phosphate, and calcium are specifically and independently associated with some of the individual symptoms in this population.
Background and Aims: COVID-19 is associated with myocardial injury and in previous studies, patients with right ventricular dysfunction had an increased risk of all-cause death. In the general population, there is evidence that right ventricular strain improves at 6 months after COVID-19, but data about the course of other myocardial performance parameters are limited. 

Method: CARDIO-SCARS in CKD is a currently ongoing observational cohort study that aims to assess the cardiovascular risk in a CKD (stages 3 to 5), dialysis and kidney transplant population following SARS-CoV2 infection, by using clinical evaluation, various techniques and both endothelial dysfunction and myocardial injury biomarkers (ClinicalTrial.gov Identifier NCT05125913). We hereby report the evolution of the main echocardiographic myocardial performance parameters at 6 months from COVID-19 disease.

Results: Our study included 222 patients (134 in the COVID-19 group and 88 in the control group). In the COVID-19 group, the echocardiography was performed at a mean distance of 2.21±1.9 months after testing positive for SARS-CoV-2. The mean age at baseline was 58.81±15.2 years and 53.41±14.14 years for the COVID-19 group and control group respectively. Atrial fibrillation, heart failure, ischemic heart disease and diabetes were more prevalent in the COVID-19 group. When analyzing the mean absolute difference between baseline and 6 months echocardiographic parameters using a two-sample t-Test, statistically significant results were observed for the left ventricular (LV) ejection fraction (EF), LV Tei Index, right ventricular (RV) Tei Index and RV free wall longitudinal strain (RVFWLS) as follows: Δ LVEF was 0.70±7.97% and -2.44±7.30% (p = 0.005), Δ LV Tei index was -0.04±0.19 and 0.0007±0.111 (p = 0.024), Δ RV Tei index was -0.04±0.17 and 0.0007±0.20 (p = 0.034) and Δ RVFWLS was 1.68±4.36% and -0.32±3.34% (p = 0.039) for the COVID-19 group and the control group respectively.

Conclusion: Our study is the first to describe the evolution of echocardiographic parameters post-COVID in a CKD population. Despite worse demographic and echocardiographic characteristics at baseline, patients from the COVID-19 group had a better evolution at 6 months, when compared to the control group. Both right and left ventricular myocardial performance indices improved for the COVID-19 patients and worsened for the control group.
Furthermore, group D had a higher positive rate of screening tests for CAD compared to the other three groups.

Conclusion: In patients with advanced CKD, ECG and TTE abnormalities were significantly associated with the occurrence of CVD events. Additionally, those with both ECG and TTE abnormalities may be at high risk for the presence of CAD.

**Conclusion:** CKD was associated with smaller initial ischemic lesions for equivalent neurological severity, and more recanalization failures. CKD was not an independent risk factor for mortality or poor functional prognosis at 3 months. CKD patients seem to benefit from thrombectomy and should not be contraindicated to this technique. AKI is associated with greater initial neurological severity, poorer functional prognosis and increased mortality at 3 months and is an independent risk factor for poor prognosis.

**Impact of mechanical thrombectomy on outcomes after an ischemic stroke.**

**Method:** Multicenter cohort study. Patients with at the acute phase of ischemic stroke following a large artery occlusion managed with mechanical thrombectomy were included. CKD was defined as eGFR < 60 mL/min/1.73m² for more than 3 months, AKI by 2012 KDIGO score, infarcted volume by ASPECTS and functional prognosis at 3 month by modified Rankin Scale (mRS).

**Results:** 296 patients were included. Sixty-three patients (22.8%) had CKD. In univariate analysis, patients with CKD had more white matter vascular lesions (Fazekas 1.7±0.8 vs. 1.0±0.8, p<0.001), had lower initial infarcted volume (ASPECTS 7.6±1.7 vs. 6.7±1.8, p = 0.003), for equivalent severity (NIHSS: 9.2±7.0 vs. 10.1±7.7, p = 0.404), and had more thrombectomy failure (12.7% vs. 3.8%, p = 0.008) compared to non-CKD patients. At 3 months, CKD was associated with equivalent functional prognosis (mRS 3–6: 51.6% vs. 42.2%, p = 0.193) but higher mortality: 24.2% vs. 9.5%, p = 0.004. Forty-eight patients (19.6%) developed an AKI. AKI was associated with increased initial gravity (NIHSS 18.8±5.2 vs. 16.7±5.7, p = 0.014, equivalent stroke volume (ASPECTS 7.3±1.9 vs. 6.8±1.8, p = 0.234). At 3 months, CKD was associated with poorer functional prognosis (mRS 3–6: 64.6% vs. 39.4%, p = 0.002) and mortality: 25.0% vs. 8.4%, p = 0.003. In multivariate analysis, AKI appeared as an independent risk factor of poor neurological outcome (OR 2.16 [1.05-4.46], p = 0.036 and mortality: OR 2.47 [0.96-6.35], p = 0.059 at 3 month, as CKD was not.

**Figure 1:** Occurrence of CVD events among study patients according to findings of ECG and TTE.
patients without diabetes, obesity may play a protective role. Diabetes is a potent predictor of outcomes irrespective of BMI, however, in group 3 (CKD and DM, n = 227) showed that patients with obesity had significant lower rates of combined outcomes compared to patients with normal BMI (HR 0.75; 95%CI = 0.63-0.89; p = 0.001 and HR 0.56; 95%CI = 0.38-0.82; p = 0.003 for group 1 and group 2 respectively). In multivariate models, obesity consistently proved to be a strong protective factor against combined outcomes (HR 0.77; 95%CI = 0.65-0.92; p = 0.005 for group 1 and HR 0.53; 95%CI = 0.34-0.83; p = 0.005 for group 2). This was independent of age, gender, HTN, angina, stroke, MI, and prescription of statins and angiotensin converting enzyme inhibitors. For group 3 (CKD and DM, n = 614), and group 4 (CKD, DM, and HF, n = 190), there was no significant difference in the combined outcomes between the different BMI groups when using univariate Cox regression analysis (for patients with obesity: HR 0.78; 95%CI = 0.61-1.01; p = 0.060 and HR 0.70; 95%CI = 0.43-1.16; p = 0.166 for both groups respectively). There was no significant difference in the incidence of RRT in any of the four groups.

Conclusion: In our largely white NDD-CKD cohort of patients, there was evidence of increasing risk of RRT or ACM as comorbidity increased irrespective of BMI. This is not surprising as ACM would be expected to increase as the burden of disease increases. However, when comparing the effect of BMI within groups, obesity was protective against combined outcomes in group 1 (CKD only) and group 2 (CKD+HF). This 'protective' effect was not seen in patients who had concomitant diabetes. These data suggest that diabetes is a potent predictor of outcomes irrespective of BMI, however, in patients without diabetes, obesity may play a protective role.

#4768
25 HYDROXYVITAMIN D ASSOCIATES WITH GASTROINTESTINAL BLEEDING IN DIALYSIS
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Background and Aims: The INSPIRE collaborative group built a prediction model that showed serum 25 hydroxyvitamin D concentration (25OH Vit D) may be a predictor of gastrointestinal bleeding (GIB) hospitalizations in dialysis patients [1]. Unexpectedly, 25OH Vit D levels in the target range (i.e., >30 ng/mL) were most associated with GIB hospitalization risk. We aimed to further investigate the association between GIB episodes and 25OH Vit D levels, considering the onset of a GIB comorbidity or a GIB hospitalization event in the next 180 days.

Method: Analysis used data from adult (age ≥18 years) dialysis patients in the United States who had one or more 25OH Vit D lab measurement between 01-Jan-2018 to 31-Mar-2021. We identified GIB episodes (comorbidity or hospitalization observations) that were within ≤180 days after a 25OH Vit D measurement. GIB episodes and types were based on ICD-10 diagnosis code clusters defined by the United States Healthcare Cost and Utilization Project [2]. We calculated the percent of GIB comorbidities that onset, or GIB hospitalizations that occurred, by categories of 25OH Vit D levels (<15, ≥15 to <30, ≥30 to <50, ≥50 to <100, or ≥100 ng/mL).

Results: Among 347,165 adult dialysis patients who had a 25OH Vit D lab measurement(s), 3.2% (n = 11,038) experienced ≥1 GIB comorbidity and 6.7% (n = 23,389) experienced ≥1 GIB hospitalization. In total, 16.5% (n = 4,873) of these patients had ≥1 GIB comorbidity and hospitalization. GIB episodes were within ≤180 days after a 25OH Vit D measurement for 5,358 GIB comorbidity and 21,862 GIB hospitalization observations. We found patients with 25OH Vit D levels that were ≥15 ng/mL or ≥50 ng/mL exhibited the lowest GIB comorbidity and GIB hospitalization rates (Figure 1A & B). Patients with 25OH Vit D levels that were between ≥15 ng/mL and <50 ng/mL had the highest GIB comorbidity and GIB hospitalization rates. This observation was consistently observed for all GIB types, including upper, lower, and unspecified GIB episodes.

Conclusion: Findings showed serum 25OH Vit D levels are associated with 180-day GIB episodes in dialysis patients. The highest GIB rates were found in patients with a 25OH Vit D level between 15–50 ng/mL versus all other levels. This finding was consistent for the onset of a GIB comorbidity and the occurrence of a GIB hospitalization, and in both cases was associated with 2-fold higher GIB rates. Outside the kidney failure population, 25OH vitamin D levels in the range of 30–100 ng/mL have been shown to be associated to higher GIB risk in warfarin users [3]. These findings may question recommendations in kidney disease that suggest repletion of 25OH Vit D levels to ≥30 ng/mL, which has been a controversy for more than a decade. Nonetheless, further analyses are needed and should consider adjustments for patient factors (e.g. age, sex, medications) and competing risks (non-GIB hospitalization events).
REFERENCES


CHARACTERISTICS OF PATIENTS WITH CKD WHO USE HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITORS: A JAPAN MEDICAL DATA CENTER DATABASE STUDY

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Background and Aims: Anemia is common among patients with chronic kidney disease (CKD) and is reported to be associated with increased cardiovascular disease and all-cause mortality, as well as reduced quality of life. The incidence of anemia increases as kidney function declines and affects approximately 32% of Japanese patients with stage 3–5 CKD.

Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) have been approved in the Japan since Sept 2019 for patients with anemia of chronic kidney disease. Available HIF-PHIs include roxadustat (approved Sept 2019), daprodustat (approved June 2020), enarodustat (approved June 2020), vadadustat (approved Sept 2020) and molidustat (approved Jan 2021). This analysis aims to provide a real-world account of patient characteristics of those initiating HIF-PHIs since the approval of HIF-PHIs in Japan, overall and by individual treatments.

Method: This retrospective cohort study leveraged data from the Japan Medical Data Center (JMDC) database from Nov 2018 – May 2022 and included patients over 18 years of age with documented CKD who initiated any HIF-PHI from Nov 2019 – Nov 2021. JMDC is a health insurance database aggregating administrative claims data, medical examination data, and ledger information of patients who are on employer-based insurance and <75 years of age. The study index date was defined as the first observed claim for any HIF-PHI during the identification period. Patients were required to have baseline period of 1 year prior to the index date and a minimum of six months of follow-up after the index date, with continuous insurance enrollment. This study assessed patient demographics, clinical characteristics, and previous anemia of CKD treatment in the baseline period.

Results: Overall, 500 patients initiated HIF-PHIs, with 47.8% (n = 239) patients initiating roxadustat, 40.8% (n = 204) patients initiating roxadustat, and 11.4% (n = 57) patients initiating other HIF-PHIs. Table 1 illustrates the patient demographic characteristics overall and by index HIF-PHI. Overall, 60.2% (n = 301) of patients were male; the mean age was 55.7 years (SD = 10.8). More than a third (37.2%) of overall patients received dialysis in the baseline period. Within the 184 patients on specified types of dialysis, 67.9% (n = 125)
had received hemodialysis and 32.1% (n = 59) had received peritoneal dialysis. In terms of prior anemia of CKD treatments, 61.8% (n = 309) of patients had any rhEPO use in the baseline period. Further breakdown is in Table 2. Nearly a third (31.6%, n = 158) of patients received any iron treatment in the baseline period, with 19.2% (n = 96) receiving oral iron and 13.8% (n = 69) receiving injectable iron. At baseline, almost all of patients initiating on HIF-PHIs had baseline comorbidities of hypertension (95.8%; n = 479) and diabetes (77.0%; n = 385).

Conclusion: Evaluating a real-world database for patients initiating HIF-PHIs within Japan allows for a more comprehensive picture of patient clinical and demographic characteristics. Our analysis found most patients initiating on HIF-PHIs were male, had previous rhEPO use, and had history of hypertension and diabetes. Understanding patient profiles in a real-world setting may guide treatment decisions in clinical practice.

REFERENCE

#5749
RATES OF SELECTED CARDIOVASCULAR AND NON-CARDIOVASCULAR EVENTS AMONG DIALYSIS PATIENTS WITH ANEMIA IN THE US MEDICARE POPULATION
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Background and Aims: The safety and efficacy of daprodustat in patients on dialysis were reported in ASCEND-D/ID trials [1,2]. Trials impose strict criteria for enrollment, making participants more narrowly selected than a broader population with disease who might benefit from treatment. We describe events, of which most were noted as safety events in ASCEND-D/ID trials, among general anemia “treatment eligible” (TE) patients on dialysis and patients similar to those in ASCEND-D/ID trials (“clinical trial-like” [CTL]) in the US.

Method: Using United States Renal Data System data, we conducted a retrospective cohort study of incident dialysis-dependent (IDD) patients from 2017–2019 and, separately, point prevalent dialysis-dependent (PDD) patients as of Jan 1 2018. Dialysis initiation date was the index date for IDD patients and Jan 1 2018 for PDD patients. We also required patients to have ≥ 6 months of continuous Medicare coverage before, and be aged ≥ 18 years on, index date. Patients with a history of kidney transplant or who had cancer during the year prior, and those who had a hospitalization for heart failure (HF), myocardial infarction (MI), or stroke in the 4 weeks before, the index date were excluded. For IDD patients, we required use of ESAs at the index date to support comparability to the PDD patients. The CTL cohort was a subset of the TE cohort, approximating eligibility in the ASCEND-D/ID trials. Patients were followed from index date to the earliest date of death, loss of Medicare coverage, kidney transplantation, or Dec 31 2019. We assessed cardiovascular (CV: all-cause death, HF, MI, stroke, thromboembolic events [TEEs], major cardiovascular events [MACE: death, MI, stroke] and MACE+HF) and non-CV (cancer, gastric erosions, ocular events, seizures, serious infections) events, derived from medical claims in the follow-up period using ICD-10 diagnosis, Healthcare Common Procedure Coding System, and Current Procedural Terminology codes. HF, MI, stroke, and serious infections were defined as inpatient events. First event rates for TE and CTL cohorts were calculated separately for IDD and PDD patients and expressed as number of events per 100 patient-years (PYs).

Results: Of IDD patients, 23,909 were in the TE and 6,962 in the CTL cohorts; corresponding numbers were 230,055 and 41,980 for PDD patients. Median follow-up was 12.6 and 13.8 months for the TE and CTL cohorts, respectively, in IDD patients; and 24 months for both TE and CTL cohorts in PDD patients. Mean ages were 70.3 and 71.0 years for the TE and CTL cohorts in IDD patients; and 63.3 and 64.1 years for the TE and CTL cohorts in PDD patients. For both IDD and PDD patients, the TE and CTL cohorts had similar demographics, but the TE cohorts had a slightly higher proportion of patients with comorbidities. First event rates are shown in the Table. TE cohorts had higher rates than CTL cohorts for most CV events (mortality, 17.3 vs 14.0 per 100 PYs in IDD and 16.8 vs 15.1 in PDD; MACE: 20.9 vs 17.5 in IDD and 20.3 vs 18.6 in PDD; MACE+HF: 25.6 vs 21.8 in IDD, 26.9 vs 25.1 in PDD). In IDD patients, HF was more common in the TE than the CTL cohort (7.1 vs 6.1) but was similar in PDD patients. MI, stroke, and TEEs (vascular access thrombosis [in hemodialysis patients only], deep venous thrombosis, and pulmonary embolism) had similar rates in the TE and CTL cohorts for both IDD and PDD patients. Serious infections were higher in the TE than the CTL cohort in both IDD and PDD patients. In PDD patients, gastric erosions were higher in the TE than the CTL cohort (40.0 vs 38.5) while ocular events and retinal hemorrhage were lower in the TE cohort.

Conclusion: Rates for most CV events were higher in TE cohorts, comprised of patients eligible for anemia treatment, compared with CTL cohorts mimicking trial participants. Rates of non-CV events did not show a consistent pattern. As expected, rates of VAT were higher in IDD than PDD patients. These findings further contextualize real-world event rates of interest in dialysis populations. Reported rates were crude (unadjusted) and should be interpreted with caution. Funding: GSK (study 217316).

REFERENCES
BONE MATERIAL STRENGTH INDEX AND DUAL ENERGY X-RAY ABSORPTIOMETRY IN EVALUATION OF BONE HEALTH IN AUTOSOMAL POLYCYSTIC KIDNEY DISEASE

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Background and Aims: Bone material strength measured with the use of impact microindentation technique (OsteoProbe®) has emerged recently as potentially beneficial tool in evaluating bone quality in metabolic bone disorders. Patients with autosomal polycystic kidney disease (ADPKD) carry an increased risk of skeletal complications, both due to deficiency of polycystins and development of chronic kidney disease-mineral bone disorder (CKD-MBD). In our preliminary study, we found that bone material strength index (BMSi) associated with bone mineral density (BMD) measured with the use of dual energy X-ray absorptiometry (DXA) in chronic kidney disease patients (CKD). The aim of the present study was to find if the same applies to patients with ADPKD. We evaluated bone health by measuring BMSi and performing DXA in patients with ADPKD.

Method: BMSi was measured (OsteoProbe®, Active Life Scientific, USA) performing DXA in patients with ADPKD.

Results: Mean values of BMSi, TBS and BMD are presented in the Table 1. BMSi in ADPKD patients was lower than average value observed in healthy individuals (85 men and 80 women). A positive linear relationship between BMSi and BMD was found in all of the examined sites with the highest standardized regression coefficient for 1/3 distal forearm (R² = 0.315, beta = 0.57, p < 0.001) and weakest for lumbar spine (R² = 0.003, beta = 0.33, p = 0.003). There was no association between BMSi and TBS.

Conclusion: This is the first report on BMSi in ADPKD patients. In agreement with the notion of a distinct bone phenotype in ADPKD, we observed a median bone material strength index in patients with ADPKD that was lower than the reference value. BMSi associated with BMD, but not with TBS. However, the association with BMD overall is weak, with BMD explaining only 3 to 31% of the variability of BMSi. This observation suggests complementarity and warrants additional studies investigating whether BMSi associates with hard bone endpoints, independent of BMD.

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EXPERIENCE IN A GERIATRIC NEPHROLOGY CONSULTATION

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Background and Aims: In the last two decades, the Spanish population over 65 years of age has increased by more than two million people. This has made the coexistence of comorbidities such as arterial hypertension (AHT) and diabetes (DM) more frequent, which act as risk factors in the onset of chronic kidney disease (CKD). This circumstance is conditioned by the presence of other factors associated with aging that condition greater frailty and a greater degree of dependency. Due to this, the application of the comprehensive geriatric assessment could be useful for its adequate stratification, obtaining a better evaluation of kidney disease and, with it, trying to improve the functionality of the patient.

Method: To analyze the parameters associated with CKD and their possible relationship with the degree of frailty and/or functionality in patients older than 75 years referred to a specific Nephrology consultation.

Material and methods: Descriptive and observational epidemiological study corresponding to a series of cases, which includes patients from the southern area of Tenerife who were referred for evaluation by the HUNSC Nephrology Service over a period of 8 months.

Results: It was obtained that, of 1263 patients referred, 41.1% of patients were older than 75 years. Of these, 19.1% of patients required face-to-face assessment in the Nephrogeriatrics consultation. When analyzing the relationship between frailty and functionality, we observed that the groups with greater frailty had both older ages and lower hemoglobin and albumin values. Likewise, it was observed that patients classified as frail had a higher risk of mortality than those who were not frail. Regarding functionality, when comparing the means of the parameters associated with CKD in relation to the degree of functionality (Barthel), it was obtained that age, creatinine, hemoglobin and albumin presented statistical significance.

Conclusion: The geriatric population represents a significant number of all consultations referred to Nephrology. The high prevalence of associated diseases that affect renal function (HBP and DM) together with the physiological changes that occur in aging make CKD an important public health problem. Carrying out adequate frailty and functionality scales may constitute one of the most important parameters to assess in nephrogeriatric patients, since it would allow us to improve the efficiency of the care process in CKD.

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Table 1: Bone material strength index (BSi), trabecular bone score (TBS) and DXA measurements expressed as mean.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BSi (SD)</th>
<th>TBS (SD)</th>
<th>BMD (SD) g/cm²</th>
<th>T score (min-max)</th>
<th>Z score (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-shaft tibia</td>
<td>74.4 (9.94)</td>
<td>n/a</td>
<td>n/a</td>
<td>1.16 (0.13)</td>
<td>0 (-2.92 – +2.16)</td>
</tr>
<tr>
<td>Whole-body</td>
<td>n/a</td>
<td>n/a</td>
<td>0.85 (0.14)</td>
<td>-0.33 (-2.78 – +2.25)</td>
<td>0.23 (-2.22 – +3.27)</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>n/a</td>
<td>n/a</td>
<td>1.0 (0.13)</td>
<td>0.05 (-2.05 – +1.73)</td>
<td>0.34 (-2.03 – +1.94)</td>
</tr>
<tr>
<td>Total hip</td>
<td>n/a</td>
<td>n/a</td>
<td>1.4 (0.12)</td>
<td>1.02 (0.13)</td>
<td>-0.43 (-2.81 – +2.49)</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>n/a</td>
<td>0.75 (0.09)</td>
<td>-0.24 (-2.65 – +1.81)</td>
<td>0.27 (-0.97 – +2.40)</td>
<td></td>
</tr>
<tr>
<td>1/3 distal forearm</td>
<td>n/a</td>
<td>n/a</td>
<td>1.94 (2.74)</td>
<td>2.25 (2.07)</td>
<td>2.74 (2.07)</td>
</tr>
</tbody>
</table>
Background and Aims: Erythropoiesis-stimulating agents (ESAs) are commonly used to treat anemia of chronic kidney disease (CKD). ESA hyporesponsiveness is prevalent in a significant portion of patients with CKD, especially those with end-stage renal disease on dialysis. Inflammation has been reported to contribute to ESA hyporesponsiveness and is associated with poor outcomes in patients with CKD. Roxadustat, an oral medication, is a hypoxia-inducible factor prolyl hydroxylase inhibitor that has previously demonstrated efficacy in patients with anemia of CKD. This pooled analysis evaluated the efficacy and safety of roxadustat in correcting hemoglobin (Hb) levels in subgroups of patients with dialysis-dependent (DD) CKD with or without inflammation at baseline.

Method: Data for this analysis were pooled from four phase 3, randomized, open-label, active comparator–controlled studies (HIMALAYAS [NCT02052310], ROCKIES [NCT02174731], PYRENEES [NCT02278341], SIERRAS [NCT02273726]) in patients with DD CKD. Outcomes evaluated were mean Hb change from baseline to Weeks 28–52 and mean weekly roxadustat dose (mg/kg) at Week 24 in patients with or without baseline inflammation (as determined by high-sensitivity C-reactive protein [hsCRP] level, divided into quintiles). Data were analyzed with an analysis of covariance model with baseline Hb as a covariate. Adjusted least-squares means, their difference, and corresponding confidence intervals were generated from datasets where missing data were imputed using missing at random-based multiple imputation, by treatment group, with baseline Hb, cardiovascular/cerebrovascular/thromboembolic history, geographical region (United States vs non–United States) and incident vs stable dialysis (<4 vs >4 months) as predictor variables. Safety data were summarized descriptively.

Results: In total, 4072 patients with DD CKD (roxadustat N = 2022; ESA N = 2050) were evaluated. At baseline, mean Hb levels (g/dL [SD]) were similar in the roxadustat (9.80 [1.29]) and ESA (9.83 [1.29]) groups, regardless of baseline hsCRP levels (roxadustat hsCRP quintiles 1–5: 9.72 [1.43], 9.78 [1.27], 9.80 [1.32], 9.90 [1.18], and 9.79 [1.23], respectively; ESA hsCRP quintiles 1–5: 9.75 [1.34], 9.92 [1.23], 9.90 [1.23], 9.96 [1.23], and 9.62 [1.38], respectively). Hb change from baseline was greater in patients treated with roxadustat compared with ESA, regardless of baseline hsCRP levels (Fig. 1). At Week 24, patients with higher baseline hsCRP levels did not require higher doses of roxadustat compared to patients with lower baseline hsCRP levels (Fig. 2). The overall percentages of patients with at least one treatment-emergent adverse event were similar for patients treated with roxadustat (hsCRP quintiles 1–5: 86.7, 88.1, 86.6, 88.7, and 90.0, respectively) or ESA (hsCRP quintiles 1–5: 83.5, 84.6, 90.5, 88.2, and 87.9, respectively) across hsCRP quintiles.

Conclusion: In patients with anemia of DD CKD, roxadustat increased Hb levels without requiring increased doses of roxadustat in patients with or without baseline inflammation. Results from the current analysis suggest that roxadustat is effective, with a comparable safety profile to ESA, regardless of inflammation status.
ASSOCIATION BETWEEN CKD-MBD AND MORTALITY IN OLDER PATIENTS WITH ADVANCED CKD – RESULTS FROM THE EQUAL STUDY

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Background and Aims: Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD) is a common complication of CKD, associated with higher mortality in dialysis patients. Its impact in non-dialysis patients remains mostly unknown. We investigate the associations between parathyroid hormone (PTH), phosphate, and calcium (and their interactions) and all-cause, cardiovascular (CV), and non-CV mortality in older non-dialysis patients with advanced CKD.

Method: We used data from the EQUAL study, which included patients aged ≥65 with eGFR ≤20 ml/min/1.73 m² from six European countries. Cox models were used to assess the association between baseline and time-dependent CKD-MBD biomarkers and all-cause, CV, and non-CV mortality. Models were sequentially adjusted for other mineral biomarkers, age, sex, country, eGFR, albumin, BMI, comorbidities and medications. Effect modification between biomarkers was also assessed.

Figure 1: Effect sizes of CKD-MBD biomarkers on all outcomes. Hazard ratios (HR) for all-cause (A), CV (B) and non-CV (C) mortality associated with 1 SD increase in baseline and time-dependent biomarkers in unadjusted and sequentially adjusted models (I, unadjusted; II, adjusted for other mineral biomarkers; III, previous further adjusted for age sex and country; IV, previous further adjusted for eGFR; V, previous further adjusted for albumin; VI, previous further adjusted for BMI; VII, previous further adjusted for pre-existing comorbidities; VIII, previous further adjusted for medications). Abbreviations: BMI, body mass index; CV, cardio-vascular; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone.
**Results:** In 1294 patients, the prevalence of CKD-MBD at baseline was 94%. Both PTH (aHR 1.12, 95%CI 1.03-1.23, p 0.01) and phosphate (aHR 1.35, 95%CI 1.00-1.84, p 0.05), but not calcium (aHR 1.11, 95%CI 0.57-2.17, p 0.76), were associated with all-cause mortality. Calcium was not independently associated with mortality, but modified the effect of phosphate, with the highest mortality risk found in patients with both hypercalcemia and hyperphosphatemia. PTH level was associated with CV mortality, but not with non-CV mortality, whereas phosphate was associated with both CV and non-CV mortality.

**Conclusion:** CKD-MBD is very common in older non-dialysis patients with advanced CKD. PTH and phosphate are independently associated with all-cause mortality in this population. While PTH level is only associated with CV mortality, phosphate seems to be associated with both CV and non-CV mortality.

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**STRUCTURAL AND FUNCTIONAL CHARACTERISTICS OF THE HEART IN ELDERLY AND OLD PATIENTS WITH CHRONIC KIDNEY DISEASE AND ATRIAL FIBRILLATION**

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**Background and Aims:** The study of cardiorenal relationships is an important area in medicine. The presence of chronic kidney disease (CKD) and atrial fibrillation (AF) in elderly and old patients requires a special integrated approach in diagnosis and treatment, taking into account the principles of patient orientation. The aim was to study of structural and functional characteristics of the heart in elderly and old patients with CKD and AF.

**Method:** 224 female and 215 male patients of elderly and old age (mean age 72.4±6.8 years) with AF were examined. Among elderly and old patients, the following types of AF were diagnosed: a permanent form was observed in 136 (30.9%), a persistent form - in 117 (26.7%), a long-term persistent form - in 98 (22.3%), a paroxysmal form - in 88 (20.1%). Glomerular filtration rate (GFR) was determined using the CKD-EPI equation. All patients underwent electrocardiography (ECG), echocardiography (EchoCG), and some patients underwent ECG monitoring by Holter with assessment of rhythm variability.

**Results:** CKD with GFR<60 ml/min/1.73m² was diagnosed in 274 (62.4%) patients with AF: stage 3a – in 184 (67.2%), stage 3b – in 82 (29.9%), 4 stage - in 8 (2.9%) patients with CKD. When analyzing the structural and functional parameters of the heart, more than half of elderly and old patients with CKD had concentric left ventricular hypertrophy - 146 (53.3%), 65 (23.7%) patients had eccentric hypertrophy. The types of remodeling in elderly and old patients did not differ depending on the presence of CKD (p=0.05). The ejection fraction (EF) of the left ventricle in elderly and old patients did not differ depending on the presence of CKD (p = 0.5). Preserved left ventricular EF
had 194 (70%) intermediate - 60 (21.7%), low - 23 (8.3%) elderly and old patients with CKD. In patients with AF and CKD, compared with patients without CKD, mitral regurgitation (p = 0.006) and aortic regurgitation (p = 0.02) were more frequently observed. Left atrial (LA) diameter, exceeding the norm, was observed in most patients regardless of the presence of CKD: in 191 (69.7%) patients with CKD and 118 (71.5%) without CKD (χ^2 = 0.03, p = 0.86). Moderate and pronounced increase in LA diameter was observed in 111 (40.1%) patients with CKD and 63 (38.1%) without CKD (χ^2 = 0.17, p = 0.67). When analyzing the LA index, an increase in size was observed significantly more often in patients with CKD than in patients without CKD: 79 (28.8%) and 25 (15.2%), respectively, χ^2 = 10.75, p = 0.001. Enlargement of the right ventricle was detected in 94 (34.3%) patients with CKD and 53 (32.1%) without CKD (χ^2 = 0.18, p = 0.67), right atrium – 35 (12.8%) patients with CKD and 19 (11.5%) without CKD (χ^2 = 0.15, p = 0.7). Attention is drawn to the differences in the spectral analysis of the heart rate in elderly and old patients with CKD compared with patients without CKD: a higher index of centralization (0.55 (0.33-0.86) and 0.36 (0.25-0.48), respectively, p = 0.03) and a lower index of vagosympathetic interaction (1.48 (0.85-2.32) and 3.16 (2.12- 4.59), p = 0.004).

Conclusion: When analyzing the structural and functional parameters of the heart in elderly and old patients with AF and CKD, there was an increase in the LA index, more frequent presence of mitral and aortic regurgitation compared to patients without CKD. Elderly and old patients with CKD had a lower index of vagosympathetic interaction compared to patients without CKD.

#4205

ESTIMATED PROXIMAL TUBULE FLUID PHOSPHATE (ePTFp) CONCENTRATION: AN EARLY MARKER OF CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDER (CKD-MBD)?

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Background and Aims: MBD develops early in CKD and is associated with kidney damage progression, but CKD-MBD markers, of initial CKD-MBD like FGF23 and α-Klotho are not available in clinical practice. Recently ePTFp has been proposed as a new early marker of MBD. In fact, the progressive reduction of nephron number, with the proportional FGF23 increments, reduce renal tubular phosphate reabsorption to maintain phosphate balance. As a consequence, PTFp concentration per single nephron progressively increases, leading to progression of kidney tubular damage. For this reason, PTFp could represent an innovative early marker of CKD-MBD. We evaluated the relationship of ePTFp with FGF23, α-Klotho and kidney damage progression.

Method: In CKD stage G2-4, we assayed serum FGF23, α-Klotho and ePTFp [ePTFp = (Phosphaturia / creatininuria) x creatininemia x 3,33]. The progression of CKD was evaluated during 5 years and the patients were splitted in two groups according to the basal ePTFp median value. 30 healthy subject provided the normal value of ePTFp.

Results: In 68 CKD patients (age 58.9 ± 15.6 y.o. eGFR 45 ± 21 mL/min), ePTFp averaged 2.4 ±1.3 mg/mg which was higher than the control group (ePTFp = 1.2±0.5; p<.01). ePTFp increased progressively along with the increasing CKD stages with values higher than the control group since stage 2 (Table 1). ePTFp showed a positive correlation with FGF23 (r: 0.69; p<.<.001) and a negative correlation with α-Klotho (r: -0.237; p<.05) and eGFR (r: -0.647; p<.001). Follow-up was available in 30 patients (Table 2) and showed a greater reduction of eGFR in the 15 patient with higher ePTFp (threshold 2 mg/dl) (Fig. 1).

Conclusion: Our data show early and progressive increments of ePTFp in CKD along with increments of FGF23 and PTH and reduction of α-Klotho, as per reciprocal pathophysiologic dependence. ePTFp values > than 2 mg/dl identified patients at highest risk of CKD progression. Accordingly, ePTFp, a surrogate of renal tubular cells phosphate overload, could represent a novel marker of CKD-MBD development and of increased risk of kidney damage potentially helpful to make therapeutic choice.
MORTALITY
CHRONICKIDNEYDISEASESTRONGLYASSOCIATEDWITH

Figure 1:

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Background and Aims: Skeletal muscle composition disturbances, like sarcopenia and myosteatosis, are common in non-dialysis chronic kidney disease (ND-CKD) patients and seem to be associated with adverse clinical outcomes. Sarcopenia and myosteatosis can be evaluated by computed tomography (CT) by measuring skeletal muscle area (SMA) and muscular attenuation (MA) in Hounsfield units (HU) at the third lumbar vertebra, respectively, but the optimal cutoff points for diagnosis and outcome prediction are not established in chronic kidney disease (CKD) patients. We aimed to evaluate the prevalence of sarcopenia and myosteatosis in ND-CKD patients and to define the optimal cutoff values of SMA and MA to predict mortality.

Method: We conducted a retrospective cohort study including non-dialysis CKD patients referred to an outpatient clinic during a two-year period, who underwent a CT as part of clinical workup and with an available serum creatinine evaluation within a 90-days timeframe. Patients with a follow-up under 26 weeks after the CT were excluded. Area under the receiver operating characteristic curve (AuROC) analysis was used to evaluate the ability of SMA and MA to predict mortality and the Youden's index was used to determine the optimal cutoff point. Cox-regression analysis was employed to identify independent predictors of mortality.

Results: 167 patients (94% Caucasian, 50.9% male, 32.3% diabetics) with a mean age of 68.3 ± 16.4 years were included, most with CKD stage 3 and 4 (53.9%; mean estimated GFR 57.6 ± 33.1 ml/min/1.73m2 at baseline). During a median follow-up of 4.9 (4.2) years, 39 patients (23.4%) died. Median SMA was 127.7 (45.8) cm² and there was a trend to increased mortality across lower SMA quartiles (1st quartile 32.6%, p = 0.026; 2nd quartile 26.8%, p = 0.095; 3rd quartile 21.4%, p = 0.261; 4th quartile 21.2% - reference). SMA showed a modest ability to predict mortality (AuROC 0.623) and the best cutoff found was 140.7 cm². Median MA was 28.4 (13.8) HU and there was a statistically significant higher mortality across lower MA quartiles (1st quartile 42.9%, p<0.001; 2nd quartile 31.0%, p = 0.001; 3rd quartile 16.7%, p = 0.028; 4th quartile 2.4% - reference). MA showed a good ability to predict mortality (AuROC 0.733) and the best cutoff was 30 HU. Using the identified cutoff points, sarcopenia (SMA < 140.7 cm²) was present in 67.1% (n = 112) and myosteatosis (MA < 30 HU) in 56.3% (n = 94) of patients. In univariate Cox-regression both sarcopenia and myosteatosis were associated with increased mortality – Hazard ratio (HR) 4.34 (95% CI 1.68-11.19, p = 0.002) and 5.32 (95% CI 2.22-12.73, p<0.001), respectively. In multivariate Cox-regression models (adjusted for age, baseline estimated GFR and presence of diabetes) only myosteatosis kept its association with mortality – HR 2.87 (95% CI 1.15-7.16, p = 0.024). This association was also present when the model was adjusted for the presence of sarcopenia. Patients with myosteatosis were older (median age 77.3 [10.8] vs 62.7 [30.1], p<0.001) and had higher frequency of diabetes (42.6% vs 19.2%, p = 0.001), arterial hypertension (87.2% vs 57.5%, p<0.001), and heart failure (24.5% vs 6.8%, p<0.003). They had also higher BMI (29.3 [7.4] vs 25.1 [6.0] kg/m², p<0.001), visceral obesity (77.7% vs 43.8%, p<0.001) and frequency of sarcopenia (75.5% vs 56.2%, p = 0.008). Myosteatosis was more frequent in CKD stage 3 to 5 patients, compared to CKD stage 1 or 2 (66.3% vs 42%, p = 0.002).

Conclusion: Sarcopenia and myosteatosis are prevalent in CKD patients, especially in advanced stages. However, reference values for this population are lacking. We found cutoff values for these muscle parameters using CT analysis in CKD patients, based on optimal stratification for mortality. Additionally, our study highlights that muscle quality (i.e., myosteatosis) may be more closely associated with mortality than muscle quantity (i.e., sarcopenia). Identifying patients at risk for these muscle abnormalities and early diagnosis are paramount for the subsequent implementation of therapeutic interventions.

#5181
MYOSTEATOSIS: A NEW MARKER OF MUSCLE QUALITY IN CHRONIC KIDNEY DISEASE STRONGLY ASSOCIATED WITH MORTALITY

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Background and Aims: Sarcopenia and myosteatosis are prevalent in CKD patients, based on optimal stratification for mortality. Additionally, our study highlights that muscle quality (i.e., myosteatosis) may be more closely associated with mortality than muscle quantity (i.e., sarcopenia). Identifying patients at risk for these muscle abnormalities and early diagnosis are paramount for the subsequent implementation of therapeutic interventions.

#2865
EARLY REPEAT HOSPITALIZATION FOR FLUID OVERLOAD IN INDIVIDUALS WITH CARDIOVASCULAR RISKS

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Background and Aims: Fluid overload is a common manifestation of cardiovascular and kidney disease and a leading cause for hospitalizations. To identify patients at risk of recurrent severe fluid overload who can benefit from strategies to reduce hospitalizations, we evaluated the incidence and risk factors associated with early repeat hospitalization for fluid overload among individuals with cardiovascular risks.

Method: Single-center retrospective cohort study of consecutive adults with an index hospitalization for fluid overload between January 2015 and December 2017 and had cardiovascular risks (older age, diabetes mellitus, hypertension, dyslipidemia, kidney disease) and/or cardiovascular disease, but excluded if lost to follow up or eGFR <15 ml/min/1.73 m². Comorbidities, biochemistry and medications were retrieved from electronic medical records. The primary outcome was early repeat hospitalization for fluid overload within 30 days of discharge. Binary logistic regression (enter method) was used to assess factors associated with repeat hospitalizations in the literature or had p<0.25 on univariate analysis. Discrimination and calibration of the model were assessed by the area (AUC) under a receiver operating characteristic (ROC) curve and Hosmer-Lemeshow goodness-of-fit test, respectively.
Results: Among 3423 unique patients with index hospitalization for fluid overload, the mean age was 73.9 ± 11.6 years and 16.7% required high-dose intravenous (IV) furosemide. The median length of stay (LOS) was 4 (2, 9) days and 95.3% were prescribed loop diuretics at discharge. Early repeat hospitalization for fluid overload occurred in 291 patients (8.5%). After adjusting for demographic factors (age, gender, ethnicity), comorbidities (recent hospitalization, cardiovascular disease, atrial fibrillation, diabetes), medications before index hospitalization (diuretic, RAS blocker, NSAID), clinical parameters during index hospitalization (systolic BP, eGFR, IV furosemide use, LOS) and medications at discharge (diuretic, RAS blocker, statin), cardiovascular disease (adjusted OR 1.66, 95% CI 1.26-2.17, p < 0.001), prior hospitalization for fluid overload within 3 months before index hospitalization (adjusted OR 2.52, 95% CI 1.17-5.44, p = 0.02), prior hospitalization for any cause in within 6 months before index hospitalization (adjusted OR 1.33, 95% CI 1.02-1.73; p = 0.04) and IV furosemide during the index hospitalization (adjusted OR 1.58, 95% CI 1.10-2.28, p = 0.01) were associated with increased early repeat hospitalization for fluid overload. Higher systolic BP on admission (adjusted OR 0.992, 95% CI 0.986-0.998, p = 0.01) and diuretic at discharge (adjusted OR 0.50, 95% CI 0.26-0.98, p = 0.04) reduced early hospitalization for fluid overload. The model accuracy was 91.5% and the Hosmer and Lemeshow Test chi-square p was 0.25. The AUC of the ROC curve was 0.639 (95% CI 0.606 – 0.671).

Conclusion: Patients with cardiovascular disease, prior hospitalization for fluid overload within 3 months or prior hospitalization for any cause in within 6 months before index hospitalization, lower systolic BP, need for IV furosemide during the index hospitalization and lack of diuretic at discharge were associated with increased early repeat hospitalization for fluid overload.

#2901
PAIN MANAGEMENT IN PATIENTS WITH CHRONIC KIDNEY DISEASE: BEWARE OF INERTIA!
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Background and Aims: Pain and pain management are major concerns when facing patients with chronic kidney disease (CKD), and it can be more challenging for practitioners other than nephrologists. In practice, one of the aspects of this challenge is the reluctance to initiate or adapt a treatment for this particular group of patients. With this in mind, we proposed to study pain management in patients with CKD by primary care givers by identifying the causes of therapeutic inertia.

Method: A survey, self-administered via internet and elaborated via Google-Forms (including multiple and unique choice questions) was carried out among primary care physicians in November 2022.

Results: Sixty primary care physicians answered our survey with a male-to-female gender-ratio of 0.36 and a mean age of 30.65 years [18-57]. Most of the practitioners enrolled in our survey worked in urban areas (98%). Half of them worked in university hospitals, 20% in regional hospitals, 23% in local community clinics and 6.7% in private offices. When asked about their immediate feeling when managing a patient with CKD for a reason other than their kidney disease, anxiety was mostly cited (55%), with indifference, fear and confidence reported respectively in 23%, 8% and 3% of practitioners. Forty-three (71%) of the participants admitted to have difficulties initiating treatment in CKD patients. The main reasons were lack of knowledge about dose adjustments (45%), fear of adverse effects (71%), unavailability of recommended treatments for CKD patient (13%) and lack of access to nephrologist’s opinion (26%). When asked about pain management in CKD patients, one out of three doctors did not prescribe the maximum dose of paracetamol for CKD patients when it was necessary. This was due to a fear of overdose (61%), fear of adverse effects (42%) and fear of interactions with other treatments (14%). Forty percent of the participants admitted delaying the increase of paracetamol doses if the initial dose is ineffective. Ninety per cent of participants did not prescribe non-steroidal anti-inflammatory drugs to CKD patients even if indicated. In this case, 61% preferred to use another therapeutic alternative, 55% feared the risk of long-term nephrotoxicity, 16% feared interactions with other treatments and 9.3% did not know how to monitor the tolerance of the treatment. Concerning not relieved by level 1 analgesic treatment pain, 55% did not reach the permitted dose of Tramadol when necessary. As for codeine, 60% of practitioners did not reach the maximum doses if indicated. In 94% of the cases, this was due to apprehension about side effects. Fifty-five per cent of the participants did not seek for a nephrologist’s opinion when initiating or modifying analgesic treatment in CKD patients. The main reasons were lack of knowledge about dose adjustments (45%), fear of adverse effects (71%), unavailability of recommended treatments for CKD patient (13%) and lack of access to nephrologist’s opinion (26%). When asked about pain management in CKD patients, one out of three doctors did not prescribe the maximum dose of paracetamol for CKD patients when it was necessary. This was due to a fear of overdose (61%), fear of adverse effects (42%) and fear of interactions with other treatments (14%). Forty percent of the participants admitted delaying the increase of paracetamol doses if the initial dose is ineffective. Ninety per cent of participants did not prescribe non-steroidal anti-inflammatory drugs to CKD patients even if indicated. In this case, 61% preferred to use another therapeutic alternative, 55% feared the risk of long-term nephrotoxicity, 16% feared interactions with other treatments and 9.3% did not know how to monitor the tolerance of the treatment. Concerning not relieved by level 1 analgesic treatment pain, 55% did not reach the permitted dose of Tramadol when necessary. As for codeine, 60% of practitioners did not reach the maximum doses if indicated. In 94% of the cases, this was due to apprehension about side effects. Fifty-five per cent of the participants did not seek for a nephrologist’s opinion when initiating or modifying analgesic treatment in CKD patients. The main reasons were lack of knowledge about dose adjustments (45%), fear of adverse effects (71%), unavailability of recommended treatments for CKD patient (13%) and lack of access to nephrologist’s opinion (26%). When asked about pain management in CKD patients, one out of three doctors did not prescribe the maximum dose of paracetamol for CKD patients when it was necessary. This was due to a fear of overdose (61%), fear of adverse effects (42%) and fear of interactions with other treatments (14%).

Figure 1: Receiver operator curve (ROC) for the clinical model to predict risk of 30-day repeat admission for fluid overload.
Abstracts

Conclusion: Managing patients with CKD calls for great caution when prescribing treatments. However, it is necessary to avoid therapeutic inertia. Our survey illustrates an example regarding a common symptom (pain) that might worsen their quality of life. We suggest that regular seminars on the topic of analgesics prescription for CKD patients should be proposed in order to improve their management.

#3258 MECHANISMS OF HEMOGLOBIN CYCLING IN ANEMIC END-STAGE RENAL DISEASE PATIENTS TREATED WITH ERYTHROPOIESIS-STIMULATING AGENTS

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Background and Aims: A considerable fraction of renal anemia patients treated with erythropoiesis-stimulating agents (ESAs) experience hemoglobin cycling behaviors during which levels periodically over- and undershoot a specified target range [1]. This is an undesired condition, which also necessitates frequent adjustment of the drug dose. The causes of hemoglobin cycling are not understood on a fundamental level. Through a combination of biomedical simulations and quantitative data analysis, we aimed at identifying mechanisms of hemoglobin cycling and the physiological and treatment-related factors contributing to cycling.

Method: We developed a biomedical modeling and simulation scheme that captures the essential features of ESA therapy involving a minimal feedback model for the delayed hemoglobin response after ESA administration and a stereotypic ESA dosing algorithm [2]. In this model, hemoglobin cycling emerged as a consequence of the delayed feedback between a patient's physiological response to ESA administrations and the resulting dose adjustments, which mutually maintain themselves in a causal loop. Guided by this model, we developed a set of statistical indicators that can detect this type of self-sustained hemoglobin cycling in clinical time series, including the Pearson cross correlation between hemoglobin levels and given ESA doses and hemoglobin standard deviation.

Results: A model analysis showed that physiological and treatment-related delays in hemoglobin response and ESA dose adjustment and administration were a major driver of hemoglobin cycling. Such delays are caused, e.g., by the cell cycle and maturation times of erythroid progenitors in response to ESA administration on one hand and restrictions in ESA dose changes and typical administration intervals on the other hand. In clinical time series, this was reflected by a systematic delay between bursts of ESA administrations and hemoglobin cycles. We quantified 1,134 such datasets from hemodialysis patients and found that more persistent cycling was associated with negative correlation coefficients between hemoglobin levels and given ESA doses. Using model simulations with similar behavior, we found that many patient- and therapy-related factors affect the hemoglobin dynamics in several (sometimes competing) ways, obfuscating their overall effect. For example, a larger RBC lifespan generally both entails higher hemoglobin levels but also prolongs the effect of ESA misdosings. However, model simulations suggested that longer RBC lifespan generally have a favorable effect in requiring less ESA on average and preventing hemoglobin cycling. Moreover, the model showed that for a given patient, ESA-specific properties such as its half-life may have a ‘sweet spot’ range of values within which hemoglobin cycling was suppressed while still showing a desired effect on the hemoglobin dynamics. Furthermore, the choice of the hemoglobin target window had an impact on hemoglobin stability. If the window was chosen too small, more frequent dose adjustments could initiate and maintain a cycling behavior.

Conclusion: Hemoglobin cycling in renal anemia patients often emerges from a complex interplay of multiple physiological and ESA treatment-related factors, with delays between ESA administration, hemoglobin response and subsequent ESA dose adjustment being a key driver of cycling. Biomedical modeling and simulation can aid in systematically exploring these interplays and find improved dosing strategies.

REFERENCES


#5342 ASSOCIATION BETWEEN LONGITUDINAL GFR TRAJECTORIES AND BMD DECLINE RATE IN PATIENTS WITH CKD STAGE 2–4

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Background and Aims: Bone mineral density (BMD) predicts fracture risk in patients with chronic kidney disease (CKD). However, there are few studies regarding BMD decline rates in CKD population. In this study, we investigated whether BMD decline rate is associated with baseline estimated glomerular filtration rate (eGFR) and further evaluated with longitudinal eGFR trajectories.

Method: A prospective cohort study of 1,006 patients with CKD stages 2 through 4 who enrolled in the Korean Cohort Study for Outcome in Patients With CKD between 2011 and 2016. BMD was measured using dual-energy X-ray absorptiometry at baseline and year 4. Estimated GFR was measured 2–5 times during 4 years of follow-up. Mixed linear regression model was used for the longitudinal analysis and trajectory analysis was performed using semiparametric group-based modeling using maximum likelihood.

Results: Declined renal function was associated with increased rate of decline in total hip BMD (Stage 2: −0.23, Stage 3A: −0.39, Stage 3B: −0.80, Stage 4: −1.20 in men; −0.86, −1.19, −1.20, −1.58% change/year respectively in women). Trajectory analysis revealed two distinct trajectories of eGFR for each CKD Stages 2 through 4: Class 1, stable group; Class 2, rapid decline group. Trajectory group that represented rapid eGFR decline showed consistent trends of increased rate of decline in total hip BMD. There was significant difference between stable and rapid decline group in Stage 3A, 3B (Stage 3A: −0.18 vs. −0.67 [p = 0.009], Stage 3B: −0.36 vs. −1.10 [p = 0.031] in men; Stage 3A: −0.79 vs. −1.67 [p = 0.006], Stage 3B: −0.60 vs. −1.52% change/year [p = 0.001] in women; p for interaction).

Conclusion: Declined renal function and faster GFR decline is associated with rapid BMD decline in CKD stage 2–4.

Figure 1: Biomedical modeling scheme that embodies prototypical anemia treatment cycles of repeated hemoglobin measurement, ESA dose adjustment and administration, increase in systemic ESA levels and delayed hemoglobin response.
SELECTED CARDIOVASCULAR (CV)/NON-CV EVENT RATES IN NON-DIALYSIS-DEPENDENT PATIENTS TREATED WITH ESAS IN US MEDICARE (2017–2019), BY CKD STAGE

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Background and Aims: The safety and efficacy of daprodustat in non-dialysis-dependent chronic kidney disease (CKD) patients have been reported in the ASCEND-ND trial [1]. However, CKD stage may affect both the need for anemia treatment as well as outcomes, including potential safety events for anemia treatment. This study describes cardiovascular (CV) and non-CV event rates by CKD stage among patients treated with erythropoietin-stimulating agents (ESAs) in the US Medicare population.

Method: Using Medicare data for all fee-for-service enrollees, we conducted a retrospective cohort study of patients who had diagnosis of CKD stages 3, 4, or 5 and a first use of ESA in 2017–2019. CKD stage was identified by ICD-10 codes; ESA use was derived using Healthcare Common Procedure Coding System (HCPCS) codes. The date of first ESA use was the index date and CKD stage was defined as the most recent diagnosis on or before index date. We further required patients to have at least 12 continuous months of Medicare Parts A and B coverage (also used as a washout period to identify new ESA users) prior to, and be aged ≥ 66 years on, the index date. Patients with a history of kidney transplant or who had cancer during the year prior, and those who had a hospitalization for heart failure (HF), myocardial infarction (MI), or stroke in the 4 weeks before, the index date were excluded. Patients were followed from index date to the earliest date of death, loss of Medicare coverage, kidney transplantation or dialysis, or December 31, 2019.

Results: This study cohort included 50,206 patients; 22,332 had stage 3, 19,177 stage 4, and 8,697 stage 5 CKD at the index date. Median follow-up time was 11.5 months for patients with CKD stage 3, 8.9 months for patients with stage 4, and 3.7 months for patients with stage 5 CKD. Patients with higher (worse) CKD stages were slightly younger (mean ages for stages 3, 4, and 5 were 79.7, 79.1, and 76.8 years); with increasingly more males (42.9%, 45.1%, and 48.5%), increasingly more individuals of non-Hispanic Black race (14.2%, 15.7%, and 19.6%), with lower income (indicated by Medicare/Medicaid dual enrolment and Medicare Part D low-income subsidy), and lower proportion of comorbidities. Rates were higher for most CV events in patients with higher (worse) CKD stages (Table): death rates were 19.5, 22.1, and 28.1 per 100 patient-years for stages 3, 4, and 5, respectively; MI rates were 2.2, 2.9, and 3.2; HF rates were 12.5, 17.2, and 19.0; MACE rates were 22.0, 25.4, and 31.8; and MACE+HF rates were 31.0, 38.7, and 47.8, respectively. Rates of stroke were similar across CKD stages; but no pattern for TEE. For non-CV events, higher (worse) CKD stage had higher rates of first ocular events (17.2, 23.3, and 27.1) and seizures (2.3, 2.7, and 3.4), but lower rates of cancer (21.8, 14.2, and 10.2) and, within this, hematological malignancies (10.4, 4.11 and 2.3).

Conclusion: Medicare-covered ESA-treated patients with higher CKD stage had higher rates for most events assessed, while malignancy rates were lower. These findings may provide important context when assessing US event rates in non-dialysis-dependent CKD patients. Further investigation could clarify some of the differences between stages, such as rates of malignancy. Rates were reported as crude (unadjusted) and so should be interpreted with caution. Limiting the analysis to ESA-treated patients may have resulted in different event rates than would be expected to occur in the general CKD population. Funding: GSK (study 217316).

Both CV (all-cause death, HF, MI, stroke, thromboembolic events [TEEs], MACE [death, stroke, MI], and MACE+HF) and non-CV (cancer, gastric erosions, ocular events, seizures, and serious infections) events were ascertained, derived from Medical claims using ICD-10 diagnosis, HCPCS, and Current Procedural Terminology codes in the follow-up period. HF, MI, stroke, and serious infection were defined as inpatient events. First event rates were calculated separately by CKD stage, expressed as number of events per 100 patient-years during the follow-up period.
REFERENCE


#4117

HYPERKALIEMIA TREATMENT APPROACH BY THE NEPHROLOGIST: A REAL-WORLD ANALYSIS (K+RENAL STUDY)

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Background and Aims: Hyperkalemia is highly prevalent among chronic kidney disease (CKD) patients and its management is determinant to allow the maintenance of therapies of demonstrated cardiovascular and renal benefit. Attitude towards hyperkalemia is variable among different guidelines and also among different clinicians. The aim of this study was to analyze nephrologist response to K serum levels > 5.5 mmol/l between July 1st and December 11th, 2022. The only exclusion criterion was being on renal replacement therapy and not obtaining patient’s informed consent.

Results: 13 centers entered the study including 339 patients with hyperK; 331 had enough data to be included in the final analysis. 258 (78%) patients had mild hyperK (5.5-5.9), 60 (18%) moderate (6.0-6.4) and 13 (3.9%) severe hyperK (>6.5). 70.7% were males, mean age 72.0 (SD 13.4) and 87.3% and 55.6% suffered hypertension or DM, respectively. 17.3% were diagnosed from heart failure (25% NYHIA type I, 63.6% TII and 11.4% TIII). Most frequent CKD diagnoses were CKD+DM 36%, nephroangioesclerosis/vascular 25.4%, glomerulor 7.2% and unknown 16.6%. Median eGFR was 29.9 ml/min/1.73m² iQR [21-41] and 40.9% had UACR > 300 mg/g. Distribution according GFR stages was homogeneous (Pearson chi2 6.4 p 0.6). Percentage of use of ACEi, ARBs, MRA and NRIAI was 41.5%, 37.9%, 13.7% and 1.52% and showed no association with higher K levels. 33.6% of the patients that suffer hyperK were on renin angiotensin system inhibitors (RAS), 46.5% on diuretics and 62.6% on potassium binders. 33.6% of the patients that suffer hyperK were on renin angiotensin system inhibitors (RAS), 46.5% on diuretics and 62.6% on potassium binders. 33.6% of the patients that suffer hyperK were on renin angiotensin system inhibitors (RAS), 46.5% on diuretics and 62.6% on potassium binders. 33.6% of the patients that suffer hyperK were on renin angiotensin system inhibitors (RAS), 46.5% on diuretics and 62.6% on potassium binders.

Conclusion: Multicentric cross-sectional study performed in the nephrology departments of Madrid analyzing the therapeutic approach to K serum levels > 5.5 mmol/l between July 1st and December 11th, 2022. The only exclusion criteria were being on renal replacement therapy and not obtaining patient’s informed consent.

Method: Retrospective observational study, includes population under follow-up in nephrology consultations in a health area, during 2018–2021. We analyzed lipid profile, renal function and whether they received statins. IBM SPSS Statistics V24 was used.

Results: 3301 prevalent patients with kidney disease were collected, excluding those on renal replacement therapy (RRT), with glomerular filtration rate (GFR), glomerular filtration rate (GFR) <10ml/min/1.73m² and proteinuria greater than 1.5g. Of these, 112 (3.4%) patients had PKD. 51% of the total CKD patients were under treatment with statins. The average number of Total Cholesterol (TC) was 170.4+/−43mg/dl, LDL 92.3+/−37mg/dl, HDL 50.3+/−15mg/dl and triglycerides (TG) 147.3+/−92mg/dl. In 37% of CKD patients, LDL was >100mg/dl and only 35% had LDL <75mg/dl. In the CKD group with a GFR <60ml/min/1.73m² (N = 2357; 71%), there was a high prevalence of patients with LDL values >100mg/dl (N = 784; 33.5%). In the case of GFR <30ml/min/1.73m² (N = 981; 29.7%), the presence of LDL>100mg/dl 30% (N = 297) was also frequent. In the subanalysis of patients with PKD, the mean TC was 182+/−40mg/dl, LDL 101.2+/−33mg/dl, HDL 56.4+/−17mg/dl, and TG 123.7+/−59mg/dl. 76% of the PKD had GFR <60ml/min/1.73m² (N = 73), of which 45% presented LDL>100mg/dl (N = 32). In PKD patients with GFR >60ml/min/1.73m² (N = 39), half (N = 22; 56.4%) also had LDL >100mg/dl. In addition, 51% were taking a statin, despite this they had a mean TC 183mg/dl+/−46, LDL 102.7+/−39, HDL 53+/−15, and TG 142+/−69mg/dl.

Conclusion: The presence of elevated LDL was frequent in CKD, especially in the group with GFR <60ml/min/1.73m² without statin and in a quarter of patients with the same GFR with statin. It is notable in the PKD group, probably due to less awareness of strict CVR control.

#6713

THE INTERACTION EFFECT OF PHASE ANGLE AND AGE ON FEMORAL NECK BONE MINERAL DENSITY IN PATIENTS WITH NON-DIALYSIS CHRONIC KIDNEY DISEASE STAGE 5

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Background and Aims: Low bone mass is common in malnourished patients with chronic kidney disease (CKD) and can lead to higher risk of fractures. Elderly and CKD patients have the same risk factors for protein energy wasting, sarcopenia, and osteoporosis. We attempted to investigate an association between phase angle (PhA) and bone mineral density (BMD) in dialysis naïve patients with stage 5 CKD, and to identify a statistical relationship between PhA and age that affects bone density.

Method: Bio-impedance spectroscopy for evaluating body composition and PhA and dual energy X-ray absorptiometry for determining the BMD were simultaneously performed in 167 consecutive patients (age: 59.65 ± 13.98 years; women: 40.1%). Two-way analysis of variance (ANOVA) was conducted to assess the potential interaction effect of PhA and two age group (young and elderly group) on femoral neck BMD (FN-BMD).

Results: Our results showed that PhA and age were independently associated with both FN-BMD and the T-score in multiple linear regressions analyses. A significant interaction effect of PhA and age on FN-BMD was found in the two-way ANOVA (P = 0.028). Average BMD values for first and second tertiles of PhA were higher in the young group than the elderly group, whereas patients in the elderly group had higher BMD in third tertiles on average.

Conclusion: A relationship between PhA and BMD in patients with advanced-stage CKD was identified in current study. The effect of PhA level on FN-BMD was different between elderly and young patients. Higher PhA levels may have protective effects on bone health in the elderly patients with stage 5 CKD and seem to be an important determinant for BMD.

#4913

ANALYSIS OF THE LIPID PROFILE IN THE RENAL PATIENT AND SUB-ANALYSIS OF THE POPULATION WITH POLYCYSTIC KIDNEY DISEASE

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Background and Aims: Dyslipidemia is frequent in patients with chronic kidney disease (CKD), it constitutes a factor of progression of both cardiovascular (CVR) and CKD itself. It has its own characteristics, which are modified with the ERC stadium. The subgroup of patients with Polycystic Kidney Disease (PKD) presents its own characteristics. The aim of the study was to analyze the lipid profile in the renal population and the differences in the PKD group.
Figure 1: The interaction between phase angle and age on femoral neck bone mineral density. BMD, bone mineral density.

#4771
PROGNOSTIC RELEVANCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES ACCORDING TO EGFR CATEGORIES

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Background and Aims: Electrocardiogram (ECG) abnormalities are associated with adverse cardiovascular outcomes in patients with chronic kidney disease (CKD), but their prognostic relevance according to estimated glomerular filtration rate (eGFR) categories remains unexplored. This study investigated the associations between no, minor, and major ECG abnormalities and fatal cardiovascular disease (CVD) according to different strata of renal function.

Method: This was a retrospective cohort study including 310,060 individuals aged ≥16 years from the Copenhagen General Practitioners' Laboratory that had an available digital ECG and creatinine measurement within 7 days from 2001–2015. eGFR was calculated using The Chronic Kidney Disease Epidemiology Collaboration equation, and data were cross-linked with...
Danish nation-wide healthcare registries to gain information on medication, comorbidity, and fatal CVD. ECG abnormalities were categorized as either no abnormalities, minor (first-degree atrioventricular block, incomplete bundle branch block or corrected QT prolongation) or major (left ventricular hypertrophy, atrial fibrillation/flutter, bundle branch block, Q waves, or ST-T deviations), as done previously [1]. Patients with both minor and major ECG abnormalities were assigned as major ECG abnormalities. ECG abnormalities and their association with fatal CVD were compared across strata of renal function [eGFR (ml/min/1.73m²) > 90, 61–90, 46–60, 31–45, 16–30 and ≤15] based on multivariable Cox-regression analysis adjusted for age, sex, and comorbidities. Counterfactual G-estimation of Hazard Ratios (HRs) standardized to age and sex was performed to estimate 5-year absolute risk of fatal CVD.

Results: The median age was 55 [IQR, 41-69] years and 46% were male. Median study follow-up time was 10.3 [IQR, 6.7-14.4] years. A total of 47,249 (17.9%) of the included patients had an eGFR < 60. The rate of fatal CVD according to ECG abnormalities and their adjusted HRs is shown in Fig.1, while 5-year standardized risk of fatal CVD is depicted in Fig.2. Generally, having minor or major ECG abnormalities, conferred a worse prognosis across all eGFR strata, with the highest 5-year absolute risk of fatal CVD being observed among patients with major ECG abnormalities and an eGFR between 31–45 [19% (95% CI, 18–20%)], eGFR 16–30 [25% (95% CI, 24–26%)] or an eGFR ≤15 [27.5% (95% CI, 24–31%)], Fig. 1–2.

Conclusion: In a population-based setting, having minor or major ECG abnormalities were associated with an increased risk of fatal CVD across all strata of renal function. Patients with an eGFR ≤45 and major ECG abnormalities represent a high-risk population, that might benefit from careful monitoring and cardiovascular risk management.

REFERENCE

Figure 2: Standardized 5-year absolute risk of fatal cardiovascular disease across no, minor and major ECG abnormalities. Absolute risks are depicted with error bars representing ± standard error.
Comparison between baseline and 6, 12 and 24 months follow-up. All other comparisons showed no statistically significant differences.

* Median value.

c-LDL, LDL-cholesterol; TC, total cholesterol; TG, triglycerides; eGFR, estimated glomerular filtration rate.

Figure 1: Percentage reduction in LDL-cholesterol, total cholesterol and triglycerides at 6, 12 and 24 months follow-up (A, B, C); median LDL-cholesterol, total cholesterol and estimated glomerular filtration rate at 6, 12 and 24 months follow-up (D, E, F).
and 48.8% at 12 months of treatment. Renal function remained stable during follow-up. No side effects or cardiovascular events were documented.

Conclusion: iPCSK9 reduce cholesterol, c-LDL and triglycerides in patients with CKD, allowing therapeutic targets to be achieved while maintaining stable renal function. Due to the apparent advantages of this drug in CKD patients, we believe that conducted clinical trials should be designed for this population.

#3394
THE VALUE OF ADVANCED CARDIAC MAGNETIC RESONANCE IN DETECTING THE CHARACTERISTICS OF CARDIAC INVOLVEMENT IN ANDERSON-FABRY DISEASE
Junlan Yang and Xiao Liang Zhang
P.R. China

Background and Aims: Anderson-Fabry disease (AFD) is a rare X-linked inherited lysosomal storage disorder caused by GLA gene mutations. With the progression of the disease, end organ damages (such as renal and cardiac) will impair quality of life. For nephrologists, it is necessary to improve the early diagnosis ability of AFD and the ability to assess the involvement of multiple organs (especially the heart). Cardiac magnetic resonance (CMR) is more accurate than echocardiography in measuring myocardial thickness and mass. Moreover, with the gradual maturation of T1 Mapping and gadolinium-enhanced cardiac magnetic resonance, CMR has also been applied to evaluate cardiomyocyte injury. In this study, clinical data of patients with AFD were collected in order to study the value and advantages of advanced CMR technologies in evaluating cardiac function, cardiac structure and cardiomyocyte injury.

Method: In this prospective observational study, clinical and echocardiography data were collected from patients with AFD diagnosed at this center from January 2022 to September 2022. T1 Mapping and gadolinium-enhanced cardiac magnetic resonance were used to evaluate the cardiac function and the degree of cardiac structural lesions, and to analyze characteristic CMR findings of cardiac involvement in AFD. To clarify the value of CMR for the assessment of cardiac involvement in AFD compared with echocardiography.

Results: 13 patients (five women, eight men) with AFD were included (Table 1). When diagnosing reduced ejection fraction, two (15.4%) met CMR, and zero (0%) met echocardiography. When diagnosing left ventricular hypertrophy, 12 (92.3%, 18.56±2.74mm) met CMR, and ten (76.9%, 16.37±2.71mm) met echocardiography. Compared with CMR, echocardiography can significantly underestimate the severity of left ventricular hypertrophy (P = 0.043). Using T1 Mapping and gadolinium-enhanced cardiac magnetic resonance, characteristic CMR findings of cardiac involvement in AFD were found in all patients (Fig.1), included decreased T1 values (12 cases, 92.3%, 1104.00±44.69ms) and late gadolinium enhancement (LGE) (six, 46.2%).

Conclusion: Characteristic CMR findings of cardiac involvement in AFD are left ventricular hypertrophy, decreased T1 values, and LGE associated with myocardial fibrosis. Advanced CMR holds promise in subclinical detection of AFD.

Table 1: Characteristics of 13 patients with AFD and genotype.

<table>
<thead>
<tr>
<th>Patient/family</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>GLA variants</th>
<th>ACMG</th>
<th>α-Gal A</th>
<th>Lyso-GL-3 (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1f</td>
<td>female</td>
<td>49</td>
<td>c.548-1G&gt;T</td>
<td>-</td>
<td>-</td>
<td>5.4</td>
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<td>F1m</td>
<td>male</td>
<td>32</td>
<td>c.548-1G&gt;T</td>
<td>unknown clinical significance</td>
<td>0.4µmol/L/h</td>
<td>86.29</td>
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<td>36</td>
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<tr>
<td>F3m</td>
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<td>32</td>
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<td>-</td>
<td>&lt;0nmol/hr/mg</td>
<td>13.12</td>
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<tr>
<td>F3f</td>
<td>female</td>
<td>57</td>
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<td>-</td>
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<td>30</td>
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<td>unknown clinical significance</td>
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<td>70.31</td>
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<td>F5m</td>
<td>male</td>
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<td>F5f2</td>
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<td>F6m1</td>
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<tr>
<td>F6f</td>
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<td>53</td>
<td>c.735G&gt;A</td>
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<td>1.4µmol/L/h</td>
<td>9.28</td>
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<td>F6m2</td>
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<tr>
<td>F7m</td>
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<td>43</td>
<td>c.263A&gt;G</td>
<td>likely pathogenic</td>
<td>0.27µmol/L/h</td>
<td>30.79</td>
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</table>

Figure 1: CMR of patients with AFD: A1-2: End-diastolic frames from cine in AFD patient (F1f): The myocardium is extensively thickened, the ventricular septal myocardium is significantly thickened, and the thickest myocardium is 19mm; B1-3: T1Mapping(3.0T) in AFD patient (F2m):Decreased T1 values, the minimum of T1 value is 1070 ms; C1-3: Gadolinium-enhanced cardiac magnetic resonance (10-15min) in AFD patient (F1f): Decreased subendocardial perfusion and LGE were observed in the apical segment, decreased myocardial perfusion and LGE in the basal inferolateral region.

Conclusion: Characteristic CMR findings of cardiac involvement in AFD are left ventricular hypertrophy, decreased T1 values, and LGE associated with myocardial fibrosis. Advanced CMR holds promise in subclinical detection of AFD.
EARLY MARKERS AND VASCULAR IMPAIRMENT IN THE PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD)

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Background and Aims: Soluble Klotho (sKlotho) is thought to decrease early in CKD, but its use as biomarker of the CKD progression is controversial. In addition, the use of non-invasive techniques to diagnose incipient vascular damage in CKD would be of clinical interest. The aims of this study were: to assess the utility of serum and urinary sKlotho as a useful biomarker of kidney impairment and, to analyse the value of carotid adventitial neovascularization and aortic stiffness in the course of CKD.

Method: Forty-three CKD patients were classified according to their estimated glomerular filtration rate (eGFR) into 4 groups (CKD-2/3a, CKD-3b, CKD-4 and CKD-5) and 38 sex and age matched controls were studied. Carotid and femoral adventitial neovascularization was assessed by ultrasonography without contrast (Superb microvascular image, SMI). Aortic pulse wave velocity (PWV) was measured to determine stiffness.

Results: No differences in age and body mass index between control group and the four CKD stages were observed. The eGFR showed a significant decrease in the CKD stages (Table 1). No changes were observed in serum Ca and serum P increased only in CKD-5 (Table 1). Serum sKlotho displayed a progressive decrease from CKD-2/3a to CKD-5, before other CKD parameters, such as FGF23 and PTH changed. A significant correlation between serum sKlotho and serum creatinine was observed (r = -0.394, p = 0.0003). Urinary sKlotho increased in CKD-2/3a stage and remained similar up to CKD-5 (Table 1). The carotid artery of CKD patients stages 4 and 5 showed a higher number of adventitial vasa vasorum in the carotid artery (r = 2.09±0.26, p = 0.002; CKD-5 vs Control) and a greater area of adventitial neovascularization (r = 0.84±0.005 vs CKD-4). Values are expressed as Median [Interquartile range] or Mean ± Standard deviation.

Conclusion: Serum sKlotho decreased before FGF23 levels begun to rise, indicating the sKlotho decrease as the earliest marker of CKD-MBD, although it remains with no changes throughout the CKD progression. Carotid adventitial neovascularization by SMI and PWV increased in advanced CKD stages, suggesting that they have a limited clinical utility as early markers of vascular damage in CKD.

Table 1: Clinical and biochemical parameters and sKlotho in CKD patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 38)</th>
<th>CKD-2/3a (n = 11)</th>
<th>CKD-3b (n = 12)</th>
<th>CKD-4 (n = 11)</th>
<th>CKD-5 (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>81.5 [75-87.8]</td>
<td>49.0 [47.0-53.0]</td>
<td>39.0 [33.8-40.3]</td>
<td>23.0 [20.5-24.5]</td>
<td>12.0 [12.0-13.0]</td>
</tr>
<tr>
<td>PTH (pg/mL)</td>
<td>52.0 [41.5-60.5]</td>
<td>56.0 [43.0-75.0]</td>
<td>86.5 [71.8-117.5]</td>
<td>114.0 [71.5-198.5]</td>
<td>176.0 [155.0-212.0]</td>
</tr>
<tr>
<td>1,25(OH)₂ D₃ (pg/mL)</td>
<td>45.56 ± 11.55</td>
<td>38.80 ± 11.50</td>
<td>29.40 ± 11.50</td>
<td>24.03 ± 11.50</td>
<td>20.58 ± 11.50</td>
</tr>
<tr>
<td>sKlotho (pg/mL)</td>
<td>809.2 [680.3-1042.2]</td>
<td>670.6 [604.2-746.0]</td>
<td>632.2 [599.8-713.0]</td>
<td>591.4 [517.2-706.8]</td>
<td>585.80 [469.40-674.20]</td>
</tr>
<tr>
<td>Proteinuria (g/L)</td>
<td>0.07 [0.05-0.09]</td>
<td>0.05 [0.03-0.16]</td>
<td>0.44 [0.15-0.77]</td>
<td>0.32 [0.09-0.70]</td>
<td>0.58 [0.26-1.06]</td>
</tr>
<tr>
<td>Urine Klotho (pg Klotho/mg urine creatinine)</td>
<td>433.4 [189.1-726.9]</td>
<td>1055.1 [918.0-2103.5]</td>
<td>1143.1 [539.4-2220.1]</td>
<td>1099.7 [905.9-1503.1]</td>
<td>1003.3 [849.3-2192.1]</td>
</tr>
</tbody>
</table>

p < 0.05, *p < 0.01 and **p < 0.001 vs Control. *p < 0.05 vs CKD 2/3a, **p < 0.01 vs CKD 2/3a.
URAEMIC CARDIOMYOPATHY AS PREMATURE PRESBYCARDIA
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Background and Aims: Presbycardia, the age-related decline in cardiac function, has been shown in the general population by demonstrating gradual decline in peak cardiac performance with advancing age [1]. Chronic kidney disease (CKD) has shown phenotypic similarities with premature aging. Studies have shown accelerated vascular aging and skeletal muscle wasting in CKD. However, it is not known whether CKD patients show age related decline in cardiac function and whether the impairment is more pronounced for the given age (premature presbycardia). In the present study, we set out to test the hypothesis that CKD patients have premature presbycardia by measuring peak cardiac power (CPO\text{peak}) non-invasively across different age groups.

Method: A cross sectional study (n = 170) of healthy male volunteers (n = 100) and male CKD patients (n = 70) spanning ages 19 to 75 years. CKD patients were grouped into early (CKD 2–3, n = 29) and late CKD (CKD 4–5, n = 41). Patients with diabetes or any known cardiovascular diseases were excluded. CPO\text{peak} was measured using a specialised cardiopulmonary exercise test (CPX) using CO₂ rebreathing method [2]. The association between age and CPO\text{peak} was evaluated. The regression lines of CKD patients and healthy volunteers were compared using ANCOVA. P < 0.05 is considered significant.

Results: The mean eGFR of early CKD and late CKD were 57.8±17.2 ml/min and 16.8±5.8 ml/min respectively. The mean CPO\text{peak} of the study groups were 5.35±0.94 W (Control), 4.93±0.71 W (early CKD) and 4.26±0.69 W (late CKD). Fig. 1 shows the association between CPO\text{peak} and age along with the regression equations for the individual study groups. Comparison of the regression lines using ANCOVA did not show any difference in slopes between the groups (P = NS). There was a diminution in CPO\text{peak} of 0.2 W per 10 years of advancing age. However, for any given age, the CPO\text{peak} was diminished by 0.38 W in early CKD (P = 0.023) and 0.93 W in late CKD (P < 10\textsuperscript{-3}) compared to control. In other words, the cardiac age was older by 19 years in early CKD and by 46.5 years in late CKD compared to healthy volunteers.

Conclusion: The results demonstrate that CKD is associated with premature presbycardia. This phenomenon may offer explanation for the high prevalence of heart failure in advanced CKD. Further studies exploring the underlying mechanisms of premature aging in CKD may be worthwhile in the future.

REFERENCES

Figure 1: Graph showing decline in peak cardiac power with age in healthy control, early CKD (CKD2-3) and late CKD (4-5).
Background and Aims: Cardiovascular disease (CVD) is the main cause of morbidity and mortality in patients with chronic kidney disease (CKD). Novel determination of clonal expansion of hematopoietic stem cells carrying mutations in certain genes is called Clonal hematopoiesis of indeterminate potential (CHIP), which is well known the association with an increased risk of hematologic malignancies but in general population, CHIP has been associated with increased mortality and increased cardiovascular risk. The aim of our study was to analyze the influence of CHIP on the risk of CVD and heart disease in the population with CKD.

Method: 128 patients with different degrees of CKD were in our prospective study in between September 1, 2020 and January 31, 2021. All of them have followed up in Nephrology clinics and any patient have previous cardiovascular pathology. For detection of silent heart disease was realized measurement of troponin I and NT-Pro-BNP in the blood using a microparticle chemiluminescence assay and the degree of coronary calcification was calculated by the computed tomography (CT): Agaston method. All the patients were prospectively followed up for 18 months, recording the occurrence of major cardiovascular events. For detection of CHIP massive sequencing was performed with Ion Chef System On-demand recording the occurrence of major cardiovascular events. For detection of silent heart disease using a microparticle chemiluminescence assay and the degree of coronary calcification was calculated by the computed tomography (CT): Agaston method. All the patients were prospectively followed up for 18 months, recording the occurrence of major cardiovascular events.

Conclusion: The presence of CHIP was not associated with a greater risk of silent heart disease or cardiovascular events, although DNMT3a mutations, analyzed independently, were associated with a greater number of cardiovascular events in our CKD population.

#4184

MALE CHRONIC KIDNEY DISEASE IS A STATE OF PREMATURE TESTICULAR AGING

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Background and Aims: Sex steroid levels have been reported to be decreased in male patients with chronic kidney disease (CKD), parallel to the severity of the kidney dysfunction. These studies, at large, used immuno-assays, a method that is inferior to gold standard chromatography measurements and, in addition, failed to give insights into the underlying pathophysiology as they lacked data on gonadotropin levels. The aim of this study was to comprehensively map the gonadal status in male CKD patients not yet on dialysis and age- and BMI-matched controls, using gold standard techniques.

Method: We performed a case-control study in 120 male CKD patients (age 59±7, BMI 26.8 kg/m²), matched (1:1) with non-CKD controls for age and BMI. We divided CKD patients into 3 categories based on CKDigo classification: CKD 1–2 (n = 24), CKD 3 (n = 42) and CKD 4–5 (n = 54). We measured total testosterone (T) and estradiol (E2) using liquid chromatography tandem mass-spectrometry. Sex hormone binding globulin (SHBG), prolactin, luteinizing hormone (LH) and follicle stimulating hormone (FSH) were measured on the Roche Cobas 8000 platform. Free T levels were calculated via Vermeulen formula. Inhibit B (a readout for testicular Sertoli cell function) was measured by ELISA.

Results: CKD patients showed lower total T (426.0 ng/dL [297.5-516.5] vs. 541.0 ng/dL [452.0-647.8]; P < 0.0001) and free T levels (7.4 ng/dL ± 3.2 vs. 9.4 ng/dL ± 2.2; P < 0.0001) as compared to non-CKD counterparts. SHBG and E2 levels, conversely, were comparable in cases and controls. Inhibit B levels were lower in CKD patients as well (112.7 pg/mL [38.1-189.0] vs. 181.1 [122.2-236.4]; P < 0.0001). LH and FSH levels were higher in CKD patients (9.1 IU/L [5.4-16.2] vs. 5.4 IU/L [3.6-8.1]; P < 0.0001 and 7.8 IU/L [5.0-20.2] vs. 5.6 IU/L [4.0-9.7]; P < 0.0001 respectively). Consequently, the T/LH ratio and inhibit B/FSH ratio, respectively reflecting Leydig and Sertoli cell function, were markedly depressed in CKD (1.8 mmol/ IU [0.7-3.0] vs. 4.0 mmol/IU [2.4-5.2]; P < 0.0001 and 14.4 ng/IU [1.2-33.6] vs. 32.2 ng/IU [3.2-146.3]; P < 0.0001). In the CKD cohort, regression analysis identified eGFR and age as independent determinants of T/LH ratio (R² 0.29). According to the T/LH ratio a male CKD patient of 45y old has a testicular age of an 81y old control.

Conclusion: Male patients with CKD not yet on dialysis show low total and free T levels, confirming CKD as a risk factor for male hypogonadism. The low T/LH and inhibit B/FSH ratio point to testicular failure as the underlying pathophysiological mechanism.
Figure 1: Kaplan-Meier showing death by tertiles of non-skeletal alkaline phosphatase.

Table 1: Cox proportional hazard model showing association of serum ALP and mortality.

<table>
<thead>
<tr>
<th>Model</th>
<th>Total ALP</th>
<th>Bone-specific ALP</th>
<th>Non-skeletal ALP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (95% CI) Per SD increase</td>
<td>P value</td>
<td>Hazard Ratio (95% CI) Per SD increase</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1.41 (1.24-1.59)</td>
<td>&lt;0.001*</td>
<td>1.09 (0.97-1.23)</td>
</tr>
<tr>
<td>Model 1a</td>
<td>1.45 (1.22-1.71)</td>
<td>&lt;0.001*</td>
<td>1.09 (0.93-1.27)</td>
</tr>
<tr>
<td>Model 2b</td>
<td>1.30 (1.09-1.56)</td>
<td>0.004*</td>
<td>1.02 (0.86-1.20)</td>
</tr>
<tr>
<td>Model 3c</td>
<td>1.30 (1.09-1.55)</td>
<td>0.004*</td>
<td>1.03 (0.87-1.20)</td>
</tr>
<tr>
<td>Model 3 + LBP</td>
<td>1.29 (1.07-1.55)</td>
<td>0.007*</td>
<td>1.03 (0.87-1.21)</td>
</tr>
</tbody>
</table>

* Adjusted for gender, age, body mass index
b Adjusted for the above and eGFR, diabetes mellitus and established cardiovascular disease
c Adjusted for the above and Framingham risk factors (systolic blood pressure, LDL, HDL, current smoker)

P = 0.051). High bone-specific ALP was not associated with increased risk of all-cause mortality.

**Conclusion:** In patients with CKD not yet on dialysis, increased non-skeletal ALP (as opposed to skeletal ALP) is associated with inflammation and increased risk of all-cause mortality. These associations are at least partly driven by metabolic endotoxemia.

#4594 INPATIENT POLYPHARMACY AND THE AGING KIDNEY
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1Griffith University, Department of Medicine, Southport, Gold Coast, Australia and 2University of Sydney, Department of Medicine, Sydney, Australia

**Background and Aims:** Individuals aged ≥80 years have been found to have some of the highest rates of polypharmacy. Nearly 50% of these people are likely to have significant renal impairment, either from chronic kidney disease or age-related decline. Since many drugs are renally excreted, reduced renal function will cause pharmacokinetic and pharmacodynamic changes. As a result, some medications are inappropriate and there is an increased risk of adverse effects which are dose-related or related to drug interactions. We aim to examine the prevalence of highly renally excreted and nephrotoxic medications taken by our oldest old medical inpatients.

**Method:** Data was obtained as part of an ongoing prospective cross-sectional observational study examining polypharmacy in elderly inpatients at Ballina Hospital, Australia. Data as of 03/01/2019 for participants aged ≥80 years were retrieved as part of this nested study involving acute medical inpatients with sufficient capacity to provide informed consent. Exclusion criteria comprised of people with insufficient working knowledge of English, cognitive impairment (including delirium) and those under the age of 80 years. Information with regards to inpatient medication use, co-morbidities and renal function (creatinine clearance, CrCl) were retrieved from inpatient medical records as part of routine clinical care. Renally excreted medications and potential nephrotoxic medications were identified via the Australian Medicines Handbook and Renal Drug Database. Cognition was assessed by the Montreal Cognitive Assessment, multimorbidity via the Charlson Co-morbidity Index and frailty using the Clinical Frailty Score. A polypharmacy questionnaire was used to further probe participant insight and aptitude towards medication use.

**Results:** One hundred and five inpatients, with mean age of 86.7 years (range 80.2 to 102.7) met the inclusion criteria and participated in the study. The patients were prescribed an average of 12 medications (range 3–26). They had multiple co-morbidities (mean CCI 6), 64% were assessed to have mild cognitive impairment and 62% were classified as frail. Also, 28% did not know the indication for their medication and 30% reported missing medications. The calculated CrCl ranged from 19–99ml/min, with the majority of patients falling between the range of 30–60ml/min (mean 49ml/min). On average, each patient was taking 1 medication that is ≥50% renally excreted unchanged (or their active metabolites), 1 medication that requires dose reduction when CrCl is 30–60ml/min, 2 medications that require dose reduction when CrCl is 10–30ml/min and 1 medication infrequently or commonly classified as nephrotoxic. The average total number of medications did not change significantly with decrease in CrCl, however, there was a non-significant increase in potentially nephrotoxic medication use. Patients experienced a similar anticholinergic or sedative load (as measured by the drug burden index) regardless of CrCl.

**Conclusion:** A substantial burden of medications was found in individuals of advanced age (≥80years) with renal impairment. The risk of medication-related harm may be further compounded by age-related barriers and challenges to managing multi-drug regimens. Regular medication reviews are essential for this vulnerable patient group.
#5534
HIF-PH INHIBITORS AND ESA IN NDD-CKD PATIENTS WITH ANEMIA COMPARING THEIR SAFETY AND EFFICACY
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Intas Pharmaceuticals Ltd, Medical Affairs, Ahmedabad, India

Background and Aims: Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) are a new class of oral medicines for the management of anemia in CKD patients. These agents are found to be efficacious in the management of renal anemia, however safety is still under scrutiny. While, ESAs (Erythropoietin stimulating agents) are available since long with a well-established clinical profile. This network meta-analysis aimed to compare the safety and efficacy of HIF-PHI vs ESA in CKD patients with anemia not undergoing dialysis.

Method: An electronic database search was carried out in EBM (Evidence Based Medicine) Reviews, Cochrane Library and PubMed from inception to July 2022 for phase III clinical trials comparing six different HIF-PHIs and ESA for treating anemia in non-dialysis-dependent (NDD) CKD patients. The outcomes included the serious adverse events (SAEs) and change in hemoglobin (Hb) levels.

Results: Total 163 records were identified out of which 6 studies involving a total of 6847 patients were eligible for analysis. Compared to ESA, all HIF-PHIs increased risk for SAEs (daprodustat of RR, 1.21[95% CI, 0.825–1.77]; desidustat, 1.38[95% CI, 0.695–2.76]; enarodustat, 1.29[95% CI, 0.568–3.02]; molidustat, 1.02[95% CI, 0.585–1.74]; roxadustat, 1.29[95% CI, 0.674–2.57] and vadadustat, 1.01[95% CI, 0.693–1.47]) although these differences were statistically non-significant. When change in Hb was analyzed, there was no statistically significant difference between the two groups. The mean difference in change in HB with various HIFs as compared to ESA were: daprodustat (MD: 0.0796, 95% CI –0.676–0.838), desidustat (MD: 0.120, 95% CI: −0.626–0.883), enarodustat (MD: -0.309, 95% CI: −1.36–0.753), molidustat (MD: 0.0402, 95% CI: −0.802–0.720).

Conclusion: In terms of safety, HIF PHIs were associated with more SAEs compared to ESA although these differences are not statistically significant. Comparing efficacy, HIF-PHIs and ESA both effectively increase Hb level in NDD-CKD patients without any significant difference. Results of our network meta-analysis suggest the need for larger and long-term studies comparing HIF-PHIs with ESAs to have better understanding of their comparative efficacy and safety profiles.

Figure 1:
THE ASSOCIATION OF FIBROBLAST GROWTH FACTOR-23 AND CARDIORENAL SYNDROME IN PATIENTS WITH DIABETES MELLITUS

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Background and Aims: Previous studies suggest that interactions between the heart and the kidney can contribute to the progressive dysfunction of both organs. Recently, there has been an increase in the prevalence of cardiovascular disease (CVD) and chronic kidney disease (CKD) due to increasing diabetes mellitus rate. It is known that fibroblast growth factor-23 (FGF-23) has been found to be related to kidney metabolism especially as a biomarker and a key factor for remodeling in the kidney field. The aim of our study was to assess potential therapeutic approaches of the use of FGF-23 in clinical settings as a potential circulating biomarker for CVD and CKD.

Method: A total of 155 patients with DT2, aged 34 to 84 years (60 [60;72]), were examined. Control group included 94 healthy people the same age. All patients underwent standard clinical and laboratory examination, with an assessment of the levels of FGF-23 in baseline plasma samples. Renal function was assessed based on the levels of serum creatinine, cystatin C, eGFR, which was calculated according to the CKD-EPI formula, and albuminuria, which was assessed as albumin/creatinine ratio (A/C). An echocardiographic examination was conducted according to the standard protocol with the calculation of dimensional, volume and speed characteristics.

Results: The levels of FGF-23 were significantly higher in DT2 patients with CKD 5 in comparison with stages 1–4. There were positive strong significant association between FGF-23 and creatinine (r = 0.71, p < 0.001).

In both unadjusted and adjusted analyses, probability of decreased eGFR was associated strongly with FGF-23 (COR: 95% CI 1.890; 1.362-2.622, p < 0.001). When evaluating the dependence of the probability of decreased eGFR on the FGF-23 using the ROC analysis, the cut-off value of FGF-23 was 0.9 pmol/l. The sensitivity and specificity of the method were 75.3% and 74.5%, respectively (AUC 0.832 [0.035 with 95% CI: 0.764-0.901, p < 0.001).

Conclusion: Our study identifies FGF-23 as a promising target of novel therapeutic interventions in cardiorenal syndrome, which should be investigated in future clinical studies.

#3115

HYPERBARIC OXYGEN TREATMENT IN CALCIFIC UREMIC ARTERIOLOPATHY PATIENTS IN ADDITION TO CONVENTIONAL MULTIDISCIPLINARY CARE

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Background and Aims: Calcific uremic arteriopathy (CUA), also referred to as calciphylaxis, is a rare and serious complication in patients with advanced kidney disease. CUA has limited treatment options and poor prognosis, with 1-year survival often reported to be below 50% after diagnosis [1,2]. Hyperbaric oxygen therapy (HBOT) may improve wound healing by increasing tissue oxygenation, and has been suggested as adjuvant treatment for CUA patients [3]. We added HBOT to our conventional multidisciplinary care of CUA patients in 2012 and this study aims to evaluate long-term outcomes of CUA patients after this.

Method: Data from all CUA patients treated at our institution from 2012 to 2022 were retrospectively retrieved from hospital records. This is a single-centre study, but patients from different Norwegian hospitals were referred for treatment at our centre. Conventional multidisciplinary care of CUA in our centre included sodium-thiosulphate, dialysis if indicated medical optimization of calcium- phosphate homeostasis, substitution of vitamin K2, withdrawal of warfarin and iron and vitamin D if used, minimization of systemic steroids, in addition to optimization of weight- and nutritional status. Our centre is restrictive with surgical revisions to CUA patients.

Results: 25 CUA patients received a total number of 1493 HBOT treatments in addition to conventional CUA multidisciplinary care in the study period. Median HBOT per patient was 45 (range 1–267). One year after CUA diagnosis, 20 out of 25 patients were alive (80%). Fifteen out of the 20 patients, who were alive at one year after CUA diagnosis, had completely resolved CUA lesions (75%). Five patients died within the first year after CUA diagnosis, due to acute cardiovascular disease (n = 3) and infection (n = 2). Our impression is that HBOT is well-tolerated and associated with less wound-associated pain.

Conclusion: Our results suggest that HBOT is well-tolerated in CUA patients. After we included HBOT in our multidisciplinary care of CUA patients, 80% of the patients were alive one year after CUA diagnosis.

REFERENCES


#4536

INFLUENCE OF REDUCTION IN THE MASS OF ACTIVE NEPHERONS ON THE EXPRESSION OF MiRNA AND NfκB IN THE MYOCARDIA AND AORT OF WKY RATS

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Pavlov First Saint Petersburg State Medical University, Department of Propadeutics of Internal Disease, Saint-Petersburg, Russia

Background and Aims: At present, there is no doubt about the relationship between the state of the kidneys and the cardiovascular system, which is reflected in the concept of the cardiorenal continuum. The emerging data suggest that miRNAs may be one of the links connecting the kidneys and the cardiovascular system. However, information about the role of epigenomic changes in the development of damage to the heart and blood vessels in chronic kidney disease remains not fully understood.

Target. The aim of the work was to evaluate changes in the expression levels of miRNA-21, 133, 203, as well as the nuclear transcription factor B (NfκB) in the tissues of the myocardium and aorta in the development of remodeling of the heart and blood vessels with a chronic reduction in the mass of active nephrons in the experiment.

Method: Systolic blood pressure (BP, mm Hg), myocardial mass index (MMI, mg/g), relative expression levels of miRNA-21, -133, -203 and NfκB in myocardium and aorta were analyzed in rats Wistar-Kyoto (WKY) with 5/6 nephrectomy (Nx) and duration of experimental exposure 2 mo (n = 9). Controls were sham operated (SO) animals (n = 9). The reverse transcription reaction for 'complementary' DNA (cDNA) preparation was carried out under the StemLoop-technology separately for the studied miRNA. The following primers were used in PCR: microRNA-21–5' GCCCGGTCGTTATCAGACGTG-3', microRNA-133–5' GCCGGTCGTTAATGGAAC-3', microRNA-203–5' GCCGGTGAATTTGAGGACG-3', and U6–5' GCCGGTCTGGAAGCTTC-3', and common reverse 5' GTGGAGGAGTCGAGG-3'. The semi-qualitative evaluation of the miRNA expression level (in relative units, RU) under the (ΔΔCt) protocol at the laboratory referent (0.09) was used in calculations. NfκB expression was quantified using a StemLoop technology and RealTimePCR compared to the expression of the reference-gene GAPDH. Data were analyzed using Student’s t-test and the Mann–Whitney, a P < 0.05 was considered statistically significant.

Results: In rats WKY with an experimental decrease of the nephron mass in comparison to control, significantly higher levels (median [interquartile range]) of blood pressure (145.5 [135.0; 155.0] vs 117.9 [110.0; 120.0] mm Hg; P < 0.001) and NfκB expression in the myocardium (1.25 [0.87; 1.87] vs 0.89 [0.31; 1.15] relative units; P < 0.001) and aorta (0.87 [0.57; 1.63] vs 0.35 [0.22; 0.87] relative units; P < 0.05). The expression level of miRNA-21 in the myocardium increased in rats with NE (1.40 [0.54; 3.73] vs 0.37 [0.06; 1.62] relative units;
P < 0.01) relative to the SO group, but did not change significantly in the aorta (p > 0.05). Relative expression levels of microRNA-133 and -203 both in the myocardium and in the aorta of WKY rats with NE were more than 10 times lower compared to those of the SO group (p < 0.001). BMI in rats 2 months after NE increased relative to the SO group (p < 0.05).

**Conclusion:** An experimental decrease in the number of functioning nephrons not only leads to an increase in blood pressure and myocardial mass in WKY rats, but also causes epigenomic changes in the myocardium and blood vessels, in particular, activation of signaling pathways associated with NFκB in the myocardium and aorta of rats. Possibly, it is accompanied by growth in expression of NFXB-associated proliferative, proinflammatory and profibrotic cytokines. It is possible that microRNA-21 is also involved in the formation of fibrosis and myocardial remodeling. However, specific mechanisms of miRNA involvement in the pathogenesis of heart and vascular remodeling require further study.

**#4554**

**FRAX® ASSOCIATION, BONE DENSITOMETRY, BIOCHEMICAL PARAMETERS OF BONE MINERAL METABOLISM AND ADVANCED CHRONIC KIDNEY DISEASE**

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Hospital Universitario Virgen del Rocio, Nephrologist, Seville, Spain

**Background and Aims:** Currently, there are calculation tools that predict the risk of fractures (fx), one of which is the Fracture Risk Assessment Tool (FRAX®). Patients with advanced chronic kidney disease (CKD) have a higher risk of fx than the general population and it is an independent factor for fx. However, this tool does not consider the presence or absence of CKD, where alterations in bone mineral metabolism have important clinical consequences and their prevention should be the objective of CKD control. The aim of our study is to evaluate the FRAX® tool in patients with advanced CKD and to analyze possible relationships with parameters of bone mineral metabolism.

**Method:** Observational, descriptive, retrospective study of a series of cases of patients with advanced chronic kidney disease in our center, where demographic data, FRAX® calculation, personal history of Diabetes Mellitus, etiology of CKD, personal history of fx, measurement of bone mineral densitometry by dual energy X-ray absorptiometry (DXA), estimated glomerular filtration rate (CKD-EPI), levels of serum calcium and phosphorus, vitamin D1, 25 levels, Parathyroid hormone (PTH), fibroblast growth factor 23 (FGF-23), use of phosphorus chelating treatment and vitamin D were collected. Descriptive results of continuous variables are expressed as mean and standard deviation or median and interquartile range (IQR) according to their distribution. For categorical data, frequency and percentage are reported. To analyze the impact of the variables on the event to be studied, a univariate and multivariate Cox regression model was used.

**Results:** 59 patients with advanced CKD with DXA performed within one year of the FRAX® analysis were analyzed. The median age was 66 years (IQR 22), 59.3% were male, 55.6% had a personal history of diabetes mellitus. The most frequent etiology of CKD was unknown etiology (41.4%), followed by vascular (16.9%). History of some type of fx (13.6%) or personal history of Diabetes Mellitus, etiology of CKD, personal history of fx, measurement of bone mineral densitometry by dual energy X-ray absorptiometry (DXA), estimated glomerular filtration rate (CKD-EPI), levels of serum calcium and phosphorus, vitamin D1, 25 levels, Parathyroid hormone (PTH), fibroblast growth factor 23 (FGF-23), use of phosphorus chelating treatment and vitamin D were collected. Descriptive results of continuous variables are expressed as mean and standard deviation or median and interquartile range (IQR) according to their distribution. For categorical data, frequency and percentage are reported. To analyze the impact of the variables on the event to be studied, a univariate and multivariate Cox regression model was used.

**Conclusion:** In patients with advanced CKD, FRAX® index identifies patients at high fracture risk for whom active treatment for osteoporosis should be instituted. In patients with advanced chronic kidney disease, FRAX® underestimates those patients with decreased bone mass and elevated risk of osteoporosis. We did not find any association with biochemical parameters of bone mineral metabolism which could guide us in anticipating the treatment of osteoporosis. The loss of renal function accelerates the loss of bone mass, so we believe that the introduction of this variable is necessary in the equation, especially in this profile of patients.

![Figure 1: Fracture risk according to FRAX® and bone densitometry. N: number of patients. FRAX®: Fracture Risk Assessment Tool. DXA: bone mineral densitometry by dual energy X-ray absorptiometry.](image1)

**#5285**

**SERUM IRON AND NUTRITIONAL STATUS ARE ASSOCIATED IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

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Taipei Tzu Chi Hospital, New Taipei City, Taiwan, Rep. of China

**Background and Aims:** Both anemia and malnutrition are highly prevalent in patients with chronic kidney disease (CKD). Iron deficiency plays a significant role in anemia of CKD. However, whether iron deficiency contributes to malnutrition in CKD is unclear.

**Method:** We examined the association of iron status with nutritional status among patients with CKD stages 3–5 not yet on dialysis. The iron indices for assessing iron status included serum iron, serum ferritin, and transferrin saturation. Nutritional status was determined using body composition assessed by anthropometric measures and multi-frequency bioelectrical impedance, serum albumin, handgrip strength, Malnutrition Inflammation Score (MIS), and dietary protein and energy intake. We performed linear regression analyses to explore the cross-sectional association between iron status and different nutritional assessment tools.

**Results:** A total of 157 patients (age 64 ± 12 years; 93 men and 64 women; diabetes 39%) with CKD [estimated glomerular filtration rate (eGFR) 24.4 ± 13.4 ml/min/1.73 m²] were included. Patients were stratified as low (<70 μg/dL) or high (≥70 μg/dL) serum iron. Compared with patients with high serum iron (n = 104), patients with low serum iron (n = 53) were more likely to be female and had a significantly lower eGFR, hemoglobin, lean tissue index, serum albumin, handgrip strength, and dietary protein intake but a significantly higher MIS. In adjusted linear regression analyses, there was a significant association of serum iron with serum albumin, handgrip strength, and MIS (all adjusted P < 0.05). Serum ferritin was not associated with nutritional status, while the association between transferrin saturation and handgrip strength was only marginal (adjusted P = 0.044).

**Conclusion:** Higher serum iron is associated with better nutritional status in patients with CKD. Serum iron may be considered a complementary tool to assess nutritional status in CKD.

![Figure 2: Bone mineral densitometry results. N: number of patients. DXA: bone mineral densitometry by dual energy X-ray absorptiometry.](image2)
#5405
MALNUTRITION DIAGNOSIS IN CKD PATIENTS
Olga Vetchinnikova, Maria Ivanova, Andrey Vatazin and Aleksei Zulkarnaev
Moscow Regional Research and Clinical Institute, Russia

**Background and Aims:** Malnutrition is a prevalent condition in patients with chronic kidney disease (CKD) receiving replacement therapy by peritoneal dialysis (PD). Geriatric nutritional risk index (GNRI) is an effective tool for screening nutritional status in maintenance hemodialysis patients. The purpose of this study was to determine the information content of GNRI for the diagnosis of protein-energy malnutrition in patients with CKD receiving replacement therapy with PD when compared to malnutrition inflammation score (MIS) and 7-point subjective global assessment (7p-SGA).

**Method:** A prospective cohort study included 222 adults PD-patients (man 100, female 112, age 44±14). All patients received continuous ambulatory peritoneal dialysis. Median duration PD before inclusion in the study was 12 months, the observation period of patients was 36 months. Nutritional status assessment included anthropometric (body mass index, triceps skinfold thickness, midupper arm muscular area) and biochemical (albumin, C-reactive protein, total iron-binding capacity, total cholesterol, hemoglobin and others) examinations as well as bioelectrical impedance analysis (BIA – fat mass). GNRI calculated according to the formula GNRI = \(1.489 \times \text{albumin (g/dL)} + [41.7 \times (\text{body wt/ideal body wt})]\), where the ideal body weight for women is: height (cm) - 100 - [(height - 152) \times 0.2], ideal body weight for men is equal to: height (cm) - 100 - [(height - 152) \times 0.4]. We used MIS and 7p-SGA as a reference standard, a score ≥ 6 and ≤ 5, respectively, defined malnutrition. The cutoff of GNRI the diagnosis of malnutrition were derived from these ROC-analysis.

**Results:** Most of the individual nutritional indexes, including the anthropometric, biochemical and BIA indexes, were significantly (P < 0.001) lower in the patients with MIS score ≥ 6 and 7p-SGA score ≤ 5, thus both nutritional screening tools were considered reasonable as a reference standard to determine the information content GNRI in PD-patients. The GNRI fluctuated in the range 66–126 (median 99), MIS score – 2–24 (median 7) and 7p-SGA score – 2–7 (median 5). The GNRI showed a significantly negative correlation with MIS (r = -0.708, p < 0.0001) and a significantly positive correlation with 7p-SGA (r = 0.636, p < 0.0001) (Fig. 1). The most accurate GNRI cutoff to identify a malnourished patient according to the MIS was ≤ 99 (Fig. 2). The frequency of malnutrition among the observed patients was 52.3% when using GNRI<99, 55.9% when using MIS≥6 and 51.4% when using 7p-SGA≤5 (n.s.). The values for sensitivity and specificity with a GNRI of ≤ 99 in predicting malnutrition based on the MIS were 77.4% (95%CI...
Background and Aims: Many chronic kidney disease (CKD) patients suffer from mineral and bone disorders like osteoporosis, which also affects a huge part of the general population, predominantly postmenopausal women. For the treatment of osteoporosis, several drug types with different mechanisms of action are available, such as bisphosphonates, PTH analogs, RANKL inhibitors and sclerostin inhibitors (some of which are contraindicated for CKD patients beyond CKD stage 3). Different drugs can be given individually or combined in various ways, simultaneously or sequentially, resulting in a huge number of theoretically possible drug combinations that are practically impossible to study in clinical studies. We aimed to study using simulations whether there are combination therapies that would work considerably better than those tested and employed in clinical practice. If so, this could be beneficial for the treatment of a large number of osteoporosis patients by leading to a higher increase in bone strength and a higher reduction in bone fracture risk than standard therapies.

Method: We developed a physiology-based mathematical model that simulates the process of bone renewal in the human body and can predict how different osteoporosis drugs (including bisphosphonates, PTH analogs, RANKL inhibitors, and sclerostin inhibitors) affect this process, alone and in combination [1].

Results: The model was validated on over 30 clinical osteoporosis studies with about 90 study arms. It predicted the time courses of bone mineral density and bone turnover markers with a high degree of accuracy based on the knowledge of the used drugs and dosing schemes alone. We used the model to study how treatment results changed when merely reshuffling the order in which different drugs were given. For example, for 3-year drug therapies involving alendronate, denosumab and romosozumab (1 year each), our simulations showed that the order in which these drugs were given can have a considerable effect on short- and long-term therapy success [1]. This is due to different drugs favorably interacting when applied in the right sequence.

Conclusion: Our findings indicate that some osteoporosis drug administration schemes are superior to others while relying on the exact same types and amounts of drugs. Therefore, there is a large potential to improve pharmacologic therapies of osteoporosis using physiological simulations. For renal patients beyond CKD stage 3, a restricted set of drug types may be considered to account for contraindications related to impaired renal clearance. If translated into clinical practice, findings obtained using our model could give rise to novel treatments using combinations of existing drugs for osteoporosis that lead to a lower bone fracture risk than standard treatments. Moreover, our model could serve as a basis for personalizing osteoporosis therapy to individual patients.

REFERENCES

#5454
DESIGN AND OPTIMIZATION OF DRUG COMBINATION THERAPIES FOR OSTEOPOROSIS VIA SIMULATIONS OF BONE TURNOVER
David Jörg1, Doris Fuertinger1 and Peter Kotanko1,3
1 Fresenius Medical Care Germany, Computational Medicine Group, Global Medical Office, Bad Homburg vor der Höhe, Germany; 2 Renal Research Institute, New York, United States of America and 3 Icahn School of Medicine at Mount Sinai, New York, United States of America

Figure 1: GRNI and 7p_SGA / MIS points correlation.

Figure 2: GRNI scale ROC-curve.
ADVERSE MUSCLE COMPOSITION ASSESSED BY MRI ASSOCIATES TO POOR FUNCTIONAL PERFORMANCE AND METABOLIC COMORBIDITIES IN CKD

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Background and Aims: CKD is associated with alterations in body composition, such as reduced muscle mass, increased amount of fat or both simultaneously. Furthermore, both sarcopenia and sarcopenic obesity are associated with worse physical functioning, poor quality of life, increased morbidity and mortality in CKD. Magnetic resonance imaging (MRI) is considered an accurate method for the study of body composition. A water/fat separated MRI scan with automated image analysis can quantify the skeletal muscle volume and allows a quantitative measure of muscle quality by assessing muscle fat infiltration. The combined observation of low muscle volume and high muscle fat infiltration, i.e. adverse muscle composition (AMC), has been shown to be linked to poor function and metabolic comorbidities within subjects with non-alcoholic fatty liver disease. The aim of this study was to investigate the prevalence of AMC and its association with poorer muscle function and metabolic comorbidity within CKD in the large UK Biobank imaging study.

Method: This is a cross-sectional and prospective study including a total of 647 UK Biobank participants with eGFR cystatin C < 60 ml/min/1.73 m². A control group was created by selecting participants (matched on sex, age, and BMI) with an eGFR cystatin ≥ 60 ml/min/1.73 m². Fat-tissue free muscle volume and muscle fat infiltration (MFI) were quantified using a rapid whole-body water and fat separated MRI protocol and automated image analysis (AMRA® Researcher). For each participant, a personalized muscle volume z-score (sex- and body size-specific) was calculated and combined with muscle fat infiltration for AMC detection. AMC was defined as having low muscle volume in combination with high muscle fat infiltration. Sarcopenia was calculated according to the last published recommendation by the European Working Group on Sarcopenia in Older People. Data describing muscle function (hand strength, walking test, stair climbing and number of falls) and metabolic comorbidity (coronary heart disease (CHD) and type 2 diabetes (T2D)) have been included and obtained from the study database linked to the study participants' electronic health records. A Cox proportional hazards ratio model, corrected for age, sex, BMI, low hand grip strength, T2D, smoking, and alcohol consumption, was used to assess the association between AMC and CHD incidence.

Results: The prevalence of AMC was 1.4x higher in CKD participants compared with the control group without CKD (27.7% vs 20.4%, p < 0.001). CKD participants had significantly higher prevalence of sarcopenia (7.2% vs 4.4%, p = 0.004), low hand grip strength (16.0% vs 11.8%, p = 0.006), slow walking pace (17.3% vs 9.9%, p < 0.001), CHD (17.4% vs 8.9%, p < 0.001) and T2D (13.7% vs 9.2%, p = 0.001) compared with the control group without CKD (Fig. 1). CKD participants with AMC (179 out of 647) had a significantly higher prevalence of sarcopenia (17.3% vs 3.5%, p < 0.001), low hand grip strength (22.8% vs 13.4%, p = 0.006), slow walking pace (27.0% vs 13.6%, p < 0.001), as well as prevalence of CHD (23.6% vs 15.0%, p = 0.014) and T2D (18.6% vs 11.8%, p = 0.033) compared with CKD participants without AMC (Fig. 2). CKD participants with prevalent CHD at the study had higher prevalence of AMC (37.5% vs 25.5%, p = 0.014) compared to CKD participants without CHD. AMC was associated with 1.9x higher incidence of CHD (95% confidence interval 1.15-3.15, p = 0.012) compared to those without AMC.

Conclusion: AMC, as determined by MRI with automated image segmentation, is highly prevalent within CKD and associates with poor function, high prevalence of metabolic comorbidities and an increased risk for CHD. CKD patients with poor muscle health is a highly vulnerable group and this technique enables them to be targeted for accurate interventions in order to improve outcomes.
Figure 1: **CKD and adverse muscle composition.** Square muscle composition plot includes prevalence of coronary heart disease and type 2 diabetes.

Figure 2: **CKD and adverse muscle composition.** Bar plots showing prevalence of poor function.
CARDIOVASCULAR RISK AND THE RISK OF KIDNEY DAMAGE IN PATIENTS WITH HYPERTENSION

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Background and Aims: A high salt content in the diet is one of the reasons for the increase in blood pressure (BP) and the development of cardiovascular disorders. However, high intake of sodium chloride does not always lead to an increase in blood pressure, but causes endothelial dysfunction and cardiac remodeling. It has been established that the introduction of soy products into the diet can have a nephro- and cardioprotective effect in chronic kidney disease. At the same time, it is not clear whether the damaging effect of a high-salt diet on the cardiovascular system can be offset by other dietary interventions, in particular, soy proteins. In this regard, the aim of the study was to study the effect of long-term use of diets with different content of sodium chloride and soy protein on myocardial remodeling in cynomolgus monkeys.

Method: A total of 18 cynomolgus male monkeys with age 6–8 years were studied. The animals were divided into three groups (six in each group). The first (control) group received the standard diet. The second group received the diet rich in common salt (8 g of NaCl/kg), and the third, the high salt diet in combination with soy protein SUPRO 760 (200 g/kg; Protein Technology International, USA). Systolic (BP) and diastolic (BPd) blood pressure (BP) in monkeys was recorded by oscillometric method on a veterinary tonometer ML-410 VET (Microlux, Russia) under anesthesia. After registration of blood pressure, an echocardiographic study (EchoCG) was performed with a sector scanner with a frequency of 3-5 MHz on an ultrasound system Chison Sonic Touch 60 (China). Echocardiography was performed in B-mode (two-dimensional scanning), M-mode (one-dimensional scanning), as well as in pulsed and tissue Doppler modes. Echocardiography and blood pressure measurements were performed at baseline, after 4 and 12 months of follow-up.

Results: BP values (group 1 - BPs: 109±10.09, BPd: 60±7.42; group 2 - BPs: 109±25.14, BPd: 57±11.86; group 3 - BPs: 101±8.59, BPd: 57±6.92 mm Hg; all p > 0.05) and heart rate (group 1 - 77±12.61, group 2 - 81±18.07, group 3-80±19.9 beats/min, all p > 0.05) in macaques did not undergo significant changes over 12 months of the study in any of the groups. In group 1, there were also no significant changes in echocardiographic parameters. Group 2 monkeys showed no early changes in LV shortening fraction (FU) and ejection fraction (EF). However, after 12 months, FU decreased by an average of 26.6%, and EF by 12.8% compared with the indicator for a period of 4 months. In addition, the speed of the transmitral flow in early diastole (E) decreased by 19.1% compared with the baseline. Long-term intake of soy proteins prevented a decrease in LV FU in macaques on a high-salt diet. Its value was 25.1% greater than in group 2. In group 3 monkeys, after 12 months, the magnitude of systolic excursion of the mitral annulus plane and the maximum rate of excursion of the fibrous ring of the mitral valve in early diastole (E') increased, the thickness of the interventricular septum in diastole decreased, and E/e' ratio. In group 3, the thickness of the posterior wall of the left ventricle decreased in systole (0.57±0.056 mm), the mass of the LV myocardium (14.9±2.94 g/m2), the average diameter of the base of the right ventricle (1.20±0.115 mm) compared with group 2 (0.69±0.040 mm), 19.6±2.83 g/m2, 1.40±0.111 mm, respectively; all p < 0.05.

Conclusion: The obtained results can be considered as confirmation of the hypothesis that high consumption of sodium chloride leads to adverse structural and functional changes in the heart and blood vessels, not associated with an increase in blood pressure. The inclusion of isolated soy proteins in the diet is likely to reduce the effects of this negative impact. The specific mechanisms of this cardioprotective effect remain to be explored.

Statistical analysis used: One-way analysis of variance for unrelated samples when comparing the data of 3 studied groups and one-way analysis of variance for related samples when studying the dynamics of the indicator in each of the groups during 12 months of observation. Results are presented as mean ± standard deviation (M ± SD). Differences were considered significant at p < 0.05.

### #6424

DIAGNOSTIC ACCURACY OF BONE TURNOVER MARKERS IN PATIENTS WITH VARIOUS DEGREES OF KIDNEY DYSFUNCTION AND PRIMARY OSTEOPOROSIS

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Background and Aims: There are limited data available on the validity of bone turnover markers (BTMs) to predict bone turnover in patients with kidney dysfunction and primary osteoporosis. Method: This is a cross-sectional retrospective study of patients with primary osteoporosis and eGFR <90 ml/min/1.73 m² who had bone biopsy for clinical purposes for a time period of 8 years. CKD-EPI equation 2021 was used to calculate eGFR based on the mean serum creatinine readings. Bone biopsy samples were evaluated qualitatively using KDIGO TMV classification.
Routine laboratory data were collected in addition to alkaline phosphatase, iPTH, cyclase activating (CAP) PTH, osteocalcin, bone specific alkaline phosphatase (BSAP), and N-telopeptide collagen (NTX).

**Results:** Study included 156 patients with mean age of 64.7 years. The majority of patients were females (93.6%). The mean BMI was 26.2 kg/m². The mean eGFR was 70 ml/min with 78% of patients had eGFR from 60-90 ml/min/1.73 m². CKD stage III was found in 19%, and 3% of patients had CKD stage IV. HTN was found in 47%, history of kidney stones in 9%, and fragility fractures in 77%. Bisphosphonates were the most used pre-biopsy bone specific medication (66%). Teriparatide was used in 10.9% and SERM was used in 7.7% of patients, while 31.4% of patients did not receive any bone anti-resorptive or anabolic medication "treatment naïve". Bone cortical thickness and cancellous volume were low in 94.2%, while high bone turnover (HBT) was found in 42.9% and low bone turnover (LBT) in 57.1%. Mineralization was defective only in 9.6%, while osteoid thickness was increased in 5.8%. Figure 1 shows the distribution of bone turnover among study group. Baseline characteristics and routine laboratory data were not different between HBT and LBT. PTH, especially PTH CAP, and alkaline phosphatase tended to be higher in HBT but did not reach statistical significance. While BTMs (osteocalcin, BSAP and NTX) were significantly higher in HBT (Table 1). Using ROC curve analysis, the area under the curve (AUC) for BSAP, NTX and osteocalcin were 0.605, 0.660, 0.642, respectively. Combining the NTX with either BSAP or osteocalcin did not result in increasing the AUC. This was also the same when the three of them were combined. BTMs were able to discriminate bone turnover status only among patients with eGFR≥60 ml/min/1.73 m² (Table 2).

**Conclusion:** Low bone turnover was found in 43% in treatment naïve patients with primary osteoporosis, with a higher prevalence among patients with eGFR≥60. In the study group, PTH and total alkaline phosphatase were not able to discriminate LBT from HBT, while BTMs showed a modest ability to discriminate the turnover status only among patients with eGFR≥60.
Elevated phosphate concentrations are associated with a significantly increased risk of cardiovascular disease and overall mortality in patients with chronic kidney disease. Current Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend lowering elevated serum phosphorus concentrations toward the normal range in patients with end-stage kidney disease on dialysis through restriction of dietary phosphorus intake, increase in clearance by dialysis, and the use of phosphate binders. However, ~75% of dialysis patients are not achieving normal phosphate concentrations, potentially due to low adherence and/or binders’ insufficient phosphate binding capacity. Therefore in patients with chronic kidney disease (CKD) death. On the other hand, elevated cardiac Troponin T (cTnT) levels are associated with cardiovascular events and mortality. Several studies have established an inverse association between CKD and cTnT, and knowledge of this association in diabetic patients would benefit their management. The objective of this study was to analyze the relationship between cTnT levels, renal function and echocardiographic parameters in diabetic patients with advanced chronic kidney disease (ACKD).

Method: A prospective study was carried out during one year of 180 patients attending for the first time for ACKD consultations, with an estimated glomerular filtration rate (eGFR) < 30 ml/min/1.72 m². The following data were analyzed: age, sex, diabetes, HBP, BMI, smoking, peripheral artery disease, coronary artery disease, non-age-adjusted Charlson index (non-age-CCI), eGFR by CKD EPI, ultrasensitive cTnT, C-reactive protein (CRP), ferritin, hemoglobin (Hb), ejection fraction (EF) and left ventricular hypertrophy (LVH), interventricular septum thickness (IVST) and left ventricular wall thickness (LVWT).

Results: Baseline characteristics are summarized in Table 1. In the group of patients, when analyzing the presence or absence of diabetes, diabetic patients were significantly older, had higher troponin levels, a higher percentage of smoking, coronary artery disease, peripheral artery disease, non-age-CCI, IVST and LVH than non-diabetic patients. In diabetic patients, troponin levels correlated significantly with eGFR (0.03) and ACR (0.09), with ACR remaining as a predictive variable (0.003). It did not correlate with echocardiographic data. In non-diabetics, the correlation was significant with age and IVST and LVH (Table 2, Figure 1). In the multivariate analysis in diabetic patients, only the association remained with ACR (0.026) and in non-diabetics with eGFR (0.038) and IVST (0.004).

Conclusion: The cTnT levels are found to be higher in diabetic patients and with higher ACR, considering it as a therapeutic target to reduce cardiovascular risk since echocardiographic data would not discriminate this risk in this profile of patients.

Table 2: AUC for BTMs in the study group and according to eGFR.

<table>
<thead>
<tr>
<th>BTMs</th>
<th>All patients</th>
<th>Patients with eGFR&lt;60</th>
<th>Patients with eGFR&lt;60</th>
<th>P-value</th>
<th>All patients</th>
<th>Patients with eGFR&lt;60</th>
<th>Patients with eGFR&lt;60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteocalcin (ng/mL)</td>
<td>0.642</td>
<td>0.670</td>
<td>0.539</td>
<td></td>
<td>0.003</td>
<td>0.002</td>
<td>0.706</td>
</tr>
<tr>
<td>BSAP (ng/L)</td>
<td>0.029</td>
<td>0.023</td>
<td>0.651</td>
<td></td>
<td>0.001</td>
<td>0.004</td>
<td>0.122</td>
</tr>
<tr>
<td>NTX (mM BCE)</td>
<td>0.660</td>
<td>0.657</td>
<td>0.660</td>
<td></td>
<td>0.001</td>
<td>0.004</td>
<td>0.474</td>
</tr>
<tr>
<td>Osteocalcin + NTX</td>
<td>0.655</td>
<td>0.675</td>
<td>0.574</td>
<td></td>
<td>0.001</td>
<td>0.004</td>
<td>0.207</td>
</tr>
<tr>
<td>BSAP + NTX</td>
<td>0.660</td>
<td>0.657</td>
<td>0.660</td>
<td></td>
<td>0.001</td>
<td>0.004</td>
<td>0.474</td>
</tr>
<tr>
<td>BSAP + Osteocalcin + NTX</td>
<td>0.660</td>
<td>0.657</td>
<td>0.660</td>
<td></td>
<td>0.002</td>
<td>0.003</td>
<td>0.396</td>
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Table 1:

<table>
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<tr>
<th></th>
<th>n: 180</th>
<th>Diabetic Patients (59.2%)</th>
<th>Non Diabetic Patients (48.2%)</th>
<th>P value</th>
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</thead>
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<tr>
<td>Age (years)</td>
<td>71,5</td>
<td>73</td>
<td>66,5</td>
<td>0,003</td>
</tr>
<tr>
<td>Sex (male) %</td>
<td>60</td>
<td>64,4</td>
<td>53,3</td>
<td>ns</td>
</tr>
<tr>
<td>BMI Kg/m²</td>
<td>30,4</td>
<td>30,17 (28,9-11,31)</td>
<td>27,2 (27,85-8,47)</td>
<td>0,013</td>
</tr>
<tr>
<td>Smoking %</td>
<td>51,6</td>
<td>58</td>
<td>43,4</td>
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</tr>
<tr>
<td>HBP %</td>
<td>94,3</td>
<td>97,1</td>
<td>90,6</td>
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<tr>
<td>Coronary heart disease %</td>
<td>26,1</td>
<td>37,9</td>
<td>10,2</td>
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<tr>
<td>Etiology of CKD %</td>
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<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>31,5</td>
<td></td>
<td>38,3</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>28,6</td>
<td>55,8</td>
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<tr>
<td>Peripheral artery disease %</td>
<td>46,5</td>
<td>61,8</td>
<td>21,3</td>
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<tr>
<td>CCI &gt; = 6%</td>
<td>28,1</td>
<td>38,8 (4,248-1,74)</td>
<td>4 (3,5-1,4)</td>
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<td>eGFR (ml/min/1,73m²)</td>
<td>19,1</td>
<td>19,2 (19,2-3,74)</td>
<td>18,6 (19,09-8,85)</td>
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<tr>
<td>ACR (mg/g)</td>
<td>702,5</td>
<td>1515 (1423-2394,5)</td>
<td>805 (667-70-684,16)</td>
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<tr>
<td>CRP (mg/dL)</td>
<td>3,8</td>
<td>4,8 (12,55-11,18)</td>
<td>2,4 (7,11-11,19)</td>
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<tr>
<td>Ferritin (mcg/L)</td>
<td>141</td>
<td>194 (207,63-153,71)</td>
<td>114 (182,18-179,87)</td>
<td>ns</td>
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<tr>
<td>Hb (g/dL)</td>
<td>11,7</td>
<td>11,6 (11-2,5)</td>
<td>11,9 (12,5-2,2)</td>
<td>ns</td>
</tr>
<tr>
<td>Tnt (ng/L)</td>
<td>39,9</td>
<td>43,8 (3,5-290)</td>
<td>30,5</td>
<td>0,021</td>
</tr>
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SD: systolic dysfunction, LVWT: Left ventricular wall thickness, IVST: Interventricular septal thickness, LVS: Left ventricular strain, LVD: Left Ventricle Diameter, LVH Left ventricle hypertrophy.

Table 2:

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
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<tbody>
<tr>
<td>Diabetic patients</td>
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<td></td>
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</tr>
<tr>
<td>Tnt (ng/L)</td>
<td>ACR, eGFR, age</td>
<td>LVH</td>
<td>&lt;0,005</td>
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<tr>
<td>Non-diabetic patients</td>
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<tr>
<td>Tnt (ng/L)</td>
<td>Age, LVH</td>
<td>eGFR</td>
<td>&lt;0,05</td>
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#6732

**EPICARDIAL ADIPOSE TISSUE AND REVERSE EPIDEMIOLOGY IN DIALYSIS PATIENTS**

**Luis D’marco¹, Ana Checa-Ros¹, Cristina Karohl², Carlos Soto³, Valmore Bermudez⁴ and Paolo Raggi⁵**

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**Background and Aims:** Conventional risk factors of cardiovascular disease and mortality in the general population such as body mass is relate to adverse outcome in dialysis patients, but often in an opposite direction (reverse epidemiology). On the contrary, epicardial adipose tissue (EAT) has reported to have a local inflammatory and proatherogenic effect. Thus, the association of EAT as direct measures of region specific adipose tissue in chronic kidney disease (CKD) has been studied.

**Method:** The study evaluated 37 CKD-5 patients in hemodialysis (mean dialysis duration 26±30 months, 70% males, 57% African-American, 48% diabetic) that underwent MSCT to measure EAT and coronary artery calcium (CAC) score. CAC distribution in quartiles of EAT was assessed. Finally, we measured patients’ body mass index (BMI) and categorized them as normal (BMI 18.5-25 kg/m²) and abnormal BMI (BMI >25 kg/m²).

**Results:** The mean BMI was 28.6±5.7 kg/m², and the mean EAT volume was 66±29 ml and 102±69 ml for normal and abnormal BMI groups. There was a direct correlation between dialysis vintage and EAT while BMI showed an inverse relationship with dialysis vintage (p = 0.05). In this small sample size, the association of CAC and EAT was only marginally significant (p = 0.7). EAT was significantly correlated with age (p = 0.02), history of cardiovascular disease (p = 0.03) and diabetes (p = 0.001).

**Conclusion:** The direct association of EAT with dialysis vintage in the face of an inverse association of BMI with dialysis duration appear to support the notion that chronic hemodialysis is a state of chronic inflammation and malnutrition.
INSULIN RESISTANCE IN PEDIATRIC CKD PATIENTS  
Dina E. Sallam  
Faculty of Medicine, Ain Shams University, Pediatric Nephology, Cairo, Egypt

**Background and Aims:** Pediatric chronic kidney disease (CKD) is associated with disturbance of glucose metabolism & insulin receptor sensitivity leading to impaired glucose tolerance & insulin resistance (IR), which are potential risk factors for cardiovascular disease (CVD). Hyperinsulinemia and IR are not extensively investigated in children with CKD, especially in different stages of CKD. The aim of our study was to detect hyperinsulinemia & IR in pediatric CKD patients.

**Method:** A total of 87 children and adolescents; 58 with chronic kidney disease (CKD); (29 CKD stage 2-4, pre-dialysis group & 29 CKD stage 5 on regular hemodialysis, CKD5d group) & 29 age & gender matched controls were enrolled in the current cross-sectional study. Homeostasis model assessment of insulin resistance (HOMA-IR) using fasting insulin & glucose, where IR was considered if HOMA-IR was 4.39.

**Results:** Fasting insulin & glucose hadn't significantly changed between CKD patients & controls (p = 0.7, 0.3 respectively), while IR represented by HOMA-IR was found in a total of 11 (12.6%) CKD patients (6, 6.89% CKD5d & 5, 5.74% CKD 2-4) with no significant difference between pre-dialysis & dialysis groups (p > 0.05), while it was significant with controls (p = 0.039), meanwhile, the total means of HOMA-IR between were no statistically significant between all CKD patients & (p = 0.64). HOMA-IR correlated positively to dialysis durations (p < 0.001, < 0.001 respectively), but hadn’t changed with BMI.

**Conclusion:** Pre-dialysis & dialysis CKD pediatric patients are at a high risk of IR & hence CVD. CKD & dialysis durations are independent risk factors for IR.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=29)</th>
<th>CKD5d (n=29)</th>
<th>CKD2-4 (n=29)</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Groups</strong></td>
<td>Mean ± SD</td>
<td>Median (IQR) N (%)</td>
<td>Mean ± SD</td>
<td>Median (IQR) N (%)</td>
</tr>
<tr>
<td>Fasting Insulin uU/ml</td>
<td>7.7 (6.4 - 8.6)</td>
<td>4.9 (2.8 - 11.9)</td>
<td>6.2 (2.7 - 10)</td>
<td>H= 0.712</td>
</tr>
<tr>
<td>Fasting Glucose mg/dL</td>
<td>88.52 ± 7.88</td>
<td>93.45 ± 20.89</td>
<td>96.03 ± 23.88</td>
<td>f= 1.187</td>
</tr>
<tr>
<td>HOMAIR</td>
<td>1.68 (1.36 - 1.9)</td>
<td>1.15 (0.54 - 3.09)</td>
<td>1.36 (0.61 - 2.33)</td>
<td>H= 0.868</td>
</tr>
<tr>
<td>IR (HOMA-IR&gt;4.39)</td>
<td>No 29 (100%)</td>
<td>23 (79.31%)</td>
<td>24 (82.75%)</td>
<td>Fisher's Exact test</td>
</tr>
<tr>
<td></td>
<td>Yes 0 (0%)</td>
<td>6 (20.68%)</td>
<td>5 (17.25%)</td>
<td></td>
</tr>
</tbody>
</table>

(1): *One Way ANOVA test of significance, (H): *Kruskal Wallis test of significance, *Post-hoc Bonferroni test was significant between: (K1) Control group Vs. (CKD5d and CKD2-4 groups).
QUALITY OF LIFE, PRURITUS BURDEN, AND TREATMENT SATISFACTION IN CHRONIC KIDNEY DISEASE PATIENTS IN GERMANY

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1CSI, Vifor, Medical Affairs, Munich, Germany, 2Nephrologisches Zentrum Villingen-Schwenningen, Villingen-Schwenningen, Germany, 3MVZ Saarpfalz GmbH, Heimdialyse Saar, Homburg, Germany and 4Bundesverband Niere eV, Mainz, Germany

Background and Aims: Chronic kidney disease (CKD) and its related symptoms significantly impact patients’ health-related quality of life (HRQoL). CKD-associated pruritus (CKD-aP) often affects patients with advanced CKD, particularly those on renal replacement therapy, and remains mostly underrecognized by both patients and medical providers. To explore the current patients’ impairment of HRQoL due to CKD-aP, we conducted a quantitative survey amongst members of a CKD patient association in Germany.

Methods: Our questionnaire was distributed via the channels of the German National Kidney Patients Association (Bundesverband Niere e.V.) from mid-June to mid-September 2022. Responses of 569 CKD-patients of a total of roughly 16,000 members were analysed regarding their general health, HRQoL, and general treatment satisfaction using multiple choice questions. Pruritus burden was assessed with a 0-10 numeric rating scale.

Results: The demographic details are displayed in Figure 1. Among the surveyed CKD patients, 33% were transplanted, 39% on hemodialysis, and 7% on peritoneal dialysis. We could confirm that most CKD patients (92%) suffered from comorbidities. Initially, 12% reported dermatological comorbidities but when asked specifically about pruritus, 62% reported this symptom which was also associated with worse HRQoL. (Figure 2). However, only one third was receiving antipruritic treatment by a physician. Furthermore, patients who were able to fully or at least partially participate in their medical decisions showed higher satisfaction and higher HRQoL (86% vs. 65% vs. 43% satisfaction, depending on full/partial/no participation, respectively) yet the patients did not always perceive that shared-decision-making was possible. Patients also showed high interest in topics outside of their primary CKD treatment, such as overall symptom control and additional psychological measures. They reported higher HRQoL when these areas were addressed by the medical team (87% vs. 55% satisfaction).

Conclusions: Our survey results emphasize the persisting need for shared or co-creative exchange between patient and physician. Improving patient education and the caregiver’s awareness of the burden of pruritus – one of the many CKD-related symptoms – could be a first step towards higher patient satisfaction and HRQoL and higher treatment rates. CKD-aP appears underreported by patients via unprovoked questioning and should be screened frequently.

Table 1:

<table>
<thead>
<tr>
<th>Sex*</th>
<th>Male n (%)</th>
<th>Female n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>245 (43 %)</td>
<td>320 (56 %)</td>
</tr>
<tr>
<td>Age at the time of the survey</td>
<td>56 years</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>19 – 88 years</td>
<td></td>
</tr>
<tr>
<td>&lt; 46 years n (%)</td>
<td>117 (21 %)</td>
<td></td>
</tr>
<tr>
<td>46 – 55 years n (%)</td>
<td>128 (22 %)</td>
<td></td>
</tr>
<tr>
<td>56 – 65 years n (%)</td>
<td>194 (34 %)</td>
<td></td>
</tr>
<tr>
<td>&gt; 65 years n (%)</td>
<td>130 (23 %)</td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td>160 (28 %)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>132 (23 %)</td>
<td></td>
</tr>
<tr>
<td>Full time employed</td>
<td>134 (24 %)</td>
<td></td>
</tr>
<tr>
<td>Part time employed</td>
<td>101 (18 %)</td>
<td></td>
</tr>
<tr>
<td>School/ Apprenticeship/ Studies</td>
<td>8 (1 %)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>33 (6 %)</td>
<td></td>
</tr>
</tbody>
</table>

*4 patients (1%) specified “diverse.”

Figure 1:
IN CHRONIC KIDNEY DISEASE, IRON DEFICIENCY-INDUCED ANEMIA IS ASSOCIATED WITH HIGHER LEVELS OF FGF23 THAT ARE NOT REDUCED BY IRON ADMINISTRATION

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Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC). Nephrology Service, Reina Sofia University Hospital. University of Córdoba (Spain), Córdoba, Spain

Background and Aims: Iron (Fe) deficiency significantly contributes to anemia in chronic kidney disease (CKD). High FGF23 levels, commonly found in CKD, are related to adverse outcomes in patients. In the normal setting, an association between Fe deficiency and FGF23 has been observed. However, it is unknown whether Fe deficiency-induced anemia might contribute to the excessive FGF23 levels in CKD. Thus, this study was intended to evaluate the interplay between Fe deficiency, CKD, and FGF23.

Method: Male Wistar rats with normal renal function received either standard (40 ppm Fe) or Fe-deficient (4 ppm Fe) diets for 6 weeks to induce anemia. Then, several normal and all the anemic rats were switched to an adenine-enriched (0.6%) diet to induce renal damage. Groups of anemic-uremic animals were treated with oral (ferric citrate, FC and ferrous sulfate, FS) or intravenous (ferric carboxymaltose, FCx) Fe at a dose of 9 mg/kg for 5 weeks. Hematological and mineral metabolism parameters were determined at sacrifice. All experimental protocols were approved by the Ethics Committee for Animal Research of the University of Córdoba.

Results: Plasma and serum biochemistries are shown in Table 1. CKD per se was associated with derangements in hematological parameters. The presence of Fe deficiency-induced anemia further decreased these parameters, being statistically significant in the case of serum Fe (P = 0.003). Iron therapy improved hematocrit, hemoglobin, and Fe levels, although statistical significance for all of them was only reached when FC was administered (P = 0.012, P = 0.038, and P = 0.002, respectively). As expected, CKD rats exhibited disturbances in mineral metabolism. Interestingly, anemic and anemic rats showed higher intact (P = 0.039) and c-terminal (P = 0.048) FGF23 levels when compared with CKD group. Despite normalization of serum Fe, intact FGF23 further increased following administration of FS (P = 0.022), and same trend was observed with all the compounds. However, cFGF23 levels remained unchanged in all the Fe-treated groups.

Conclusion: The presence of Fe-induced anemia in an experimental model of CKD is associated with further increases in the levels of both intact and c-terminal FGF23. Thus, other factors distinct than serum Fe might influence FGF23 levels. Our results support the need for investigating the precise mechanisms underlying the relationship between Fe and FGF23 to optimize the clinical management of anemia, particularly in the context of renal dysfunction.

Audiological assessment in pediatric CKD patients

Dina E. Sallam

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Background and Aims: Many similarities exist between the nephron & ear infrastructures, making them vulnerable to same risk factors. Idiopathic sensory neural hearing loss is frequent in pediatric patients with chronic kidney disease (CKD). Our aims were to determine the prevalence, type, & degree of hearing impairment in pediatric CKD patients.

Method: This cross-sectional study was carried out at pediatric dialysis & nephrology unit at Children's hospital & Audiology unit, Faculty of Medicine Ain Shams University, included 45 CKD patients’ stage 2-4, 45 CKD patients’ stage 5 on hemodialysis, & 90 children as controls. Detailed history, physical, otological examinations & audiological assessment by standard pure tone audiometry, speech audiometry & tympanometry, IQ test, in addition to some laboratory investigations were done for all our studied patients.

Results: The mean IQ was significantly lower in CKD patients than the controls, however, it was significantly higher in dialysis than non-dialysis groups (P = 0.05). Pure tone audiometry showed 16.6% of out CKD patients had hearing loss, which was mainly sensory neural (SNHL); (53.3%), that was significantly higher compared to the control group (P < 0.001). A mild degree of high-frequency hearing loss was frequently reported. These findings weren’t significantly different between dialysis & non-dialysis patients, but were significant compared to control group (P < 0.001). Regarding speech discrimination scores, controls had a higher significant change compared to CKD patients. Regarding Tympanometry test results, most of CKD patients & the controls had normal middle ear pressure. The most determining factor affecting the hearing loss in our patients was the IQ.

Conclusion: High-frequency SNHL is not uncommon in CKD pediatric patients, in addition to low IQ. It’s recommended to do a routine audiological evaluation & follow up for early diagnosis & intervention.

Table 1: Plasma and serum biochemistry of the animals included in the study. Data are expressed as mean ± SEM.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CKD</th>
<th>CKD-Anemia</th>
<th>CKD-Anemia + FC</th>
<th>CKD-Anemia + FS</th>
<th>CKD-Anemia + FCx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron (mg/dl)</td>
<td>166 ± 14</td>
<td>122 ± 4a</td>
<td>71 ± 6b</td>
<td>142 ± 13a</td>
<td>234 ± 41bc</td>
<td>91 ± 28a</td>
</tr>
<tr>
<td>Hemoglobin (g/l)</td>
<td>14.7 ± 0.5</td>
<td>10.1 ± 0.8a</td>
<td>9.0 ± 0.6a</td>
<td>12.0 ± 13a</td>
<td>10.4 ± 1.0a</td>
<td>10.1 ± 0.3a</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>43.3 ± 0.6</td>
<td>25.3 ± 1.4a</td>
<td>22.9 ± 1.6a</td>
<td>31.7 ± 1.7abc</td>
<td>30.5 ± 1.7abc</td>
<td>27.7 ± 1.5a</td>
</tr>
<tr>
<td>Ionized calcium (mM)</td>
<td>1.25 ± 0.03</td>
<td>1.21 ± 0.02</td>
<td>1.32 ± 0.03b</td>
<td>1.35 ± 0.06</td>
<td>1.29 ± 0.03</td>
<td>1.28 ± 0.02</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>5.2 ± 0.5</td>
<td>25.2 ± 2.5a</td>
<td>17.7 ± 1.3ab</td>
<td>18.3 ± 2.7a</td>
<td>14.8 ± 1.9b</td>
<td>24.1 ± 2.2ab</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.53 ± 0.02</td>
<td>4.33 ± 0.67a</td>
<td>4.68 ± 0.70a</td>
<td>6.94 ± 0.83ab</td>
<td>5.03 ± 0.17a</td>
<td>8.18 ± 0.58abc</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>127 ± 9</td>
<td>504 ± 64a</td>
<td>578 ± 108a</td>
<td>715 ± 238a</td>
<td>395 ± 101a</td>
<td>969 ± 517a</td>
</tr>
<tr>
<td>Intact FGF23 (fold change vs. Control)</td>
<td>1 ± 0.1</td>
<td>91 ± 32a</td>
<td>196 ± 33b</td>
<td>282 ± 43ab</td>
<td>346 ± 41bc</td>
<td>323 ± 35ab</td>
</tr>
<tr>
<td>C-terminal FGF23 (fold change vs. Control)</td>
<td>1 ± 0.2</td>
<td>47 ± 13a</td>
<td>126 ± 28b</td>
<td>161 ± 38ab</td>
<td>137 ± 42ab</td>
<td>201 ± 27ab</td>
</tr>
</tbody>
</table>

CKD: chronic kidney disease, FC: ferric citrate, FS: ferrous sulfate, FCx: ferric carboxymaltose

#5517

#3935
**Table 1: Auditory findings in patients & controls.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patient (n = 90)</th>
<th>Control (n = 90)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hearing assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>75</td>
<td>89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Impaired</td>
<td>15</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Type of the impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNHL</td>
<td>8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>CHL</td>
<td>5</td>
<td>1</td>
<td>0.049</td>
</tr>
<tr>
<td>Mixed</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Thresholds of hearing loss</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flat frequency</td>
<td>1</td>
<td>0</td>
<td>0.080</td>
</tr>
<tr>
<td>Low frequency</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>High frequency</td>
<td>10</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1: Comparison of clinical and patient reported outcomes before and after program.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before program</th>
<th>After 4-week program</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP, mmHg</td>
<td>162 (120-198)</td>
<td>141 (109-179)</td>
<td>0.046</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>74 (58-83)</td>
<td>68 (57-81)</td>
<td>0.12</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>190 (80-401)</td>
<td>215 (162-586)</td>
<td>0.89</td>
</tr>
<tr>
<td>Partner in Health total score</td>
<td>57 (10-94)</td>
<td>84 (72-96)</td>
<td>0.04</td>
</tr>
<tr>
<td>EuroQOL-5 dimensions total score</td>
<td>5 (5-9)</td>
<td>5 (5-6)</td>
<td>0.16</td>
</tr>
<tr>
<td>Modified Health Care Climate Questionnaire total score</td>
<td>-</td>
<td>42 (36-42)</td>
<td></td>
</tr>
</tbody>
</table>

Continuous data presented as median (minimum-maximum) and compared using Wilcoxon signed rank test for related samples.
Table 1: Baseline demographic and clinical findings.

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 18)</th>
<th>Control (n = 20)</th>
<th>p</th>
<th>TOTAL (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6 (33%)</td>
<td>11 (55%)</td>
<td>0.23</td>
<td>17 (44%)</td>
</tr>
<tr>
<td>Male</td>
<td>12 (67%)</td>
<td>9 (45%)</td>
<td>0.76</td>
<td>21 (56%)</td>
</tr>
<tr>
<td>Age (median) (Range)*</td>
<td>44 (22-50)</td>
<td>42 (27-48)</td>
<td>0.001</td>
<td>86 (43-50)</td>
</tr>
<tr>
<td>BMI (median) (Range)</td>
<td>25.3 (20.7-33.2)</td>
<td>28.3 (21.6-37.5)</td>
<td>0.21</td>
<td>28.06 (20.7-37.5)</td>
</tr>
<tr>
<td>GFR (median) (Range)*</td>
<td>19 (6-28)</td>
<td>110.5 (63.7-120)</td>
<td>&lt;0.0001</td>
<td>28 (6-120)</td>
</tr>
<tr>
<td>Calcium (median) (Range)</td>
<td>9.06 (7.2-9.9)</td>
<td>3.97 (8.1-10.2)</td>
<td>0.049</td>
<td>9.09 (7.2-10.2)</td>
</tr>
<tr>
<td>Phosphorus (median) (Range)*</td>
<td>4.3 (3.1-6.5)</td>
<td>4.05 (3.1-4.05)</td>
<td>0.12</td>
<td>4.1 (3.1-6.5)</td>
</tr>
<tr>
<td>Parathormone (median) (Range)*</td>
<td>140 (19-630)</td>
<td>40.2 (23-87.3)</td>
<td>&lt;0.0001</td>
<td>64.8 (19-630)</td>
</tr>
<tr>
<td>Vitamine D (median) (Range)</td>
<td>13.8 (5.1-35)</td>
<td>14.5 (3-35)</td>
<td>0.13</td>
<td>13.8 (3-35)</td>
</tr>
<tr>
<td>DXA (n = 33)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal T-Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>10 (62%)</td>
<td>12 (71%)</td>
<td>0.62</td>
<td>22 (67%)</td>
</tr>
<tr>
<td>Osteopenia/Osteoporoz</td>
<td>6 (38%)</td>
<td>5 (29%)</td>
<td>0.46</td>
<td>11 (33%)</td>
</tr>
<tr>
<td>Femoral Neck T-Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>9 (56%)</td>
<td>11 (65%)</td>
<td>0.61</td>
<td>20 (61%)</td>
</tr>
<tr>
<td>Osteopenia/Osteoporoz</td>
<td>7 (44%)</td>
<td>6 (35%)</td>
<td>0.39</td>
<td>13 (39%)</td>
</tr>
<tr>
<td>Total T SCORE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>6 (38%)</td>
<td>10 (59%)</td>
<td>0.22</td>
<td>16 (48%)</td>
</tr>
<tr>
<td>Osteopenia/Osteoporoz</td>
<td>10 (62%)</td>
<td>7 (41%)</td>
<td>0.17</td>
<td>17 (52%)</td>
</tr>
<tr>
<td>QCT (n = 33)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>12 (80%)</td>
<td>15 (82%)</td>
<td>0.80</td>
<td>27 (81%)</td>
</tr>
<tr>
<td>Osteopenia/Osteoporoz</td>
<td>3 (20%)</td>
<td>3 (18%)</td>
<td>0.19</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Femoral Neck BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>10 (67%)</td>
<td>13 (71%)</td>
<td>0.73</td>
<td>23 (69%)</td>
</tr>
<tr>
<td>Osteopenia/Osteoporoz</td>
<td>5 (33%)</td>
<td>5 (29%)</td>
<td>0.31</td>
<td>10 (31%)</td>
</tr>
<tr>
<td>Total BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>9 (60%)</td>
<td>12 (67%)</td>
<td>0.69</td>
<td>21 (64%)</td>
</tr>
<tr>
<td>Osteopenia/Osteoporoz</td>
<td>6 (40%)</td>
<td>6 (33%)</td>
<td>0.13</td>
<td>12 (36%)</td>
</tr>
</tbody>
</table>

Table 2: The results of bone status in lumbar spine and femoral neck in the whole cohort.

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Control</th>
<th>p</th>
<th>Health control group</th>
<th>CRF group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QCT</td>
<td>QCT</td>
<td></td>
<td>QCT</td>
<td>QCT</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Osteopenia+Osteoporoz</td>
<td>Total</td>
<td>p</td>
<td>Normal</td>
</tr>
<tr>
<td>DXA L1-L4*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>9 (100%)</td>
<td>0</td>
<td>9 (100%)</td>
<td>0.01</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>Osteopenia+Osteoporoz</td>
<td>3 (50%)</td>
<td>3 (50%)</td>
<td>6 (100%)</td>
<td></td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Total</td>
<td>12 (80%)</td>
<td>3 (20%)</td>
<td>15 (100%)</td>
<td></td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Femoral Neck**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>7 (88%)</td>
<td>1 (12%)</td>
<td>8 (100%)</td>
<td>0.06</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Osteopenia+Osteoporoz</td>
<td>3 (43%)</td>
<td>4 (57%)</td>
<td>7 (100%)</td>
<td></td>
<td>1 (16%)</td>
</tr>
<tr>
<td>Total</td>
<td>10 (67%)</td>
<td>5 (33%)</td>
<td>15 (100%)</td>
<td></td>
<td>11 (69%)</td>
</tr>
<tr>
<td>Total BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>5 (100%)</td>
<td>0</td>
<td>5 (100%)</td>
<td>0.02</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>Osteopenia+Osteoporoz</td>
<td>4 (40%)</td>
<td>6 (60%)</td>
<td>10 (100%)</td>
<td></td>
<td>2 (28%)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (60%)</td>
<td>6 (40%)</td>
<td>15 (100%)</td>
<td></td>
<td>10 (63%)</td>
</tr>
</tbody>
</table>

Method: We performed control cross-sectional study in single center in Turkey between 2019, and 2022. We evaluated two groups aged 18-50 years. Patients groups; consisted of patients with stage 4 - 5 chronic kidney disease, and control healthy groups; consisted of healthy participants. The bone status of thirty-three participants was evaluated using both cQCT and DXA. Diagnostic discordance was assessed between the lumbar spine and femoral neck from DXA and cQCT.

Results: Thirty-eight participants were included in the study and BMD of 33 was evaluated with DXA and cQCT. The median age was 44 years (range 22-50) in the patient’s group (33% female), and 42 years (range 27-48) in controls (55% female). Baseline variables were outlined in Table 1. Using the DXA T score and cQCT; the incidence of osteopenia or osteoporosis was not statistically different in the patient and control groups (for DXA; spine and femoral neck, p: 0.62 and 0.61 respectively, for cQCT; spine and femoral neck, p:0.8 and 0.73 respectively). Regarding the lumbar spine, DXA diagnosed osteopenia or osteoporosis more frequently compared to QCT in the patient’s group [6 (40%) vs 3 (20%), p = 0.01]. Three of 6 patients (50%) diagnosed with osteopenia or osteoporosis by DXA were evaluated as having normal bone status by QCT. There was no statistical difference between the two methods in the control group. The results of bone status in lumbar spine and femoral neck in the whole cohort were summarized in Table 2.

Conclusion: According to our result, in young or middle-aged patients with stage 4-5 CKD, DEXA might overdiagnosis osteopenia or osteoporosis compared to QCT.

#4795
PEAK SYSTOLIC VELOCITY IN THE KIDNEY INTERLOBAR ARTERIES AS A POSSIBLE SCREENING MARKER OF CKD IN PREGNANT WOMEN
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1Moscow Regional Research Institute of Obstetrics and Gynecology, Moscow, Russia, 2Moscow Regional Research Clinical Institute, Moscow, Russia and 3Ural Federal University, Ekaterinburg, Russia

Background and Aims: Currently, pregnancy is increasingly occurring in patients with CKD including patients with chronic renal failure (CRF) - CKD grade 3-5. Physiological renal hyperperfusion and glomerular hyperfiltration in pregnant women leads to a temporary decrease in serum creatinine values even in patients with CRF. Consequently, the CKD diagnosis during pregnancy may be difficult in women without a history of kidney disease, and the degree of kidney damage may be underestimated [1]. The aim of our study was to

Table 1: Study groups of patients.

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health control group</td>
<td>50</td>
</tr>
<tr>
<td>CKD group</td>
<td>233</td>
</tr>
<tr>
<td>CKD1</td>
<td>143</td>
</tr>
<tr>
<td>CKD2</td>
<td>34</td>
</tr>
<tr>
<td>CRF group</td>
<td>45</td>
</tr>
<tr>
<td>CRF1</td>
<td>7</td>
</tr>
<tr>
<td>CRF2</td>
<td>56</td>
</tr>
<tr>
<td>CRF3</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>283</td>
</tr>
</tbody>
</table>
estimate Doppler sonography of the renal arteries as a possible CKD screening method in pregnant women.

**Method:** The study included 283 pregnant women (Table 1). Doppler sonography was performed in the main renal, segmental, interlobar and interlobular arteries in left and right kidney at the first, second and third trimesters of pregnancy. Peak systolic velocity (PSV), end-diastolic velocity, pulse index, resistive index and systolic-diastolic ratio were analyzed.

**Results:** PSV in the renal arteries was significantly lower in pregnant women with CKD 3-5 compared with healthy control group since 22 weeks of pregnancy. However, PSV in the interlobar arteries had a higher diagnostic value. The values of this parameter were significantly lower in pregnant women with all stages CKD compared with healthy control group. We found cut-off points of right and left interlobar arteries PSV linear combination at the second and third trimesters of pregnancy. Peak systolic velocity (PSV), end-diastolic velocity, pulse index, resistive index and systolic-diastolic ratio were analyzed.

**Conclusion:** In pregnant women, interlobar renal arteries PSV can be used as screening marker of CKD. Additionally, it allows to identify pregnant women with advanced stages of CKD. The linear combination of right and left interlobar arteries PSV has the greatest diagnostic value.

### Table 2: Cut-off points of interlobar arteries PSV (cm/sec) and linear combination of right and left interlobar arteries PSV (cm/sec) for CKD and CRF diagnosing in pregnant women; sensitivity (Se) and specificity (Sp) of method.

<table>
<thead>
<tr>
<th>Screening target</th>
<th>Interlobar artery</th>
<th>First trimester</th>
<th>Second trimester</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PSV Se Sp</td>
<td>PSV Se Sp</td>
<td>PSV Se Sp</td>
</tr>
<tr>
<td>CKD diagnosing</td>
<td>Right</td>
<td>24.7 81.2% 81.2%</td>
<td>31.5 75% 75%</td>
<td>32 77% 76%</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>24.5 80% 80%</td>
<td>32 77% 76%</td>
<td>32 77% 76%</td>
</tr>
<tr>
<td></td>
<td>Linear combination formula*</td>
<td>0.057*PSV right + 87% 83%</td>
<td>0.074*PSV right + 81% 81%</td>
<td>0.074*PSV right + 81% 81%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.26 -0.98</td>
<td>4.64 0.19</td>
<td>4.64 0.19</td>
</tr>
<tr>
<td>CRF diagnosing</td>
<td>Right</td>
<td>23.6 73% 83%</td>
<td>24 82% 84%</td>
<td>23 82% 80%</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>22.6 78% 75%</td>
<td>24 82% 84%</td>
<td>24 82% 84%</td>
</tr>
<tr>
<td></td>
<td>Linear combination formula*</td>
<td>0.063*PSV right + 80% 81%</td>
<td>0.069*PSV right + 84% 84%</td>
<td>0.057*PSV right + 84% 84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.85 -0.55</td>
<td>3.94 -0.91</td>
<td>3.94 -0.91</td>
</tr>
</tbody>
</table>

*Linear combination of right and left interlobar arteries PSV was founded by linear discriminant analysis.

#4368

THE PERSISTENT UNDERREPRESENTATION OF PEOPLE WITH CHRONIC KIDNEY DISEASE IN CARDIOVASCULAR TRIALS: A SYSTEMATIC REVIEW AND EVIDENCE MAP

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1UMC Utrecht, Department of Nephrology and hypertension, Utrecht, Netherlands, 2UMC Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands, 3Cochrane Netherlands, Julius Centre for Health Sciences and Primary Care, UMC Utrecht, Utrecht, Netherlands, 4Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Cardiovascular Sciences, Amsterdam, Department of Cardiology, Amsterdam, Netherlands and 5Amsterdam UMC, University of Amsterdam, Amsterdam Public Health, Medical library, Amsterdam, Netherlands

**Background and Aims:** People with chronic kidney disease (CKD) have a markedly higher risk for cardiovascular disease. Systematic underrepresentation of people with CKD in cardiovascular randomised controlled trials (RCTs) limits evidence to guide cardiovascular risk management (CVRM). In this systematic review we aimed to identify evidence gaps regarding CVRM medication for people with CKD and evaluated the prevalence of exclusion of people with CKD from cardiovascular RCTs.

**Method:** We searched Clinicaltrials.gov through the Cochrane Central Register of Controlled Trials from inception until October 2021. Eligible studies were randomised controlled trials (RCTs) that investigate the efficacy of guideline-recommended CVRM medications on (cardiovascular) mortality, cardiovascular morbidity, and end-stage kidney disease in adults with a history of cardiovascular disease or one or more major risk factors for cardiovascular disease. Two reviewers independently determined the eligibility of references and extracted data. Outcomes were an overview of studies that report results for people with CKD, evidence gaps in results, and the rate of exclusion of people with CKD.

**Results:** We included 2794 eligible RCTs involving 2,158,869 participants (mean age 63±6 years, 36% female). Overall, 841 (71%) RCTs excluded (subgroups of) people with CKD based on heterogenous exclusion criteria. Since 2000, this prevalence has increased from 70% to 73%. Of included RCTs, only 157 (13%) reported results for people with CKD (again in heterogenous subgroups). The prevalence of RCTs with results for people with CKD has increased since 2000 to 10% to 23%. Nevertheless, significant evidence gaps remain for most CVRM interventions, particularly for those with an eGFR <30 ml/min/1.73m² (22 RCTs), and people who are treated with dialysis (14 RCTs) or received a kidney transplant (1 RCTs).

**Conclusion:** The majority of cardiovascular RCTs continues to exclude (subgroups of) people with CKD and this has only increased over the years. Although more RCTs report results for people with CKD, evidence gaps for the efficacy most CVRM medications persist, particularly for those with severe CKD.

##REFERENCE

Figure 1: Heatmap of (subgroup) analyses for MACE for people with different stages CKD. Panel A shows the analyses for people with CKD for antihypertensives, panel B for lipid-lowering drugs, panel C for antiplatelets and anticoagulants, panel D for glucose-lowering drugs, and panel E for a combination of these of these drug groups.

Abbreviations: ACE-i, ace-inhibitor; ARB, angiotensin receptor blocker; ARNi Angiotensin Receptor-Neprilysin Inhibitor; CCB, calcium channel blocker; DAPT, double antiplatelet therapy; DOAC, direct oral anticoagulant; DPP-4, dipeptidyl peptidase-4; GLP-1, Glucagon-like peptide 1; MRA, mineralocorticoid receptor antagonist; PCSK-9, proprotein convertase subtilisin/kexin-9; renin-i, renin-inhibitor; SAPT, single antiplatelet therapy; SGLT-2, sodium-glucose cotransporter 2; TAPT, triple antiplatelet therapy; VKA, vitamin K antagonist.

Figure 1: continued

#5026

ESTIMATED PROXIMAL TUBULE FLUID PHOSPHATE CONCENTRATION AS AN ELEMENT OF DECREASED RENAL FUNCTION IN PATIENTS UNDERGOING UNILATERAL NEPHRECTOMY

Lida Tartaglione, Silverio Rotondi, Francesca Franco, Marzia Pasquali, Francesca Tinti and Sandro Mazzaferro

Sapienza University of Rome, Roma, Italy

Background and Aims: Patients with chronic renal failure (CRF) develop early alterations in mineral metabolism called Chronic Kidney Disease Mineral Bone Disorders (CKD-MBD), detectable with the available markers (PTH, Ca, P) only in the most advanced stages of disease. Recent evidence suggests that the early development of CKD-MBD is related to the nutritional phosphorus intake and the reduction of the number of nephrons (renal functional reserve). In fact, with the reduction in the nephrons number, compensation systems must be activated for the maintenance of the phosphoric balance with an increase in urinary phosphate and in the concentration of phosphorus in the single nephron (ePTFp). Therefore, the measurement of ePTFp has been proposed as a new early marker of CKD-MBD and effective renal functional reserve. Threshold values of ePTFp (2.2 mg/dl) have been identified to indicate patients with reduced renal functional reserve and therefore at increased risk of progression of renal damage. The measurement of residual renal function with ePTFp may be a useful parameter to be evaluated in patients who undergo unilateral nephrectomy due to renal neoplasia. In fact, post-nephrectomy some patients have a high reduction of the renal function not identified by preoperative GFR assessment or other risk factors. In these patients, ePTFp could represent a measure of pre nephrectomy kidney functional reserve and thus indicate the risk of reduce renal function after nephrectomy. The aim of the study was to evaluate the relationship between pre-operative ePTFp and renal function after nephrectomy.

Methods: This is a transversal monocentric observational study. From January 2022 to November 2022, we enrolled patients diagnosed with renal cell carcinoma for which has been indicated unilateral nephrectomy surgery. In all patients we evaluated pre nephrectomy and three months after surgery, renal function, and ePTFp with the formula \[ ePTFp = \frac{\text{Phosphaturia}}{\text{creatininuria}} \times \text{ creatininemia} \times 3.33 \]. 30 subjects with normal renal function (eGFR 100 ± 10 ml/min, no proteinuria) were evaluated for the ePTFp preference values.

Results: We evaluated 13 patients: age 57.5 ± 13.6; Cr 1.48 ± 0.7 mg/dl; eGFR 58.5 ± 23.3, ml/min; Pi, mg/dl 3.2 ± 0.6; Ca 9.9 ± 0.6 mg/dl; PTH 38.8 ± 41 pg/ml FA 176.7 ± 108 IU/L, proteinuría 500 ± 150 mg. Compared to the control population (GFR 100 ml/min) the 24-hour phosphaturia was no different while ePTFp was increased 2.1 ± 0.9 vs 1.2 ± 0.2 mg/dl; p: 0.05. In the post-nephrectomy assessment, creatinine and GFR were stable (Cr 1.48±0.7 vs 1.5 ± 0.7 mg/dl; p: n.s; eGFR 58.5 ± 23.3, vs 56.5 ± 22.3, ml/min; p: n.s), while ePTFp was increased (ePTFp pre 2.1 ± 0.9 vs ePTFp post 3.3 ± 2.7; p<0.01). Patients with pre-nephrectomy ePTFp ≥ 2.2 mg/dl (n. 6, eGFR 56.5 ± 20.3, proteinuría 500±100 mg/24h) had a greater renal function reduction post nephrectomy (mean GFR delta -9.5±2 ml/min) respect to patients with pre-nephrectomy ePTFp <2.2 mg/dl (n. 7, eGFR 59.7 ± 24.3, proteinuría 500±200 mg/24h; mean GFR delta -0.5±2 ml/min; p: 0.05). In all the population there was direct correlation between ePTFp and the reduction of GFR post nephrectomy (r: 0.667; p: 0.05).
Conclusion: In our patients ePTFp was higher than the control group and correlate with the entity of the GFR reduction post nephrectomy. The group with a preoperative ePTFp ≥ 2.2 mg/dl had a higher post nephrectomy GFR reduction. These results suggest that ePTFp identify the pre nephrectomy kidney functional reserve. In particular and ePTFp higher than limits highlighted in the literature (2.2 mg/dl) pre nephrectomy identify a greater risk of kidney function reduction post nephrectomy. ePTFp may be proposed as a parameter to identify patients with higher risk of decreased renal function post nephrectomy.

ASSOCIATION BETWEEN FIBROBLAST GROWTH FACTOR 23 AND TRABECULAR BONE SCORE IN EARLY STAGES OF CKD

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1Comenius University Faculty of Medicine, University Hospital Bratislava, 5th department of Internal Medicine, Bratislava, Slovakia and 2Comenius University Faculty of Medicine, University Hospital Bratislava, 5th department of Internal Medicine, Bratislava, Slovakia

Background and Aims: Newer markers of kidney damage and mineral and bone changes in chronic kidney disease (CKD) are needed. The fracture risk increases with worsening of CKD with highest incidence in later stages. Thus methods for early bone status assessment and laboratory marker of kidney function is needed. Aim of the study was to evaluate bone mineral density (BMD) and trabecular bone scores (TBS) – a novel surrogate of trabecular bone microstructure, in relationship with newer laboratory markers of CKD, such as fibroblast growth factor 23 (FGF23) and klotho.

Method: A cross-sectional study during July 2018-July 2019 was conducted. Plasma levels of soluble klotho and FGF23 were determined by ELISA (enzyme-linked immuno - assay). All patients underwent bone mineral density (BMD) and trabecular bone scores (TBS) measurement. Patients were divided into 2 groups as follows: A - patients in stages G1 - G3; B - patients in stages G4 – 5 according to KDIGO.

Results: A total of 74 CKD patients (42 males and 32 females; mean age 68.8 years) were included in the study. Greater FGF23 levels in group B(N = 15) in comparison to group A (N = 59)(p = 0.01) were observed. FGF23 was associated with glomerular filtration (GF)(R = -0.43; p = 0.003), with greater levels of FGF23 at GF less than 0.8 ml/s. Significant difference in TBS within first 3 CKD stages (mean TBS in G1 = 1.374 vs. G2 = 1.304 vs. G3a = 1.24; p = 0.03) and negative correlation of FGF23 and TBS (R = -0.33; p = 0.05) and a positive correlation between klotho and TBS (R = 0.419; p = 0.04) was observed.

Conclusion: This study confirmed that FGF23 is associated with TBS. However, TBS reflects kidney function decline only in first 3 stages of CKD. Thus, FGF23 together with TBS are promising markers of early trabecular bone impairment in CKD.

EFFECT OF DAPAGLIFLOZIN IN PATIENTS WITH CKD ACROSS THE SPECTRUM OF AGE AND BY SEX

Margaret Yu1, Priya Vart2, Hiddo Lambers Heerspink3,4, Niels Jong1, Ricardo Correa-Rotter4, John McMurray5, Peter Rossing6,7, Anna Maria Langkilde8, Robert Toto9, David C. Wheeler10 and Glenn Chertow11

1Stanford University School of Medicine, Department of Medicine, United States of America, 2University of Groningen, Department of Clinical Pharmacy and Pharmacology, Groningen, Netherlands, 3The George Institute for Global Health, Australia, 4The National Medical Science and Nutrition Institute Salvador Zubiran, Mexico, 5University of Glasgow, Institute of Cardiovascular and Medical Sciences, United Kingdom, 6Steno Diabetes Center Copenhagen, Denmark, 7University of Copenhagen, Department of Clinical Medicine, Denmark, 8AstraZeneca, BioPharmaceuticals R&D, Sweden, 9UT Southwestern Medical Center, Department of Internal Medicine, United States of America, 10University College London, Department of Renal Medicine, United Kingdom and 11Stanford University School of Medicine, Departments of Medicine and Epidemiology and Population Health, United States of America

Background and Aims: The SGLT2 inhibitor dapagliflozin reduces the risk of progressive kidney disease and cardiovascular events in patients with and without type 2 diabetes. Among patients with CKD, baseline risks of cardiovascular disease and CKD progression vary based on age and sex. Whether the effects of dapagliflozin are uniform among patients across the spectrum of age and among men and women is unknown. Therefore, we performed a pre-specified analysis from the DAPA-CKD trial to evaluate efficacy and safety of dapagliflozin according to baseline age and sex.

Method: We randomized 4304 adults with baseline estimated glomerular filtration rate (eGFR) 25–75 ml/min/1.73m² and urinary albumin-to-creatinine ratio 200–5000 mg/g to dapagliflozin 10 mg or placebo once daily. The primary endpoint was a composite of ≥50% eGFR decline, end-stage kidney disease, and kidney or cardiovascular death. Secondary endpoints included a kidney composite endpoint (primary composite endpoint without cardiovascular death), a cardiovascular composite endpoint (hospitalized heart failure or cardiovascular death), and all-cause mortality. Study participants were categorized based on decades of age (<50, 50-59, 60-69, 70-79, ≥80 years). Sex was based on self-report. We conducted time-to-event analyses using a proportional hazards (Cox) regression stratified by randomization factors (diabetes status and UACR), adjusting for baseline eGFR, and analyzed the effects of dapagliflozin on total and chronic eGFR slopes using a mixed effects linear spline model.

Results: Median follow-up was 2.4 years. 671 (15.6%), 935 (21.7%), 1501 (34.9%), 999 (23.2%), and 198 (4.6%) participants were <50, 50-59, 60-69, 70-79, and ≥80 years of age, respectively; 1425 (33.1%) were women and 2879 (66.9%) were men. Racial composition varied by age and sex; older patients were more likely to be white, younger patients were more likely to be Asian, and a higher proportion of women were black. As expected, absolute risks of the cardiovascular composite endpoint and all-cause mortality were higher in older patients; absolute risks of the kidney composite endpoint were highest in patients <50 (10.7 and 6.2 per 100 patient-years in the placebo and dapagliflozin groups, respectively) and lowest in patients ≥80 years (3.0 and 1.2 per 100 patient-years in the placebo and dapagliflozin groups, respectively). There was no evidence of heterogeneity of the relative effects of dapagliflozin on the primary composite or secondary endpoints based on age or sex. Neither age nor sex modified the effects of dapagliflozin on total or chronic eGFR slope (Figure 1).

Conclusion: Benefits of dapagliflozin were evident across the spectrum of age and among women and men. Although younger trial participants with CKD and albuminuria were more likely to experience CKD progression, dapagliflozin reduced the risks of mortality, cardiovascular events, and CKD progression in older patients, including in more than 25% septuagenarians and octogenarians. Ageism and/or therapeutic nihilism should not diminish the use of dapagliflozin in older patients who are likely to experience considerable benefit.
THE SYSTEMIC AND RENAL HAEMODYNAMIC EFFECTS OF APELIN IN HEALTH AND CHRONIC KIDNEY DISEASE

Fiona Chapman1, Vanessa Melville3, Lorraine Bruce3, Janet Maguire3, Anthony Davenport4, David Newby1 and Neeraj Dhaun1

1University of Edinburgh, Centre for Cardiovascular Science, Queen’s Medical Research Institute, Edinburgh, United Kingdom, 2University of Edinburgh, Clinical Research Centre, Edinburgh, United Kingdom, 3Queen’s College, Cambridge, United Kingdom and 4University of Cambridge, Experimental Medicine & Immunotherapeutics, Cambridge, United Kingdom

Background and Aims: Chronic kidney disease (CKD) is a leading cause of global morbidity and mortality and is independently associated with cardiovascular disease. Indeed, patients with CKD are more likely to die of cardiovascular disease than they are to progress to kidney failure. Despite current standard of care, outcomes remain poor and newer therapies are needed. Apelin, an endothelium-dependent vasodilator and potent inotrope, is a potential novel treatment for CKD. There are no clinical studies of the renal actions of apelin, but pre-clinical data show that it regulates glomerular haemodynamics and promotes aquaresis. We investigated the cardiovascular and renal actions of apelin in healthy volunteers and in patients with CKD.

Method: Patients with stable, non-diabetic CKD and age- and sex-matched healthy volunteers were recruited to a prospective, randomised, double-blind and placebo-controlled study. Subjects received either pyroglutamated apelin-13 (Pyr1-apelin-13, 1 nmol/min and 30 nmol/min) or placebo on two separate visits. Cardiovascular assessments included blood pressure, impedance cardiology and pulse wave velocity; iohexol and para-aminohippurate clearance were used to assess glomerular filtration rate (GFR) and renal blood flow, respectively. Tubular function was examined via urinary sodium, potassium and free water excretion.

Results: Twelve patients with CKD and 12 healthy volunteers were recruited and completed both phases of the study protocol. Baseline characteristics are shown in Table 1. Whilst infusion of 1 nmol/min [Pyr1]apelin-13 did not affect systemic haemodynamics, 30 nmol/min [Pyr1]apelin-13 led to significant changes. Compared to placebo, mean arterial pressure fell by 3 mmHg and 4 mmHg in health and CKD, respectively (p<0.05 for both groups), and systemic vascular resistance index fell by 309 dynes*s*cm⁻⁵ m² and 407 dynes*s*cm⁻⁵ m², respectively (p<0.01 for both groups). Cardiac index increased by 0.3 L/min/m² and 0.2 L/min/m², respectively (p<0.05 for both groups compared to placebo). In contrast, both 1 nmol/min and 30 nmol/min [Pyr1]apelin-13 had similar effects on renal haemodynamics. Effective renal blood flow increased by ~15% in health and CKD (p<0.01 compared to placebo for both groups). GFR fell by ~4 mL/min compared to placebo in patients with CKD (p<0.01) but we observed no change in healthy volunteers. As a result of these changes in effective renal blood flow and GFR, filtration fraction fell by ~3% in CKD, reflected by a fall in proteinuria of ~25% (p<0.001 compared to placebo for both). Both low and high doses of [Pyr1]apelin-13 promoted natriuresis and free water clearance in health and CKD. In comparison to placebo, sodium excretion increased by ~30% and free water clearance by ~15% in both groups (p<0.05 for all comparisons). Overall, the effects of apelin were prolonged in CKD.

Conclusion: Apelin offers systemic and renal haemodynamic benefits to patients with CKD. If these effects were maintained longer-term they would translate to improved cardiovascular and renal outcomes in this at-risk patient group. Clinical trials of long-acting, oral apelin analogues are now justified in CKD and other conditions with impaired salt and water balance.
Table 1: Baseline characteristics of participants.

<table>
<thead>
<tr>
<th></th>
<th>Healthy volunteers</th>
<th>Chronic kidney disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>48±4</td>
<td>48±4</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>8 (67)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>90±6</td>
<td>95±8</td>
</tr>
<tr>
<td>Systemic vascular resistance index, dynes·cm⁻²·m⁻²</td>
<td>2548±397</td>
<td>3013±613</td>
</tr>
<tr>
<td>Cardiac index, L/min/m²</td>
<td>2.9±0.3</td>
<td>2.6±0.6</td>
</tr>
<tr>
<td>Pulse wave velocity, m/s</td>
<td>5.8±0.2</td>
<td>6.6±0.3</td>
</tr>
<tr>
<td>Glomerular filtration rate, mL/min</td>
<td>98±5</td>
<td>41±5</td>
</tr>
<tr>
<td>Effective renal blood flow, mL/min</td>
<td>843±68</td>
<td>325±50</td>
</tr>
<tr>
<td>Protein:creatinine ratio, mg/mmol</td>
<td>0</td>
<td>39 (16-144)</td>
</tr>
<tr>
<td>Urinary sodium excretion, μmol/min</td>
<td>232±17</td>
<td>242±22</td>
</tr>
<tr>
<td>Free water clearance, mL/min</td>
<td>6.0±0.4</td>
<td>4.1±0.5</td>
</tr>
</tbody>
</table>

#2999

# APABETALONE REDUCES CARDIAC EVENTS IN CKD PATIENTS BY DOWNREGULATING FIBROTIC AND INFLAMMATORY PROCESSES

Dean Gilham 1, Sylwia Wasial 1, Brooke Rakai 1, LI Fu 1, Laura Tsujikawa 1, Christopher Sarsons 1, Jan Johansson 2, Michael Sweeney 2, Kamyar Kalantar-Zadeh 1 and Ewelina Kulikowski 1

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**Background and Aims:** Major adverse cardiac events (MACE) are a leading cause of mortality in patients with chronic kidney disease (CKD). Apabetalone is an orally available inhibitor of bromodomain & extraterminal (BET) proteins – epigenetic readers that modulate gene expression involved in fibrosis & inflammation. In the phase 3 BETonMACE trial in patients with CVD & diabetes mellitus (NCT02586155), apabetalone reduced MACE by 50% in the population with CKD (eGFR < 60 mL/min/1.73 m²). HR 0.50 95% CI 0.26,0.96 p = 0.04 indicating favorable response along the kidney-heart axis. This study examines effects of apabetalone in human renal mesangial cells (HRMCs) on fibrotic & inflammatory pathways. In the clinic, we assess plasma levels of fibrotic factors in CKD patients & matched controls after receiving apabetalone.

**Method:** TGF-β1 is a pro-fibrotic cytokine that activates HRMCs to over-produce extracellular matrix (ECM). HRMCs were stimulated with TGF-β1 or LPS ±1-25 μM apabetalone 0.15-0.5 μM JQ1 or 0.1 μM MZI - BET inhibitors (BETi) with chemical scaffolds different than apabetalone. Gene expression was measured by RNA-seq & real-time PCR. RNA-seq was evaluated by Gene Ontology (GO) & Ingenuity Pathway Analysis (IPA). Proteins were measured by immunofluorescence microscopy or ELISA. Collagen gel contraction was assessed in 3D culture. In human subjects, proteomic analysis of plasma was performed via SOMAscan 1.3k 12 hours after 100 mg of apabetalone in CKD patients (n = 8 eGFR < 30 stage 4 or 5) and matched controls (n = 8 eGFR > 60).

**Results:** GO analysis of RNA-seq from TGF-β1 stimulated HRMCs showed multiple gene sets associated with ECM production & remodeling in the top 20 affected by BETi. IPA predicted NRκ-B-RelA and NRκB (complex) were inhibited by apabetalone, consistent with suppressed inflammation. IPA also predicted apabetalone activated pathways of glucose utilization & tolerance of ROS production, including Oxidative Phosphorylation (z-score 5.7, p = 2.95 × 10⁻³ at 25 μM) & NRF2-Mediated Oxidative Stress Response (z score 2.3, p = 7.9 × 10⁻¹² at 25 μM; z-score 1.6, p = 1.5 × 10⁻³ at 5 μM). Predicted changes may allow tolerance of elevated glucose. Mechanically, apabetalone suppressed TGF-β1 induced α-smooth muscle actin (α-SMA) gene expression, a marker of activation, up to 89% (p = 2.8 × 10⁻⁸ at 25 μM), and abolished α-SMA filament formation. Consequently, apabetalone opposed TGF-β1 induced collagen gel contraction up to 24% (p = 0.031 at 25 μM). Further, apabetalone countered TGF-β1 induced expression & protein production of key drivers of fibrosis including (a) thrombospondin, an activator of latent TGF-β1 (b) fibronectin, a key ECM component (c) peristin, a promoter of ECM production (d) osteonectin, a regulator of TGF-β1 expression and (e) IL6, a pro-inflammatory cytokine (Table 1). In addition, apabetalone dose dependently opposed LPS stimulated expression of inflammatory genes: IL6 up to 94%, IL1B up to 95% and PTGS2 up to 94% (p<0.001 for each). In all studies, JQ1 or MZI had similar activity as apabetalone, confirming on-target BETi effects. In humans, plasma levels of probiotic and inflammatory markers were reduced 12 hours after receiving apabetalone specifically in those with CKD. Only peristin was reduced in subjects without renal impairment (Table 1).

**Conclusion:** Through epigenetic regulation of transcription in HRMCs, apabetalone reduces production of fibrotic & inflammatory factors known to signal along the kidney-heart axis & exacerbate kidney dysfunction. Predicted changes in energy metabolism suggest apabetalone facilitates adaptation to high glucose in kidneys. In a clinical trial, plasma levels of fibrotic & inflammatory factors were reduced specifically in CKD patients receiving apabetalone. Our results provide mechanistic insights into reduced MACE in CKD patients receiving apabetalone in the phase 3 BETonMACE trial & will be further evaluated in an upcoming Phase 3 trial.

#5214

# RENAL TOLERABILITY OF SGLT-2 INHIBITORS COMBINING WITH RENIN-ANGIOTENSIN SYSTEM BLOCKERS AND MINERALOCORTICOID RECEPTOR ANTAGONISTS IN CKD

Saul Pampa Saico, Simona Alexandru, Aida Frias, M. Soledad Pizarro-Sánchez, Elena Burgos, María López-Picasso and Laura García Puente-Suárez

Spain

**Background and aims:** Recently the sodium glucose cotransporter-2 (SGLT-2) inhibitors combining with angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor II blocker (ARBs) or angiotensin-receptor neprilysin inhibitor (ARNI)) and mineralocorticoid receptor antagonist (MRA) (triple therapy (TT)), would help prevent further progression of renal and cardiovascular (CV) endpoints including progression of end-stage kidney disease (ESKD). The degree to which data on TT initiation and discontinuation in chronic kidney disease (CKD) patients can be generalized to patients in real-world practice is unclear.

**Aims:** to evaluate renal tolerability to the TT at target doses as well as clinical incidents and dosage adjustments. To analyze the risk factors for TT discontinuation.

**Method:** A retrospective cohort study was carried out in patients ≥18 years old with chronic kidney disease (CKD) treated with TT in Rey Juan Carlos Hospital between January 2019 to December 2022. The collected clinical data included age, gender, associated morbidities, serum creatinine (Scr), estimated
glomerular filtration rate (eGFR), potassium, sodium levels, dose adjustments before administration of TT and in the first year of follow up. Multivariate logistic models were performed to evaluate the risk factors to dosage adjusted and discontinuation of TT.

Results: Among 104 patients treated with TT were included. Medium age was 69 years old (range, 37-91). Most of them were men, 78% (81). The main cause to initiate TT was cardiorenal syndrome 59% (61). Before to initiate TT, in 35% patients the treatment was adjusted. The main modification was reduced or discontinuation of diuretics (loop or thiazide) therapy 23% (24/104). In the first year of follow up, in 69 patients (66%) it was necessary dosage adjustments, being the reduced of MRA (spironolactone and eplerenone) the main modification treatment 38% (26/69). The major cause of dose adjustment was developed of acute kidney injury (AKI) in 43 patients (41%). According to KDIGO criteria, 38 patients (88%) reached stage 1; 4 patients (9%) stage 2 and 1 case (2%) stage 3. The independent risk factor associated with dosage adjustment were AKI development (OR: 28.57; 95% CI 6.04-134.4; P = 0.0001) adjusted by sex and age. Despite the dosage adjustment and titers, in 29 patients (28%) TT was discontinued in a median time of 4 months (IQR 2–11) after its initiation. The risk factor associated with TT discontinuation were AKI developed (P = 0.003) and eGFR at the 12 months of follow up (P = 0.01). There were no significant excess risks of symptomatic hypotension, volume depletion, and hyperkalemia after a year of follow up.

Conclusions: The renal tolerability of use to triple therapy in chronic kidney disease appears to be low. The AKI development was the main risk factor of dosage adjustment and discontinuation of TT. Its necessary to clarify which is the best way to maximizing renal tolerability in this complex groups of patients. The use of early combination therapy requires careful assessment. Its important to find strategies to guide clinicians about the steps and challenges to improving overall use of triple therapy tolerability and dosage adjustment.

#4483
THE 2021 KDIGO BLOOD PRESSURE TARGET AND THE PROGRESSION OF CHRONIC KIDNEY DISEASE: FINDINGS FROM THE KNOW-CKD
Hyun Jung Lee1, Cheol Ho Park1, Hyung Woo Kim1, Jung Tak Park1, Tae Ik Chang1, Tae-Hyun Yoo1, Shin-Wook Kang1 and Seung Hyoek Han1
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Background and Aims: The 2021 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for management of blood pressure (BP) in chronic kidney disease (CKD) recommends a target systolic BP of <120 mmHg because this lower target can provide cardiovascular benefits. However, whether implementing the new BP target could improve kidney outcome remains unknown.

Method: We examined the association of the 2021 KDIGO BP target with CKD progression compared with the 2012 KDIGO BP target among 1724 participants from the Korean Cohort Study for Outcomes in Patients With CKD. The main exposure was BP status categorized according to the 2012 or 2021 KDIGO guideline: 1) controlled within 2021 target; 2) controlled within 2012 target only; and 3) above both targets. The primary outcome was a composite kidney outcome of ≥50% decline in estimated glomerular filtration rate from baseline measurement or the initiation of kidney replacement therapy during the follow-up.

Results: During 8,078 person-years of follow-up (median, 4.9 years), the composite kidney outcome occurred in 650 (37.7%) participants. The incidence rates of this outcome were 55, 66.5, and 116.4 per 1,000 person-years in BP controlled within the 2012 and 2012 KDIGO targets, and BP above both targets, respectively. In the multivariable cause-specific hazard model, hazard ratios for the composite outcome were 0.76 (95% confidence interval, 0.60-0.95) for BP controlled within the 2021 target and 1.36 (95% confidence interval, 1.13-1.64) for BP above both targets, compared with BP controlled within 2012 target only.

Conclusion: The newly lowered BP target by the 2021 KDIGO guideline was associated with improved kidney outcome compared with BP target by the 2012 KDIGO guideline.

#5123
EFFICACY AND SAFETY OF PATIROMER IN THE TREATMENT OF CHRONIC HYPERKALEMIA IN ASTURIAS: THE K-ASTUR STUDY
Jose Emilio Sanchez-Alvarez1, Maria del Carmen Merino Bueno1, Anna Gallardo Perez1, Cristina Sango1, Carlos Ruiz Zorrilla1 and Catalina Ulloa2
1Hospital de Cabueñes, Nephrology, Gijón, Spain and 2Fundacion Hospital Jove: Gynecology and Obstetrics, Nephrology, Gijón, Spain

Background and Aims: Hyperkalemia is a frequent problem in patients with chronic kidney disease (CKD), especially in those on hemodialysis (HD) and confers increased morbidity and mortality. It is common to carry out urgent HD sessions or increase the number of weekly sessions due to toxic hyperkalemia. Hyperkalemia also prevents the administration or adequate titration of drugs such as renin-angiotensin-aldosterone system (RAAS) inhibitors despite the evidence of their cardiovascular benefits and on the progression of CKD. New drugs have recently entered the market that can help treat chronic hyperkalemia. The aim of the present study was to analyse the efficacy and safety of Patiromer in patients with CKD.

Method: Multicenter, prospective, clinical practice study in patients with CKD stages 3-5. Patiromer was administered with the indication of chronic hyperkalemia. Epidemiological and clinical data were analyzed; the evolution of serum potassium and elements involved in bone and mineral metabolism were taken into account.

Results: Finally, 52 patients (71±12 years old, 75% male, 63% diabetic, 54% with heart failure, and 42% receiving RAAS inhibitors) were included in the study. Regarding CKD, 17% were in stage 3b, 31% in stage 4, 38% in stage 5 (not on dialysis) and 13% were on HD. Of the 52 patients included, 46 reached 6 months of follow-up, 2 died, 2 underwent a kidney transplant and 2 were transferred to another center. The initial dose of Patiromer was in all cases 8.4 g administered orally in a single dose. Only one patient required doubling the dose because the therapeutic objectives were not achieved. Taking Patiromer was associated with a decrease in the levels of serum potassium of 27% (5.9 vs 4.6 mEq/L; P<0.001), a decrease that was more pronounced in the first month of treatment. There were no changes in the concentration of serum calcium and magnesium. We did find a decrease of 18% in serum phosphorus (5.1 vs 4.2 mg/dl; P 0.022), with no changes in diet or phosphate binders. Patiromer was well tolerated and only 2 patients reported mild constipation; none discontinued the medication due to adverse effects.

Conclusion: Patiromer is effective and safe in reducing serum potassium concentrations. Due to its calcium content, it is possible that it favors the reduction in phosphoremia due to a decrease in the intestinal absorption of phosphorus. The use of this drug can help us control potassium levels in patients with CKD, properly titrate the use of ISRAAs, and even reduce the number of HD sessions or dialysis emergencies in some patients.

#6823
THE NUTRITIONAL AND NEPHROLOGICAL IMPACT OF A LOW-NORMAL PROTEIN HIGH CALORIE DIET ON THE ONCOLOGICAL SOLITARY KIDNEY: TIME FOR A NEW PERSPECTIVE?
Francesco Trevisiani1, Matteo Paccagnella2, Francesco Fiorio3, Fabiana Laurenti1, Riccardo Vago1, Federico Di Marco1, Matteo Floris4, Umberto Capitanio1, Michele Ghidini5, Andrea Salonia1, Francesco Montorsi1 and Arianna Bettiga4
1IRCCS San Raffaele Scientific Institute, Department of Urology and Division of Experimental Oncology, Milan, Italy, 2Carle Hospital, Laboratory of Oncology Translation, Cuneo, Italy, 3University of Aquila, Department of Clinical Medicine, Public Health, Science of ambiental and life (MeSVA), Aquila, Italy, 4San Michele Hospital, ARNAS G. Brotzu, Department of Medical Science and Public Health, Cagliari, Italy and 5Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Medical Oncology Unit, Milan, Italy

Background and Aims: Nutritional therapy (NT) based on controlled protein intake represents a cornerstone in the management of chronic kidney disease (CKD). However the international guidelines do not precisely define an adequate protein intake for nephrological patients affected by cancer, the onco-nephrological ones. Among them, there is a precise asset where a personalized nutritional strategy can make the difference; the oncological patients who...
Method: A consecutive cohort of 44 pts was enrolled in the Urological Department at San Raffaele Scientific Institute between 2018-2021. Inclusion criteria were: Age (>18 years old), eGFR (<60 ml/min/1.73 m²), Malnutritional Screening Tool (MST<2), Solitary kidney for radical nephrectomy for renal cancer, informed consent (signed). Each patient underwent an initial nephrological and nutritional evaluation and was subsequently subjected to a conventional CKD LNPHC diet integrated with aprotic foods (0.7-1 g/kg/die: calories: 30-35 kcal per kg body weight/die) for a period of 6 months (+/- 2 moths). The diet was based on the estimated Glomerular Filtration Rate (CKD-EPI 2021 Creatinin formula), comorbidities and nutritional status. MST, Body Mass Index (BMI), Phase Angle (PA), Fat Mass percentage (FM%), Fat-Free Mass Index (FFMI), body cell mass index (BCM1), extracellular/intracellular water ratio (ECW/ICW), waist/hip circumference ratio (WHC), lab test exams and clinical variables were examined at baseline and after 6 months. Statistical analysis: Kruskal-Wallis rank sum test; Data analysis: R programming language and RStudio integrated development environment.

Results: Descriptive analysis is showed in Table 1. Our results clearly highlighted that LNPHC was able to generate a significant improvement in all the investigated nutritional parameters (Table 2 and 3) avoiding malnutrition or catabolism. Moreover, regarding the nephrological asset, LNPHC was responsible for a significant decrease of urea, the most important parameter influencing general status. The non-significant increase of serum creatinine and therefore decrease of eGFR was related to the augmented muscle mass (Table 4).

Conclusion: LNPHC represents a new important therapeutic strategy to apply in the onco-nephrological patients with solitary kidney due to renal cancer.

ASSOCIATION OF PLANT PROTEIN INTAKE AND RISK OF INCIDENT CHRONIC KIDNEY DISEASE: THE UK BIOBANK STUDY

Ga Young Heo 1, Hee Byung Koh 1, Hye Jeong Kim 1, Kyung Won Kim 1, Chan-Young Jung 1, Hyung Woo Kim 1, Jung Tak Park 1, Tae Ik Chang 1, Tae Hyun Yoo 1, Shin-Wook Kang 1 and Seung Hyeok Han 1

1Yonsei University College of Medicine, Seoul, Rep. of South Korea and 2NHIS Ilsan Hospital, Department of Internal Medicine, Goyang-si, Rep. of South Korea

Background and Aims: Dietary intake from various protein sources can affect health differently. However, the association between plant protein intake and incident chronic kidney disease (CKD) is uncertain.

Method: Using the UK Biobank prospective cohort, we included 117,809 participants who completed more than one dietary questionnaire and had an estimated glomerular filtration rate (eGFR) ≥60 ml/min/1.73 m², urinary albumin-to-creatinine ratio (UACR) <30 mg/g, and no prior history of CKD. The main predictor was the daily plant protein intake, assessed with a web-based 24-hour recall questionnaire. The primary outcome was incident CKD, based on the International Classification of Diseases, 10th Revision (ICD-10) or Office of Population Censuses and Surveys Classification of Interventions and Procedures, version 4 (OPCS-4) codes. We additionally analyzed this association in 37,955 participants with primary care-linked data for eGFR and UACR. We used strictly defined CKD based on ICD-10 and OPCS-4 codes or two consecutive measures of eGFR <60 ml/min/1.73 m² or UACR >30 mg/g.

Results: During the median follow-up of 9.9 years, incident CKD occurred in 3745 (3.2%) participants (incidence rate, 3.2 per 1,000 person-years). In a multivariable cause-specific model, the adjusted hazard ratios (aHRs; 95% confidence intervals [CIs]) for the second, third, and highest quartiles were 0.91 (0.83-0.99), 0.79 (0.71-0.87), and 0.75 (0.64-0.85), respectively, compared with the lowest quartile. In a continuous model, the aHR (95% CIs) per 0.1 g/kg/day increase in plant protein intake was 0.91 (0.88-0.94). This beneficial association was also consistent in the secondary analysis with strictly defined CKD and various sensitivity analyses.

Conclusion: This large prospective cohort study showed that increased dietary plant protein intake was associated with a lower risk of CKD.

#4318

ASSOCIATION OF PLANT PROTEIN INTAKE AND RISK OF INCIDENT CHRONIC KIDNEY DISEASE: THE UK BIOBANK STUDY

Ga Young Heo 1, Hee Byung Koh 1, Hye Jeong Kim 1, Kyung Won Kim 1, Chan-Young Jung 1, Hyung Woo Kim 1, Jung Tak Park 1, Tae Ik Chang 1, Tae Hyun Yoo 1, Shin-Wook Kang 1 and Seung Hyeok Han 1

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Conclusion: This large prospective cohort study showed that increased dietary plant protein intake was associated with a lower risk of CKD.
Table 1: Incidence rates of incident CKD according to quartile of plant protein intake.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Total (N = 117,809)</th>
<th>Quartile of plant protein intake (g/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Q1 (&lt;0.28)</td>
</tr>
<tr>
<td>Total No. of participants</td>
<td>117,809</td>
<td>29453</td>
</tr>
<tr>
<td>Incident chronic kidney disease</td>
<td>37.45 (3.2)</td>
<td>1155 (3.9)</td>
</tr>
<tr>
<td>Incidence rate per 1000 person-years</td>
<td>3.2 (3.1-3.3)</td>
<td>4.0 (3.8-4.2)</td>
</tr>
</tbody>
</table>

Subcohort

<table>
<thead>
<tr>
<th>No. of participants Incident CKD (strictly defined)a</th>
<th>37,995</th>
<th>9499</th>
<th>9499</th>
<th>9499</th>
<th>9498</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of outcome, n (%)</td>
<td>2637 (6.9)</td>
<td>794 (8.4)</td>
<td>725 (7.6)</td>
<td>607 (6.4)</td>
<td>511 (5.4)</td>
</tr>
<tr>
<td>Incidence rate per 1000 person-years</td>
<td>7.4 (7.1-7.7)</td>
<td>9.0 (8.4-9.7)</td>
<td>8.2 (7.6-8.8)</td>
<td>6.8 (6.2-7.3)</td>
<td>5.6 (5.2-6.1)</td>
</tr>
</tbody>
</table>

Note: Model was adjusted for age, sex, BMI, ethnic background, socioeconomic status, alcohol status, smoking status, physical activity, dietary intake (total energy, total fat, total protein, total carbohydrate, and total sodium intake), comorbidities (hypertension, diabetes, cardiovascular disease, chronic pulmonary disease, and liver disease), the use of medications (renin-angiotensin-aldosterone system blockers, diuretics, and statins) and laboratory measurements (total cholesterol, LDL-C, triglyceride, and hs-CRP).

#4486

VALIDATION OF A CKD PROGRESSION RISK PREDICTION MODEL IN THE FIDELITY TRIAL POPULATION

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Background and Aims: Chronic kidney disease (CKD) is often underrecognised until later stages when most of the kidney function is lost and the therapeutic window for disease-modifying therapy is narrow [1]. We previously developed a lab-based risk prediction model to accurately predict CKD progression in adults at all stages of CKD [2]. Here, we describe a validation of our model in the clinical trial population of FIDELITY, a prespecified post hoc analysis of the phase III FIDELIO-DKD (NCT02545049) and FIGARO-DKD (NCT02545409) trials for the nonsteroidal mineralocorticoid receptor antagonist finerenone [3].

Method: We performed a post hoc analysis of all participants from the FIDELITY database, irrespective of estimated glomerular filtration rate (eGFR) or albuminuria stage. Baseline values for the underlying laboratory tests required for the model, Klinrisk, were extracted from the complete blood count, comprehensive metabolic panel and urine albumin-to-creatinine ratio (UACR). The predicted outcome was a ≥40% decline in eGFR or kidney failure. We calculated discrimination ability of the model and calibration using area under the curve (AUC), Brier scores and calibration plots in the overall population, and stratified by treatment assignment. Sensitivity analyses examined the accuracy of the models in predicting CKD failure. We calculated discrimination ability of the model and calibration (UACR). The predicted outcome was a ≥57% decline in eGFR, as well as the change in risk score over time. Kidney Disease: Improving Global Outcomes (KDIGO) heat map categories were used as the reference standard.

Results: We included 13,026 participants with a mean age of 64.8 ± 9.5 years, mean eGFR of 57.6 ± 21.7 ml/min/1.73 m², and median UACR of 58.2 mg/mmol (interquartile range 22.4–129.6). At time horizons of 2 and 4 years,
894 and 1795 patients experienced a primary outcome event, respectively. The Klinrisk risk model accurately predicted progression in all four randomized groups (AUC of 0.81 [95% CI: 0.76–0.85] at 3 years), which is characterized by poor renal outcomes and mortality in patients with DKD. However, an effective, well-tolerated treatment of progressive renal disease driven by inflammation has remained elusive.

Inhibition of IL-33 may provide a novel opportunity to improve glomerular endothelial health as indicated by decreased cellular inflammation and reduced release of pro-inflammatory cytokines such as IL-1β, IL-6, IL-8, TNFR-1, and CCL2.

**Conclusion:** Taken together, inhibition of IL-33 may be beneficial in patients with DKD on standard of care, who have elevated biomarkers of inflammation such as TNFR-1 and/or CCL2. This hypothesis is currently being tested in the FRONTIER-1 phase 2b clinical study. To identify the patients most likely to benefit from immunomodulatory treatment with tozorakimab, the study will consist of a retrospective analysis of albuminuria and other biomarkers. The primary analysis of the study is planned for the second half of 2023.

#5413

**FRONTIER-1: A PHASE 2B STUDY OF IL-33 BLOCKADE IN DIABETIC KIDNEY DISEASE**

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**Background and Aims:** Several biomarkers of inflammation have been correlated with poor renal outcomes and mortality in DKD. However, an effective, well-tolerated treatment of progressive renal disease driven by inflammation has remained elusive. Inhibition of IL-33 may provide a novel opportunity to address this unmet medical need in high-risk patients. Here, we: 1) show that tozorakimab, a high-affinity IL-33-neutralizing mAb, promotes glomerular health in inflammation; 2) describe the clinical study to test tozorakimab in patients with DKD; and 3) present participant baseline characteristics, safety and efficacy, and biomarker response to independent reference cohorts (N = 775). The inflammatory state of participants at baseline was assessed in preclinical models of DKD and demonstrated with improved glomerular endothelial health as indicated by decreased cellular inflammation and reduced release of pro-inflammatory cytokines such as IL-1β, IL-6, IL-8, TNFR-1, and CCL2.

**Method:** FRONTIER-1 (NCT04170543) is a phase 2b, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy, safety, pharmacokinetics (PK), and immunogenicity of tozorakimab in patients with DKD; defined as T2DM with an eGFR of 25-75 mL/min/1.73 m² and a UACR in the range of 100-3000 mg/g. All participants are expected to receive an ACEI/ARB for > 6 weeks before the treatment period. Approximately 556 patients from multiple countries will be randomized to four dose levels of tozorakimab, or volume-matched placebo dosed subcutaneously every 28 days over a 4-week treatment period. All participants will receive 10 mg dapagliflozin Day 85-168. The primary objective of the study is to evaluate the safety and tolerability of tozorakimab and with and without SGLT2i, evaluate the effect of tozorakimab in combination with ACEI or ARB with and without SGLT2i on albuminuria, and describe the PK and immunogenicity of tozorakimab.

**Key exploratory objective is to assess baseline and treatment-response for urine albumin and circulating biomarkers of inflammation, including hsCRP, IL-33/sIL1RL1, CCL2, and TNFR-1/2. Biomarker response was, furthermore, evaluated in pre-clinical models of DKD, and respective distributions and risk were assessed in four independent DKD cohorts (N > 200).**

**Results:** Transcriptomic profiling of kidney biopsies from patients with DKD indicated a significant glomerular up-regulation of IL-33. Inhibition of IL-33 signalling reduced glomerular damage and albuminuria in the urine/macromolecules-dib/db model associated with improved glomerular endothelial health as indicated by decreased cellular inflammation and reduced release of pro-inflammatory cytokines such as IL-1β, IL-6, IL-8, TNFR-1, and CCL2. Hence, FRONTIER-1 was started in 2019. So far, all trial groups are well-balanced and in line with our expectations for this patient population (N = 574). At baseline, > 95% were receiving ACEI/ARBs and approximately 25% were receiving SGLT2i. The mean eGFR was 47.8 mL/min/1.73 m² (± 14.7) and mean UACR was 765 mg/g (± 775). The inflammatory state of participants at baseline was assessed in urine and urine by hsCRP, TNFR-1 and CCL2 and showed that 6-week treatment of dapagliflozin did not alter these biomarkers significantly.

**Conclusion:** Taken together, inhibition of IL-33 may be beneficial in patients with DKD on standard of care, who have elevated biomarkers of inflammation such as TNFR-1 and/or CCL2. This hypothesis is currently being tested in the FRONTIER-1 phase 2b clinical study. To identify the patients most likely to benefit from immunomodulatory treatment with tozorakimab, the study will consist of a retrospective analysis of albuminuria and other biomarkers. The primary analysis of the study is planned for the second half of 2023.

#3034

**PHASE 3 TRIAL OF TOLVAPTAN IN PEDIATRIC AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): TWO YEARS OF DATA FROM AN OPEN-LABEL EXTENSION**

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**Background and Aims:** The 1-year, randomized, placebo-controlled phase (Phase A) of a 2-part trial of tolvaptan in children/adolescents with ADPKD (NCT02964273) demonstrated acceptable safety/tolerability and evidence of vasopressin type 2 receptor antagonism. A 2-year, open-label extension (Phase B) evaluated longer-term outcomes.

**Method:** By entry criteria, participants at Phase A baseline were aged 4-17 years, had a diagnosis of ADPKD, estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m², and body weight ≥20 kg. Participants in the tolvaptan and placebo arms who completed Phase A could enter Phase B to receive open-label tolvaptan for 24 months. Dosing was based on body weight and tolerability, with tolvaptan re-initiated in participants who had received tolvaptan in Phase A to preserve the blind until Phase A completion. Phase B post-baseline study visits occurred at Week 1, Months 1, 6, 12, 18, and 24. Laboratory safety assessments were performed monthly, with more frequent liver function testing if any indication of liver injury was detected. eGFR and height-adjusted total kidney volume (htTKV) were calculated using the mixed model repeated measures method with model terms treatment, visit, treatment by visit, and baseline by visit interaction. To exclude the acute hemodynamic effect of tolvaptan, change in eGFR after week 1 of treatment is shown.
Results: Of 83 Phase A completers, 81 (42 prior tolvaptan, 39 prior placebo) enrolled in Phase B; 33/42 (78.6%) prior tolvaptan and 30/39 (76.9%) prior placebo participants completed the Phase B Month 24 visit on tolvaptan. The average daily tolvaptan dose was 41.1 mg in the prior tolvaptan group (mean [SD] age 14.3 [3.2] years) and 38.0 mg in the prior placebo group (13.9 [2.9] years). Adherence determined by returned drug was ≥90% in 32/42 (76.2%) participants in the prior tolvaptan group and 28/39 (71.8%) in prior placebo. In Phase A, eGFR increased in the tolvaptan group and decreased in the placebo group (significant difference at Month 6), with significant benefit maintained at most assessment visits in Phase B for the prior tolvaptan group compared to the prior placebo group (Figure 1A). Growth in htTKV on MRI (participants ages 12-17) was slowest during the first year of tolvaptan treatment, as shown by the slope of htTKV during Phase A in the tolvaptan group and during year 1 of Phase B in the prior placebo group (Figure 1B), with growth rates higher thereafter, although sample sizes did not permit meaningful statistical comparison of the changes. Scores on pediatric health-related quality of life assessment instruments, including the PedsQL Generic Core Scale and the PedsQL Multidimensional Fatigue Scale, remained stable during both phases and indicated low health-related quality of life burden and high functioning. The most common adverse events in Phase B (>15% participants overall: prior tolvaptan and prior placebo, respectively) were headache (36%, 44%), nasopharyngitis (26%, 33%), rhinitis (26%, 10%), oropharyngeal pain (21%, 18%), pyrexia (19%, 18%), cough (17%, 21%), abdominal pain (12%, 31%), polyuria (5%, 33%). Eleven participants overall experienced elevated liver enzymes by investigator report (no prespecified enzyme levels were required to report an event): 6 recovered without intervention, treatment was interrupted in 4, and in 1 tolvaptan was withdrawn for a reason other than the hepatic event. No participant met predefined laboratory criteria for serious drug-induced liver injury in either phase. There were no notable differences between prior tolvaptan and prior placebo in Tanner staging progression or change from baseline in growth percentile in Phase B.

Conclusion: Consistent with adult data in the TEMPO 3:4 and TEMPO 4:4 trials, children and adolescents who received tolvaptan during a randomized trial exhibited eGFR benefit relative to those who received placebo, a difference that was preserved during a 2-year, open-label extension. As in adults, kidney volume growth was higher after 1 year of treatment. Tolvaptan exhibited...
acceptable safety and good tolerability, with few discontinuations and a low quality of life burden.

THE EFFECT OF DAPRODUSTAT ON INTRAVENOUS IRON USE IN PATIENTS WITH CKD-RELATED ANAEMIA ON DIALYSIS IN THE ASCEND TRIALS

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Background and Aims: Intravenous (IV) iron is frequently needed in patients with chronic kidney disease (CKD) to ensure sufficient iron is available for erythropoiesis. However, high doses of IV iron and erythropoiesis stimulating agents (ESAs) may be associated with risks in these patients [1]. The hypoxia-inducible factor-prolyl hydroxylase domain inhibitor daprodustat was non-inferior to comparator ESAs for the primary endpoint of efficacy (change-in-Hb) in the multicentre, randomised, Phase 3 trials ASCEND-D (NCT02879305) [2] and ASCEND-TD (NCT03400033) [3], also for the safety (major adverse cardiovascular [CV] events) coprimary endpoint in ASCEND-D [2]. This analysis of ASCEND-D and ASCEND-TD compared daprodustat to active ESAs on measures of IV iron use in dialysis patients.

Method: Daprodustat and ESAs were compared in patients with CKD anaemia on haemodialysis/peritoneal dialysis (ASCEND-D); haemodialysis (ASCEND-TD). ASCEND-D (N = 2,964) was an open-label CV outcome study using daprodustat once daily, while ASCEND-TD (N = 407) was a double-blind, double-dummy, 52-week study investigating three times weekly dosing of daprodustat. In both studies, following randomisation, treatment dosage was titrated to achieve the Hb target range of 10.0–11.0 g/dL, with Hb efficacy assessed during the evaluation period (EP), Weeks 28–52. All patients were required to have ferritin > 100 ng/mL and/or transferrin saturation (TSAT) > 20% at baseline for inclusion. Throughout the study, iron therapy was administered if ferritin was ≤ 100 ng/mL and/or TSAT was ≤ 20% so patients would remain iron replete throughout the study. Investigators chose the route and dose of iron administration per patient iron status and clinical judgement. Stopping threshold criteria of 800 ng/mL ferritin + TSAT > 20%, or TSAT > 40% were implemented to avoid iron overload, but investigators could stop administration of iron at levels below the protocol-defined stopping thresholds. The average monthly IV iron dose (mg/patient to Week 52 was a principal secondary endpoint, while the proportion of patients who met iron management criteria with a decrease in monthly IV iron dose during the EP relative to baseline and until patients received first transfusion were exploratory endpoints. The baseline monthly IV iron dose was defined as the average monthly IV iron (mg) over the 16 weeks prior to randomisation for ASCEND-D and over the 12 weeks prior to randomisation for ASCEND-TD.

Results: The proportion of patients with IV iron use at baseline was similar in patients with chronic kidney disease (CKD) to ensure sufficient iron is available for erythropoiesis. However, high doses of IV iron and erythropoiesis stimulating agents (ESAs) may be associated with risks in these patients [1]. The hypoxia-inducible factor-prolyl hydroxylase domain inhibitor daprodustat was non-inferior to comparator ESAs for the primary endpoint of efficacy (change-in-Hb) in the multicentre, randomised, Phase 3 trials ASCEND-D (NCT02879305) [2] and ASCEND-TD (NCT03400033) [3], also for the safety (major adverse cardiovascular [CV] events) coprimary endpoint in ASCEND-D [2]. This analysis of ASCEND-D and ASCEND-TD compared daprodustat to active ESAs on measures of IV iron use in dialysis patients.

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Results: The proportion of patients with IV iron use at baseline was similar in both treatment arms for ASCEND-D (64%) but lower in the daprodustat group in ASCEND-TD (63% vs 72% in the ESA group). In both studies the proportion of patients receiving IV iron during the EP decreased (ASCEND-
Daprodustat 49%, ESA 52%; ASCEND-TD: daprodustat 38%, ESA 40%). The average monthly IV iron dose during the EP and from Day 1 to Week 52 was lower than monthly IV iron dose at baseline, however daprodustat was not associated with a statistically significant reduction in monthly IV iron per patient to Week 52 vs ESA comparator (Table 1). After a period of IV iron requirements decreasing, based on adjustment to protocol-specified levels, IV iron dosage remained relatively stable for daprodustat and ESA (Figure 1). In ASCEND-D, 3 of 23 pre-defined subgroups (prior ESA dose group, ESA hyporesponder group, history of myocardial infarction) showed a trend towards heterogeneity (interaction p-value < 0.1), with differences in monthly IV iron use in the prior ESA dose group receiving ≥ 7000 U/week (-21.2 mg/month) and in the ESA hyporesponder group (-31.7 mg/month) in favour of daprodustat. Fewer patients met the criteria for stopping iron while on daprodustat vs ESA, whereas the converse was observed in ASCEND-TD (Table 1).

Conclusion: In ASCEND-D and -TD, no clinically or statistically significant reduction in monthly IV iron use was seen with daprodustat vs ESA comparators, although there was a numerical decrease in the proportion of patients receiving IV iron during the EP for the daprodustat group in both studies.

REFERENCES

ASSESSING ACCURACY OF POINT-OF-CARE CREATININE AND POTASSIUM TESTING IN A MULTI-ETHNIC SOUTH LONDON POPULATION

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Background and Aims: Point-of-care (POC) testing allows rapid analysis of blood samples without delay of laboratory testing. For patients with chronic kidney disease (CKD), this allows for instant identification of changes in kidney function, such as acute kidney injury or hyperkalaemia, and assists in timely decision-making in outpatient or community settings (e.g. commencing or up-titrating medications dependent on renal function). It also provides an opportunity for early recognition of CKD in high-risk populations by providing screening in more convenient and trusted settings. To achieve these aims, it is essential to confirm that POC systems can produce accurate results in real world settings with diverse patient populations. This pilot validation study assessed accuracy of the Siemens Epoc Blood Analysis System venous creatinine and potassium compared with laboratory assays in a diverse UK renal patient population.

Method: Venous blood samples from 57 patients, aged ≥ 18 years old and receiving care at a London teaching hospital, were analysed using the Siemens Epoc Blood Analysis System. POC-Creatinine (POC-Cr) and Potassium (POC-K) measurements were compared with laboratory (IDMS-traceable Siemens enzymatic and Roche) assays. Demographics (age, ethnicity and sex) were recorded for each patient. Passing-Bablock regression analysis were used to compare the results using both methods. Comparison between testing
methods was assessed using a Bland-Altman plot. Limits of agreement were compared with CLIA criteria for acceptable performance for creatinine and potassium.

**Results:** The mean age was 55.6 ± 15.3 years old and 64.9% were male (n = 37). The majority of patients were of White (N = 23; 40.4%), Black (N = 21; 36.8%) or South Asian (N = 9; 15.8%) ethnicity respectively. Median POC-Cr was 216 μmol/L (interquartile range (IQR) 111, 396 μmol/L) versus median venous creatinine 212 μmol/L (IQR 114, 380 μmol/L). The median bias for creatinine was +1.0 (IQR -3.0, +8.0). Limits of agreement on Bland-Altman plot were +36.5 μmol/L and –34.4 μmol/L (Figure 1). Overall, there remained a strong positive correlation between POC-Cr and IDMS-traceable enzymatic creatinine assays (R = 0.997; P < 0.0001) (Figure 2). Median POC-K was 4.3 mmol/L, IQR 4.0, 4.8 mmol/L versus median venous potassium 5.0, IQR 4.3, 5.3 mmol/L. The median bias for potassium was +0.4 (IQR +0.2, +0.5). Limits of agreement on Bland-Altman plot were +0.16 mmol/L and –0.91 mmol/L (Figure 3). A strong positive correlation between POC-K and laboratory potassium assays was also confirmed (R = 0.937; P < 0.0001) (Figure 4).

**Conclusion:** There was strong positive correlation between POC and laboratory analysis of venous creatinine, comparable to product literature (R = 0.997 vs 0.998). Limits of agreement were outside the CLIA criteria for acceptable performance (+/- 27 μmol/L). POC and laboratory potassium levels were also strongly correlated and comparable to product literature (R = 0.937 vs 0.997). Limits of agreement were outside the CLIA criteria for acceptable performance (+/- 0.5 mmol/L). This discrepancy is likely due to haemolysis in some blood samples and small sample size. Overall, this pilot study demonstrated a strong correlation between POC and laboratory testing. Larger scale evaluation is still required in a multi-ethnic population, prior to assessing feasibility in community-led protocolized pathways.
Background and Aims: Well-based therapies may repair diseased nephrons and stabilize and enhance kidney function to delay the onset of end-stage kidney disease and improve co-morbidities. REACT™ is a novel product formed of cryopreserved autologous homologous selected renal cells, undergoing phase III clinical trials for diabetic kidney disease (DKD). We describe an open label phase II study to evaluate how patients respond to
REACT™ injections in both kidneys and a redosing trigger, as being evaluated in a Phase III blinded data trial (proact 1 & 2 trials).

Method: REGEN 007 is a multi-center Phase II, open label 1:1 randomized controlled trial enrolling up to 50 patients ages 30-80 years with DKD, who have an eGFR of 20 - 50 mL/min/1.73 m². Each patient undergoes a percutaneous kidney biopsy and ex vivo culture expansion of their selected renal cells. Patients are then randomized to an arm where they receive two REACT™ injections, one in each kidney, three months apart if they meet inclusion criteria, or an arm with an initial single REACT™ dose in one kidney and a 2nd REACT™ dose in the contralateral kidney > 90 days apart, based on a sustained eGFR decline of ≥ 20%, and/or an increase in the urine albumin to creatinine ratio (UACR) from baseline of ≥ 30% and ≥ 30 mg/g. CT-guided bilateral percutaneous renal cortex injections of REACT™ are performed under conscious sedation. Trial design, inclusion and exclusion criteria can be found at the National Clinical Trial Registry (Trial number 05018416).

Results: Thirty-one of the targeted 30 participants have been enrolled with the following characteristics at screening: 64.0% males, 97.0% Non-Hispanic/Latino. Mean age 62.9 years, serum creatinine (sCr) 2.0 mg/dL ±0.50, Cystatin C 2.0 mg/L ±0.40, eGFR (sCr + Cystatin C) 31.2 mL/min/1.72m² ±7.88, HgbA1C 7.4% ± 1.14, Hgb 12.9 g/dL ± 1.78, K⁺ 4.6 mEq/L ± 0.44, Bicarbonate 20.3 mEq/L ± 3.0, and a median UACR 662 mg/g [SD 705.8]. Percent baseline medications are: Angiotensin Converting Enzyme inhibitors 25.8, Angiotensin Converting Enzyme receptor Blockers 48.4, beta blockers 64.5, diuretics 64.4, glucose lowering agents 100, Sodium glucose Cotransporter 2 inhibitors 32.3, and platelet inhibitors 67.7. Efficacy endpoint is an eGFR slope improvement from first injection to 18 months after last injection. REACT™ and procedure related serious adverse events are expected to be commensurate with ongoing trials and standard of care.

Conclusion: REACT™ cell-based therapy has the potential to effect nephron structure and function by stabilizing or improving DKD progression and its comorbidities. Current phase II and III trials are underway to determine structure and function by stabilizing or improving DKD progression and its comorbidities. Current phase II and III trials are underway to determine.

KIDNEY FUNCTION ESTIMATORS FOR DRUG DOSE ADJUSTMENT OF DIRECT ORAL ANTICOAGULANTS IN OLDER ADULTS WITH ATRIAL FIBRILLATION

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Background and Aims: The Food and Drug Administration and the European Medicines Agency (EMA) recommend using the Cockcroft-Gault equation (CG) for drug dose adjustment of direct oral anticoagulant drugs (DOACs) in non-valvular atrial fibrillation (NVAF), whereas Cardiology guidelines recommend using estimated glomerular filtration rate (eGFR). This issue is of great importance in older adults, which are more prone to adverse drug reactions and have higher prevalence of atrial fibrillation as compared to younger adults, and in whom CG has worse diagnostic performance than most eGFR equations. We aimed to assess if prognosis was similar according to drug dose status using different kidney function estimators based on creatinine and/or cystatin C in older adults with NVAF.

Method: We used data from the Berlin Initiative Study (BIS): a population-based prospective cohort study initiated in 2009, with five biennial study visits. Participants with a history of NVAF (based on ICD-10 codes) and a dispensed prescription of DOAC four months prior to baseline or a follow-up visit according to claims data were included. Drug dose status was defined according to the EMA guidelines. CG and/ or cystatin C (xg) and/or cystatin C-based (CGstation) and deindexed (in ml/min) creatinine and/or cystatin C-based (BIS 2 (creatinine- and cystatin C-based) equations were included. Associations between dosing status and mortality, stroke or systemic embolism, and bleeding events were assessed using marginal structural Cox models with time-advancing variables and taking account of various confounders. Subgroup analyses were performed in rivaroxaban and apixaban users, but not in dabigatran and edoxaban users because of too small sample sizes.

Results: Two hundred forty four patients treated with DOACs were included in this analysis (median age 87 years, median eGFR (EPA) 56 ml/min/1.73m², median follow-up length 40 months for the mortality analysis). Of those, 99 (44%) were taking rivaroxaban, 86 (38%) apixaban, 21 (9%) edoxaban, and 18 (8%) dabigatran. Using CG, 154 (69%) had appropriate DOAC dose at baseline, 52 (23%) were underdosed, and 18 (8%) were overdosed. Discrepancies were found by comparing dosing status according to CG and eGFR equations (Figure 1). During the follow-up period, 109 (14.9/100 person-years) participants died, 25 (3.6/100 person-years) experienced a stroke or systemic embolism, and 60 (9/100 person-years) experienced a bleeding event. Drug dose status was not significantly associated with mortality and the occurrence of stroke or systemic embolism, whatever equation was used. Underdose status was associated with a significantly lower risk of bleeding events with all the equations but overdose status was not associated with a higher risk of bleeding events (Figure 2). In subgroup analyses, drug dose status was not associated with mortality and bleeding event in apixaban users, whatever equation was used. In rivaroxaban users, underdose status was associated with a significant higher risk of death by using CG, eGFR (EPA), and BIS 2, and a lower risk of bleeding event by using eGFR (EPA). Conclusion: In this population of very old adults with NVAF, drug dose status of DOAC was not associated with mortality or the occurrence of stroke or systemic embolism for any of the studied equations. However, underdose status was associated with bleeding events occurrence regardless of the equation used.

Figure 1: Dosing status of direct oral anticoagulants at baseline according to kidney function estimators in older adults with non-valvular atrial fibrillation (percentages).
These associations differed according to the used drug, but this should be interpreted with caution due to small sample sizes. Our results do not allow us to provide any guidance which equation to use in this context. A study including a larger group of patients with discrepancy in dose status according to the used equations would be of great interest.

#4011
LESSONS LEARNT FROM VIRTUAL RECRUITMENT TO A MULTICENTRE RANDOMISED CONTROLLED TRIAL EVALUATING A DIGITAL HEALTH INTERVENTION FOR CKD
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Background and Aims: The post-COVID era has seen an escalation in the use of digital health interventions (DHIs), which have the potential to provide a widely accessible and cost-efficient approach to aspects of health service delivery such as patient education. Robust effectiveness evaluation is essential for all novel interventions to enable appropriate and sustained implementation. We have developed an education/self-management DHI named “My Kidneys & Me” (MK&M) for chronic kidney disease (CKD). A multi-centre randomised controlled trial (RCT) (SMILE-K) with virtual study processes allowing for minimal face-to-face participant contact was conducted to pragmatically deliver and evaluate MK&M. Here we report the recruitment metrics of SMILE-K to inform and improve future design of virtual trials and delivery of DHIs.

Method: The SMILE-K virtual study design involved outcome measures collected via an online survey, and 2:1 randomisation to intervention or control group. The recruitment process is summarised in Figure 1. Briefly, eligible adult CKD patients were identified by their clinical teams and given or sent a study invitation. If interested, patients emailed the study team, who then sent sequential emailed links to: 1) the information sheet and consent form; 2) the baseline outcome measure survey; and 3) (if randomised to intervention), MK&M.

Results: 26 hospital sites in England recruited to SMILE-K between May 2021 and December 2022. 6693 invitations were issued: 4942 (74%) by mail, 883 (13%) in-person, 616 (9%) by mail following remote consultation; and 252 (4%) by email. 13% (875/6693 invited) invitees expressed interest, of which 60% (533/875) consented. Of the 533 consented, 5% (265/4942) had been invited via mail, 14% (120/883) in-person, 17% (103/616) via mail following remote appointment, and 2% (5/252) via email. Of those consented, 80% (424/533) completed the baseline survey and were subsequently randomised. The mean age of recruited participants was 74 years (±9.0; range: 20-88) and 94% were White British. The median time from expression of interest to consent was 1 day (IQR:0-5), and consent to randomisation was 6 days (IQR:2.5-11).

Conclusion: Our experience shows that a virtual strategy for DHI RCT recruitment provides the opportunity to reach a high number of eligible participants. However, only 13% of invited patients expressed interest, and just 7% were recruited into the study. Most invitations were sent via mail with no prior approach or explanation. This method resulted in a markedly lower response rate than invitations issued after discussion with a healthcare professional, either remotely or in-person, underlining the importance of personal contact. Substantial attrition occurred at the consent stage, indicating that reading the information sheet and completing the online consent form unassisted was a barrier. Despite the need for internet access and digital skills, there was a wide participant age range, including those in their 80s. However, we noted a disproportionate representation of White ethnicity. This highlights the need to embed specific strategies to engage minority ethnic communities and other disadvantaged groups in the design of DHIs and future virtual trials to maximise reach and access to their potential benefits.
Abstracts

Figure 1: SMILE-K Recruitment Process.

#3318

PHASE II DOSE-SELECTION, RANDOMISED DOUBLE-BLIND TRIAL OF THE ASI, BI 690517, ALONE AND IN COMBINATION WITH EMPA IN PEOPLE WITH CKD

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Background and Aims: Elevated aldosterone levels are associated with chronic kidney disease (CKD) progression and adverse kidney and cardiovascular disease outcomes. Therapy with an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) improves clinical outcomes, yet elevated aldosterone levels often persist. BI 690517 is a first-in-class, selective aldosterone synthase inhibitor (ASI) that may reduce deleterious mineralocorticoid receptor-dependent and -independent actions of aldosterone. Co-administration of BI 690517 with a sodium–glucose cotransporter-2 inhibitor could mitigate the risk of hyperkalaemia. This study is investigating the efficacy and safety of three doses of BI 690517, alone and in combination with empagliflozin (EMPA), on top of an ACEi or ARB, for treatment of CKD with or without type 2 diabetes.

Method: A randomised, double-blind, placebo-controlled, parallel-dose Phase II trial (NCT05182840) in adults with or without type 2 diabetes who had an estimated glomerular filtration rate (eGFR) ≥30 and <90 mL/min/1.73 m², urine albumin:creatinine ratio (UACR) ≥200 and <5000 mg/g, and serum potassium ≤4.8 mmol/L on stable background therapy with an ACEi or ARB. After an 8-week run-in period to assigned background therapy (EMPA 10 mg or matched placebo randomised 1:1), participants were randomised 1:1:1:1 to BI 690517 (low, medium or high dose) or matched placebo for 14 weeks. Primary outcome was the change in UACR measured in a first morning void (UACR_{1MV}) from baseline to Week 14. Secondary outcomes were the proportion of participants with ≥15 and 30% decreases in UACR_{1MV}. Safety outcomes and changes in eGFR and serum potassium were also evaluated.

Results: Recruitment is complete, with 1719 participants from 168 sites in 29 countries screened. In total, 714 were randomised and entered the run-in period (last randomisation on 30 December 2022). The trial is currently ongoing; data on baseline characteristics will become available and shared.

Conclusion: This study will provide key data on the potential synergistic kidney-protective effects and safety of combination therapy with BI 690517 plus EMPA, as well as data on monotherapy, for CKD with or without type 2 diabetes. Findings will inform BI 690517 dose selection for further clinical trial development.

#3749

QUANTIFICATION OF URINE PROTEINS FOR DISCOVERY OF BIOMARKERS FOR KIDNEY INJURIES BY DIA-PROTEOMICS

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Background and Aims: Recent advances in proteomics have enabled to quantify proteins comprehensively. We aimed to establish a platform of urine quantitative proteomics for selection of the biomarkers and assessment of health conditions. Since plasma proteins of varying amounts of were present in urine especially from proteinuric patients, we subtracted the plasma protein contents from total urine proteomes after the quantitative proteomics for discovery of biomarkers for kidney injuries. On the other hand, urine proteins excreted from plasma may be indicators of pathophysiological conditions in the body, suggesting that the urine proteome profiles figure out health conditions and early discovery of any diseases in the future.

Method: More than 120,000 urine samples (∼10 ml each) have been collected from ∼15,000 patients with various diseases and healthy volunteers (HV) and stored in -20°C freezers. In this study, urine samples were selected from HV, diabetic patients (DM) with or without microalbuminuria and other CKD patients. Proteins were precipitated by a methanol/chloroform precipitation method from 1 ml urine. The protein fractions were digested with trypsin and the tryptic peptides were purified by C18 column chromatography. The tryptic peptides of 200 ng each were analyzed by LC-MS (tims-TOFPro, Bruker) by quantitative Data-independent acquisition (DIA) proteomics and proteins were quantified by the DIA method. Major top 30 plasma proteins were removed from the quantitative proteomics data and kidney- and other urinary tract organ-derived proteins were normalized to compare their proportions in urine.

Results: Approximately 2,500 proteins were quantified by the DIA analysis. In urine from HV, proportions of plasma proteins were small, however, in urine from DM patients with microalbuminuria or CKD patients, the plasma protein contents were increased, resulting in relative decreases of urine proportions of other proteins derived from the kidney or other urinary tract organs. By subtraction of the plasma proteins from total urine proteins, protein proportions were comparable to select candidates of biomarkers for kidney injuries. Comparison of total urine protein profiles between HV and DM elucidated their differences, which might indicate changes of pathophysiological conditions.

Conclusion: By recent quantitative proteomics urine proteins were quantified comprehensively, facilitating discovery of biomarkers for kidney injuries and also evaluation of health conditions in the body.
Figure 1: A urine protein proportions before and after subtraction of plasma proteins.

#6184

PULSE WAVE VELOCITY AND AMBULATORY BLOOD PRESSURE IN PATIENTS WITH RENAL HYPERFILTRATION

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Background and Aims: Recent studies have been implicated that abnormally increased glomerular filtration rate, defined as renal hyperfiltration, may be a risk factor for the development of renal damage and cardiovascular disease. Herein, we aimed to investigate the possible relationship between renal hyperfiltration (RHf) and pulse wave velocity, ambulatory blood pressure measurements and clinical parameters.

Method: All individuals included the study were between 18 and 65 years old. The eGFR (CKD-EPI) values of above 140 ml/min/1.73 m² were defined as RHf. Nineteen individuals in the renal hyperfiltration group and 20 in the control group were included. Blood and urine samples of the cases were examined. The individuals with diabetes, obesity, pregnancy, hypertension, cardiovascular disease, peripheral artery disease, cerebrovascular disease, chronic rheumatological disease, and thyroid dysfunction were excluded from the study. The parameters related arterial stiffness and ambulatory blood pressure measurements were obtained in all cases. The results were analyzed statistically.

Results: The two groups were similar in terms of gender, age, BMI and smoking. In RHf group, total cholesterol, 24-hour urine proteinuria and albuminuria, SBP, DBP, MAP and PP values were found higher than control group. Interestingly, the differences of “night time” measurements of all these hemodynamic parameters were more pronounced in RHf group. The trend of “non-dipper” pattern was to be higher in the hyperfiltration group. In arterial stiffness parameters the augmentation pressure (AP), central systolic pressure and pulse wave amplification (PPA) were found significantly different. Pearson’s correlation analysis revealed that AP, CSP, CBP was the positively; Pearson’s correlation analysis.

Conclusion: We found that augmentation pressure is the most important independent parameter correlated with RHf among arterial stiffness measurements. The vascular risk may be increased in this population.

#3704

EU REGION-SPECIFIC CARDIOVASCULAR EVENT DATA FOR DAPRODUSTAT IN ASCEND-D AND ASCEND-ND

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Background and Aims: Daprodustat (GSK1278863) is a hypoxia-inducible factor prolyl hydroxylase inhibitor under investigation for the treatment of anaemia of chronic kidney disease. Phase 3 studies in dialysis (ASCEND-D) and non-dialysis (ASCEND-ND) patients demonstrated the non-inferiority of daprodustat vs recombinant human erythropoietin (rhEPO) control (in ASCEND-D) or darbepoetin alfa (ASCEND-ND) control in terms of the mean change in haemoglobin levels between Weeks 28 and 52 versus baseline and the first occurrence of a composite major adverse cardiovascular (CV) event (MACE) [1, 2]. Post-hoc analyses were conducted to evaluate prespecified CV endpoints for patients enrolled in these studies from participating countries in Europe (EU patients) versus elsewhere (non-EU patients).

Table 1: Laboratory, hemodynamic and arterial stiffness parameters found to be different statistically in both groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group(n = 20)</th>
<th>RHF group (n = 19)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (CKD-EPI), ml/min/1.73 m²</td>
<td>Mean(±SD)</td>
<td>Mean(±SD)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Cholesterol, mg/dL</td>
<td>106.4(±11.4)</td>
<td>156.0(±20.4)</td>
<td></td>
</tr>
<tr>
<td>Proteinuria, (24-hour), mg/day</td>
<td>114.2(±51.6)</td>
<td>185.4(±52.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albuminuria, (24-hour), mg/day median, (IQR)</td>
<td>4.0(4.9)</td>
<td>9.2(7.6)</td>
<td>0.007**</td>
</tr>
<tr>
<td>SBP, (whole day), mm Hg</td>
<td>109.5(±6.1)</td>
<td>119.8(±10.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>DBP, (whole day), mm Hg</td>
<td>70.8(±6.1)</td>
<td>76.3(±10.1)</td>
<td>0.048</td>
</tr>
<tr>
<td>MAP, (whole day), mm Hg</td>
<td>83.6(±7.4)</td>
<td>95.5(±11.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PP, (whole day), mm Hg</td>
<td>40.1(±3.5)</td>
<td>44.6(±5.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>AP, mm Hg</td>
<td>8.9(±5.9)</td>
<td>24.0(±11.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RM, %</td>
<td>66.2(±7.6)</td>
<td>59.6(±9.4)</td>
<td>0.021</td>
</tr>
<tr>
<td>CSP, mm Hg</td>
<td>113.0(±8.4)</td>
<td>119.1(±9.2)</td>
<td>0.037</td>
</tr>
<tr>
<td>PPA, mm Hg</td>
<td>1.3(±0.1)</td>
<td>1.4(±0.2)</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Student t, *Chi square and **Mann Whitney U tests were used, accordingly. p<0.05 was considered significant. RHf: renal hyperfiltration, IQR: interquartile range. SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure, PP: pulse pressure, AP: augmentation pressure, RM: reflection magnitude, CSP: central systolic pressure, PPA: pulse pressure amplification.

Table 2: Correlation analysis of parameters found to be different statistically.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria, (24-hour), mg/day</td>
<td>0.396</td>
<td>0.013</td>
</tr>
<tr>
<td>SBP, (day time), mm Hg</td>
<td>0.347</td>
<td>0.030</td>
</tr>
<tr>
<td>(night time), mm Hg</td>
<td>0.453</td>
<td>0.004</td>
</tr>
<tr>
<td>(whole day), mm Hg</td>
<td>0.449</td>
<td>0.004</td>
</tr>
<tr>
<td>MAP, (day time), mm Hg</td>
<td>0.411</td>
<td>0.009</td>
</tr>
<tr>
<td>(night time), mm Hg</td>
<td>0.494</td>
<td>0.001</td>
</tr>
<tr>
<td>(whole day), mm Hg</td>
<td>0.485</td>
<td>0.002</td>
</tr>
<tr>
<td>PP, (day time), mm Hg</td>
<td>0.433</td>
<td>0.006</td>
</tr>
<tr>
<td>(whole day), mm Hg</td>
<td>0.365</td>
<td>0.022</td>
</tr>
<tr>
<td>CSP, mm Hg</td>
<td>0.425</td>
<td>0.007</td>
</tr>
<tr>
<td>AP, mm Hg</td>
<td>0.572</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RM, %</td>
<td>-0.436</td>
<td>0.006</td>
</tr>
<tr>
<td>PPA, mm Hg</td>
<td>0.370</td>
<td>0.020</td>
</tr>
</tbody>
</table>

Pearson’s correlation analysis. p < 0.05 was considered significant.
Method: Post-hoc time to the first adjudicated MACE (death from any cause, non-fatal myocardial infarction or non-fatal stroke), time to the first adjudicated MACE or thromboembolic event (TEE; deep vein thrombosis, pulmonary embolism or vascular access thrombosis), and time to the first adjudicated MACE or hospitalisation for heart failure (HHF) were analysed for EU (enrolled from Austria, Belgium, Bulgaria, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Italy, the Netherlands, Norway, Poland, Portugal, Romania, Spain, Sweden and the UK; not all countries participated in both studies) and non-EU (all other participating countries) patients. Hazard ratios (HRs) and associated 95% confidence intervals were calculated to evaluate the likelihood of CV events with daprodustat versus alternative therapy in both studies. HRs for EU and non-EU patients were compared for each endpoint in each study and p-values were calculated to assess the statistical significance of observed differences. Significance was defined at the 10% level (interaction p-value <0.1).

Results: ASCEND-D included 415 EU patients and 1072 non-EU patients randomised to daprodustat, and 440 EU and 1037 non-EU patients randomised to rhEPO. ASCEND-Nd included 410 EU patients and 1527 non-EU patients randomised to daprodustat, and 407 EU and 1037 non-EU patients randomised to rhEPO. No significant heterogeneity was observed between EU and non-EU patients in terms of the prespecified CV endpoints (p=0.1979). In ASCEND-D and ASCEND-Nd, the results for MACE, MACE+TEE and MACE+HHF for the EU subgroup were consistent with the non-EU subgroup (Table, as well as with the co-primary analysis [1, 2]. Efficacy and additional safety data for EU versus non-EU patients are being explored and will be included in the subsequent presentation.

Conclusion: Non-inferiority in terms of the first occurrence of MACE was demonstrated for daprodustat versus rhEPO in ASCEND-D and versus darbeepoetin alfa in ASCEND-Nd.1,2 Results for EU and non-EU patients in the current analysis were consistent with the global outcomes from both studies.

REFERENCES

#3696
THE PROACT 2 PHASE 3 STUDY DESIGN: A RANDOMIZED CONTROLLED STUDY OF REACT IN PARTICIPANTS WITH TYPE 2 DIABETES AND CHRONIC KIDNEY DISEASE
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Background and Aims: The global burden of chronic kidney disease (CKD) is estimated at 850 million people worldwide, with diabetic kidney disease (DKD) being the main cause. Existing medical therapies may delay the deterioration of kidney function; however, many patients continue to progress to kidney failure. REACT (Renal Autologous Cell Therapy), a cell-based advanced therapy, is being developed to decrease the risk of CKD progression. REACT is composed of selected renal cells (SRC), isolated from a patient’s own kidney, which are involved in the process of kidney repair and regeneration. Preclinical studies in multiple animal models of DKD have demonstrated that SRC injected directly into the kidney cortex produced a regenerative response improving overall kidney function and histology. Encouraging early clinical results from phase 2 studies with REACT resulted in RMAT (Regenerative Medicine Advanced Therapy) designation by the Food and Drug Administration in the USA.

Method: Description of therapy - REACT is derived from the participant’s own kidney tissue obtained by percutaneous biopsy in an outpatient setting. Renal cells are culture expanded ex vivo, and SRC are isolated. SRC are cryopreserved at a concentration of 100 × 10^6 cells/mL and shipped to the clinical site approximately 12 weeks after the biopsy. REACT will be percutaneously re injected by specially trained interventional proceduralists utilizing CT guidance and a non-cutting 25-gauge needle inserted into the kidney cortex. A single REACT dose will be injected into each kidney, approximately 3 months apart. Participants - The study will enroll 600 participants from approximately 250 global sites (including 38 sites in the EU) with up to 60 months of follow-up. Patients aged 30-80 years with type 2 diabetes who have an estimated glomerular filtration rate (eGFR) of 20-50 mL/min/1.73 m^2, and urine albumin-to-creatinine ratio (UACR) 300-5000 mg/g will be eligible. Participants will be randomized 1:1 to REACT or sham biopsy/injection in a single blind manner. Standard-of-care therapies including renin angiotensin system inhibitors and sodium glucose cotransporter inhibitors may be given as per local guidance.

Results: Study Endpoints - The primary endpoint for proact 2 is the time from first injection to the earliest of ≥40% eGFR decline, eGFR < 15 mL/min/1.73m^2 sustained for 30 days, initiation of chronic dialysis or kidney transplantation, or cardiovascular or renal death. proact 2 is an endpoint driven trial with 80% power to detect a hazard ratio of 0.6 for the primary outcome. Key secondary outcomes will include time to these individual components as well as annualized change in eGFR and change from baseline in UACR.

Conclusion: proact 2 is a global Phase 3 randomized controlled trial that will evaluate the safety and efficacy of REACT on major kidney disease endpoints, among participants with type 2 diabetes and moderate-severe CKD. This trial is part of a comprehensive phase 3 development program with an estimated start date of June 2023. REACT, a novel autologous cell therapy composed of SRC, has the potential to directly improve kidney function with a goal to prevent kidney failure.

#4406
INCREASE IN HOSPITALIZED DAYS AFTER HYPERKALEMIA-RELATED REDUCTION IN RAASI USE: AN OBSERVATIONAL STUDY ON CARDIORENAL PATIENTS IN SWEDEN AND JAPAN
Maria Eriksson Svensson1, Toyoaki Murohara2, Johan Sundström3,4, Eva Lesén5, Matthew Arnold5, Thomas Cars6, Krister Järbrink7, Gengshi Chen8, Naru Morita9, Sudhir Venkatesan10 and Eiichiro Kanda11

1Uppsala University, Department of Medical Sciences, Renal Medicine, Uppsala, Sweden, 2Nagoya University Graduate School of Medicine, Division of Cardiology, Department of Internal Medicine, Nagoya, Japan, 3Uppsala
Background and Aims: Guidelines recommend renin-angiotensin-aldosterone system inhibitor (RAASI) therapy at the maximum tolerated dose to achieve optimal treatment benefits in chronic kidney disease (CKD) and heart failure (HF). However, hyperkalaemia (HK) is a barrier to achieving guideline-directed target dosing, with RAASI treatment often down-titrated or discontinued in patients who experience HK. Current international guidelines recommend novel oral anti-HK treatments to manage HK and facilitate maintenance of RAASI therapy. The aim of this study was to describe the extent of RAASI reduction (down-titration or discontinuation) following an HK episode, and the associated change in inpatient days, in patients with cardio renal disease in Sweden and Japan.

Methods: This observational study used data from health registers and hospital records in Sweden (national registers linked with health records from two large regions) and Japan (Medical Data Vision). Patients with an index HK episode, defined as ICD-10 code E87.5 (Japan and Sweden) or potassium >5.0 mmol/L (Sweden only), during March 2018 to July 2020 (Sweden) or May 2020 to February 2022 (Japan), with a prior diagnosis of CKD and/or HF, and RAASI use at index were included. RAASI classes included angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA), and an angiotensin receptor-neprilysin inhibitor (ARNI). Patients were defined as having reduced or maintained their pre-HK RAASI treatment based on filled prescriptions, or lack thereof, within 90 (Japan) or 120 (Sweden) days before versus after the index HK episode. Propensity score matching (1:1) was applied to balance lack thereof, within 90 (Japan) or 120 (Sweden) days before versus after the index HK episode. The change in number of all-cause, CKD-, and HF-related inpatient days (per person-years of follow-up) was described from 6 months before to 6 months after the index HK episode.

Results: In total, 20,824 patients from Sweden and 7789 from Japan were included. The mean age was 76 (Sweden) and 74 (Japan) years, 57% and 65%, respectively, were male. In Sweden, 86% had CKD and 57% had HF; in Japan, 49% had CKD and 75% had HF. The most common RAASI classes in Sweden were ACEi (used by 49%), ARB (44%), and MRA (30%). In Japan, ARB was the most common class (73%), followed by MRA (28%), and ACEi (17%). Overall, 42% (n = 8716) of patients in Sweden and 38% (n = 2976) in Japan reduced their RAASI treatment after the HK episode. In the propensity score matched cohorts, the increase in number of all-cause inpatient days following an HK episode in those with reduced RAASI treatment was 18.2 days in Sweden (n = 6998) and 17.9 days in Japan (n = 2092) (Figure 1A and B). For reference, the increase in those who maintained their RAASI treatment was 9.4 and 8.5 days in Sweden and Japan, respectively. Similar patterns were observed for CKD- and HF-related inpatient days.

Conclusion: In clinical practice, an episode of hyperkalaemia was often followed by reduced RAASI treatment. Reduced RAASI treatment was associated with a greater increase in the number of inpatient days, compared with maintained RAASI treatment. A better understanding of how guideline adherence can be increased to maintain RAASI treatment in patients experiencing HK is needed to achieve optimal treatment benefits in chronic kidney disease (CKD) and heart failure (HF).
THE VALUE OF MANAGING DIABETIC KIDNEY DISEASE: CONTRASTING FINDINGS FROM THE INDIVIDUAL PATIENT AND POPULATION LEVEL PERSPECTIVES

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Background and Aims: The management of diabetic kidney disease (DKD) is associated with considerable resource utilisation. Within the context of the broader healthcare system, understanding the health economic implications of adopting strategies to ameliorate the progression of DKD is imperative for fully informed decision-making. The objective of this study was to estimate the UK whole healthcare system economic value, from the individual patient and population perspectives, associated with modifying the progression of DKD through attenuating the decline in eGFR by values consistent with those observed in recent randomised clinical outcome trials.

Method: Since type 2 diabetes (T2D) is the commonest single cause of chronic kidney disease (CKD), we developed a deterministic model utilising published estimates of disease progression stratified by stages: stage 1/2, stage 3a, stage 3b and stage 4/5. Patient characteristics and mean annual decline in eGFR were aligned to the placebo arm of DECLARE-TIMI 58 (-2.44 ml/min/1.732). We explored scenarios where a sustained attenuation in the rate of eGFR decline by 1 and 2ml/min/1.732 per year was realised. T2D specific and all-cause mortality were captured using UKPDS risk equations. CKD stage specific costs and changes in health utility were drawn from NICE guidelines (NG203). Per-patient and population level costs (indexed to 2022) and quality adjusted life years (QALYs) were estimated, and both discounted at 3.5%.

Results: We estimated there were 3.2M, 0.6M, 0.2M and 0.04M DKD patients in stages 1/2, 3a, 3b and 4/5 respectively. Declining kidney function was associated with increasing per-patient lifetime costs and decreasing QALYs: stage 1/2 £36,714, 8.1 QALYs; stage 3a £90,666, 6.5 QALYs; stage 3b £126,931, 5.2 QALYs; stage 4/5 £168,604, 3.7 QALYs. A sustained attenuation in the rate of eGFR decline by 1 and 2ml/min/1.732 per year had the greatest impact in those in stage 3b: with cost savings of £23,690 and £47,463 and gains in QALYs of 0.68 and 1.46 for 1 and 2ml/min/1.732 respectively. At the population level, however, total lifetime cost for DKD was greatest in those in stage 1/2 £30.3Bn; followed by stage 3a, £19.2Bn; stage 3b £9.5Bn; stage 4/5 £146M. A sustained attenuation in eGFR resulted in the largest cost savings in those in stage 1/2: £16.9 Bn and £22.3 Bn for 1 and 2ml/min/1.732 respectively, and the greatest gains in QALYs of 0.8M and 1.1M for 1 and 2ml/min/1.732 respectively. In contrast, population level stage 4 cost savings and QALY gains were modest at £70.7M and £281.6M and 0.02M and 0.4M for 1 and 2ml/min/1.732 respectively.

Conclusion: The notion of value in healthcare is influenced by stakeholder perspective. From the clinician’s and patient’s perspective the greatest value in attenuating the progression of DKD is in those with more advanced disease. However, from the health care provider perspective, at the population level, modest cost-savings and QALY gains are realised in such patients. By contrast, those at an earlier disease stage deliver much greater population level return on investment consequent upon larger numbers of such individuals. This study illustrates that attenuating DKD progression provides value at both the individual and public health levels, irrespective of disease stage.

#6355

EFFECTS OF SODIUM-GLUCOSE CO-TRANSPORTER 2 INHIBITORS ON HEART FAILURE IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Sodium-glucose co-transporter 2 (SGLT-2) inhibitors significantly reduce the risk for hospitalizations for heart failure (HF) in patients with diabetes, and HF; findings in patients with chronic kidney disease (CKD) are not uniform. Objectives: We aimed to perform a meta-analysis exploring the effect of SGLT-2 inhibitors on HF events in patients with CKD and across subgroups defined by baseline kidney function.

Method: A systematic search in major electronic databases was performed. Randomized controlled trials providing data on the effect of SGLT-2 inhibitors on the primary outcome, time to hospitalization or urgent visit for worsening HF in patients with prevalent CKD at baseline or across subgroups stratified by baseline estimated glomerular-filtration-rate (eGFR) were included.

Results: Twelve studies (n = 89,191 participants) were included in the meta-analysis. In patients with CKD, treatment with SGLT-2 inhibitors reduced the risk for HF events by 32% compared to placebo (hazard ratio [HR] 0.68, 95% CI 0.63-0.73). Reduction in HF events with SGLT-2 inhibitors was more prominent in patients with eGFR < 60 ml/min/1.732 (HR 0.68; 95%CI 0.63-0.74) than in those with eGFR > = 60 ml/min/1.732 (HR 0.76; 95%CI 0.69-0.83). Subgroup analysis according to type of SGLT-2 inhibitor showed a consistent treatment effect across all studied agents (p subgroup-activity analysis = 0.44). Sensitivity analysis including data from studies including only diabetic patients showed an even more pronounced effect in eGFR subgroup <60ml/min/1.732 (HR 0.62; 95%CI 0.54-0.70).

Conclusion: Treatment with SGLT-2 inhibitors led to a significant reduction in HF events in patients with CKD. These findings may change the landscape of HF treatment in patients with advanced CKD.
the present study was to examine the long-term health effects of a dietary intervention with NNRD in patients with CKD stage 3-4 [2].

Method: A 26-week randomized, controlled, non-blinded trial comparing the effect of NNRD vs. non-restricted habitual diet. Patients in the NNRD group received weekly home delivery of fresh food items (free of charge) and recipes for five days of the week, and on the remaining two days they were instructed to prepare meals according to the NNRD food principles. The study was designed with seven follow-up visits in the outpatient clinic where fasting blood samples and 24-hour urine collection were delivered. Linear mixed-effects models were used to assess the effects of the intervention, time, and the potential interaction between intervention and time. The primary endpoint was the difference in 24-hour urine phosphorus excretion between the two study groups. Secondary endpoints included fractional phosphorus excretion and plasma fibroblast growth factor 23 (p-FGF23).

Results: Sixty patients (mean age 54 years, 31 women) with mean eGFR of 34 ml/min/1.73 m² were included. Two patients were withdrawn due to dialysis initiation. In the NNRD-group (n = 29), mean 24-hour urine phosphorus excretion during the intervention period was 651 mg (SD, 35 mg) vs. 930 mg (SD, 84 mg) in the control group (n = 29), between-group difference 279 mg (95% CI; -372, -91; P < 0.001) (Figure 1). Mean fractional phosphorus excretion was 11% (SD, 5%) in the NNRD-group and 14% (SD, 7%) in the control group, between-group difference 3% (95% CI; -6.4, -0.8; P = 0.01). Mean p-FGF23 was 162 pg/ml (SD, 130 pg/ml) in the NNRD-group and 215 pg/ml (SD, 230 pg/ml) in the control group, between-group difference 52 pg/ml (95% CI; -5.3, -0.2, P = 0.03) and 24-h urine bicarbonate excretion was 4.1 mmol higher in the NNRD group (95% CI; 0.7, 7.5, P = 0.01). There was no difference between study groups in p-calcium, p-creatinine, p-potassium, p-calcium, p-lipids, or proteinuria.

Conclusion: NNRD intervention in the context of fresh food delivery and recipes was feasible and had a major beneficial effect on phosphorus parameters in patients with CKD 3-4.

REFERENCES

#3804 ASSOCIATION BETWEEN PLASMA XOR AND OUTCOMES IN CKD PATIENTS
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Background and Aims: Plasma xanthine oxidoreductase (pXOR) is an enzyme plays a key role in uric acid (UA) production and produces reactive oxygen species (ROS), and it has been reported that pXOR activity is related with cardiovascular events in the general population. However, the relationship between pXOR activity and prognosis in patients with chronic kidney disease (CKD) remains unclear.

Method: We measured pXOR activity by Liquid chromatography tandem quadruple mass spectrometer (LC-TQMS method) in 415 outpatients with CKD, and compared demographic and laboratory data between two groups based on the median pXOR activity. Furthermore, we examined the association between pXOR activity and outcomes; renal replacement therapy (RRT), major adverse cardiovascular events (MACE), and all-cause mortality, using multivariate Cox proportional hazards model.

Results: Median age and eGFR were 71 years old and 21.6 ml/min/1.73 m², respectively. Median pXOR activity is 3.33 pmol/h/ml and 26.3 pmol/h/ml in the lower and higher pXOR activity groups, respectively. eGFR was significantly lower and UA was significantly higher in the lower pXOR activity group compared with the higher pXOR group (eGFR, 18.9 vs 27.4, P < 0.001; UA, 5.7 vs 6.1, P < 0.001). During the follow-up period of 38 months, the incidence of each outcome including RRT, MACE, or all-cause mortality were significantly higher in the lower pXOR group (log rank test, P < 0.001). Multivariate Cox proportional hazards analysis including eGFR and UA levels showed that lower pXOR activity was significantly associated with poor renal outcome (HR, 1.4; 95% CI, 1.0–2.1; P = 0.038). Furthermore, in subgroup analysis with or without antihyperuricemic use, univariate Cox analysis showed similar association between pXOR and each outcome.

Conclusion: In patients with CKD, lower pXOR activity has a significantly higher risk of all outcome (RRT, MACE, and all-cause mortality).

#4878 STUDYING THE EFFECTIVENESS OF PRASUGREL AND CLOPIDOGEL IN PATIENTS WITH CHRONIC LOWER LIMB ISCHEMIA WITH STAGE 2 CKD
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Background and Aims: To compare the clinical and rheological efficacy of prasugrel and clopidogrel in patients with chronic lower limb ischemia with stage 2 chronic kidney disease. According to statistics, in Europe, peripheral arterial disease is common in more than 40 million Europeans. According to the developed tactics, not only stroke should be recognized as a serious, life-threatening condition, but other peripheral vascular diseases can lead to disability and death.

Methods: The study included 101 patients with critical lower limb ischemia of atherosclerotic origin. The mean age of the patients was 51.51±8.33 years. As a control group, 20 healthy volunteers (mean age 53.90 ± 9.05 years) were examined without signs of pathology of the cardiovascular system, including those of a vegetative nature. All patients included in the study were hospitalized in the Department of Interventional Cardiology of the Republican Specialized Scientific and Practical Center for Therapy and Medical Rehabilitation, Tashkent city.

Results: In 94 patients (93.07%), CLCI was accompanied by hemodynamically significant multifocal atherosclerotic lesions. The first place in frequency of combined lesions was occupied by the coronary vessels, the second place - by the arteries of the brachiocephalic basin. 82 patients (81.19%) had previously suffered arterial occlusion, also most often in the form of acute myocardial infarction, somewhat less often - acute cerebrovascular accident. 47 patients (46.53%) underwent revascularization earlier, mainly coronary artery stenting, coronary artery bypass grafting, carotid endarterectomy. 8 patients (7.92%) underwent revascularization of the contralateral leg. The study studied spontaneous (SAT) and ADP-induced platelet aggregation. In the CG, SAT was noted only in 50% of cases and in all patients of the CLCI group. After comparing the results in the groups of patients with CLCI and representatives of the CG, in whom SAT was noted, it was found that both the rate and degree of SAT in the group of patients were significantly higher than in healthy individuals (2.95±0.59% versus 0.55±0.21% and 6.05±1.54% versus 1.24±0.21%, respectively, p<0.001 significance of the intergroup difference of both parameters). All patients due to CINC underwent endovascular revascularization of the affected leg. After the procedure, patients were prescribed an antiplatelet agent at a maintenance dose (prasugrel 10 mg/day, clopidogrel 75 mg/day). After 3 months, a control examination was carried out, during which the dynamics of platelet aggregation activity was studied. It was found that the indicators of CAT and ADP induced aggregation decreased by 22-37%. During the test, patients with resistance to antiplatelet agents were identified - in whom the decrease in the degree of ADP5 induced aggregation was less than 20%. Such resistance was found in 19 patients: 1 patient in the prasugrel group (1.69%) and 18 patients in the clopidogrel group (42.86%, chi square = 27.00, p<0.001). Isolation of patients with normal and reduced response to the loading dose of clopidogrel revealed some differences (Table 3.3). So, already initially in this group of patients, the degree of ADP5-induced aggregation was lower than in the group of patients with an antiplatelet response of more than 20%. After the application of a loading dose of clopidogrel, differences in relative dynamics were noted only in terms of the degree of ADP%-induced aggregation (p<0.001).

Conclusions: Thus, the present study revealed that in patients with CLCI, there is a significant activation of CAT and an increase in the aggregation response to the introduction of high doses of the inducer of ADP5 aggregation. The loading dose of antiplatelet agents contributed to a significant decrease in platelet aggregation activity after 2 hours with a large effect of prasugrel. Chronic antiplatelet therapy led to a decrease in the rate and degree of aggregation, both spontaneous and ADP-induced, a decrease in the endogenous ADP release response, also with a great effect in patients taking prasugrel.

#4355

THE INFLUENCE OF ANTIRETROVIRAL DRUGS AND HIV RESISTANCE MUTATIONS ON THE SHEDDING OF HIV-1 INTO PERITONEAL DIALYSIS EFFLUENT

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Background and Aims: Antiretroviral therapy (ART) is effective HIV management even in HIV-positive patients with end-stage kidney failure (ESKF). However, drug resistance mutations are important determinants of therapeutic effects. The study aimed to determine the prevalence of HIV resistance mutations and ART drug penetration in the peritoneal compartment and their effect on the shedding of HIV-1 into continuous ambulatory peritoneal dialysis (CAPD) effluents.

Method: This prospective cross-sectional study of HIV-positive ESKF patients managed with ART and CAPD at Universitas Academic Hospital collected enrolled patients’ background information and clinical and laboratory data. HIV-1 was detected using quantitative polymerase chain reaction (qPCR) and sequenced by the Sanger method, while ART levels were quantified using LC-MS/MS.

Results: There were 38 patients recruited with a median age of 41.8 (IQR, 36.15–48.0) years and were predominantly on abacavir (89.5%), lamivudine (100%) and efavirenz (76.3%) for a median duration of 8 (IQR, 6–11) years. Among participants with detectable HIV in CAPD effluents, the prevalence of ARV-drug resistance mutations was 71.4% (5/7) compared to 12.9% (4/31) among those with undetectable HIV-1 (p = 0.004) with NNRTI resistance mutations predominating. Participants with detectable HIV-1 had lower abacavir (0.0182 vs 5.68 ng/μl; p = 0.021), lamivudine (0.0152 vs 1.09 ng/μl; p = 0.001) and efavirenz (3,605 vs. 57.8 ng/μl; p = 0.004) plasma levels compared to those with undetectable HIV-1. Measured lamivudine (0.455 vs 0.342 ng/μl; p = 0.007) and efavirenz (46.5 vs 2.34 ng/μl; p < 0.001) drug levels are significantly higher in plasma than CAPD effluents.

Conclusion: ART resistance mutations, lower drug levels and poor compartment penetration are suggested significant factors for HIV-1 shedding into CAPD effluents.
Figure 1: A representation of factors hypothesized to be contributing to HIV-1 shedding into peritoneal dialysis (PD) effluents. Figure 1: Shows the association of environmental, underlying diseases (communicable and non-communicable) (A) and genetic factors (B) associated with HIV-1 particle-induced kidney failure (D) and shedding of the particles into PD waste (F). Virological failure due to HIV-1 mutations on Gag, Pol and Env segments (C, C1 and D) and altered anti-retroviral therapy (ART) pharmacodynamics (D2) in individuals who are carriers or non-carriers of either homozygous or heterozygous pair of renal risk alleles (B1). Moreover, single nucleotide polymorphisms and frame-shift deletion mutations on G1 and G2, respectively, induces a nonsynonymous substitution and Insertion that alters SRA binding domain of apolipoprotein 1 (B2). This in synergy with continuous viral replication alters the behaviour and function of tubular and podocyte cells (D3), thus impairing the renal tubule and glomerulus capacity to filter out nitrogenous waste from the blood (D4 - D5) and possibly leads to acute and chronic kidney failure which may be reversible until stage 3B (E1). Progression to stage 4 and 5 may imply a complete loss of kidney function in terms of the glomerular filtration which is usually managed by dialysis, either haemodialysis or PD (E2). The shedding of HIV-1 particles has been observed mainly in peritoneal effluent in a setting of HIV positive patients complying to their respective renal friendly ART, most likely due to lowered ART dosage regimen and modified ART pharmacokinetics as well as HIV-1 mutations and other factors (F1), Figure created with Biorender.com.

#4385

RELEVANCE OF REPEATED ALBUMINURIA AND GLOMERULAR FILTRATION RATE IN A LARGE COHORT OF SICKLE CELL ANEMIA CHILDREN LIVING IN A RESOURCE-LIMITED AREA

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Background and Aims: Chronic kidney disease (CKD) is associated with significant morbidity and mortality among patients with sickle cell anemia (SCA). Glomerular hyperfiltration (GHF) and albuminuria are known as early manifestations of kidney disease occurring in early childhood and can predict the progression to CKD in these patients. Studies reported the prevalence of these kidney abnormalities in SCA children using a single measure and their association with genetic risk factors, especially the co-inheritance of APOL1 risk variants (RVs). However, data on the prevalence of persistent kidney abnormalities (based on the KDIGO CKD definition) and their association with APOL1 RVs are limited in SCA children, particularly those living in sub-Saharan Africa. This study aimed: (i) to determine the prevalence of persistent kidney abnormalities (albuminuria and/or GHF) in SCA children living in the Democratic Republic of Congo (DRC); and (ii) to assess the association between persistent kidney abnormalities with clinical and genetic risk factors.

Method: From March 2021 to December 2022, we prospectively enrolled 585 steady state SCA children aged 2 to 18 years (male gender 278/585; 47.5%). The SCA status was confirmed through the molecular sequencing of beta-globin gene. Clinical and biological parameters were obtained. All participants were genotyped for apolipoprotein-L1 (APOL1) G1 (rs73885319, rs60910145) and G2 (rs71785313) variants. APOL1 high-risk genotype (HRG) was defined by the presence of 2 risk variants (G1/G1, G2/G2, and G1/G2), and low-risk genotype (LRG) by the presence of 0 or 1 risk variant. Albuminuria was defined as urinary albumin-to-creatinine ratio (ACR) ≥ 30mg/g. The estimated glomerular filtration rate (eGFRcr) was calculated using the original Schwartz formula and GHF was defined as eGFRcr ≥ 180 ml/min/1.73 m² for...
children between 2-10 years of age and > 140 ml/min/1.73 m² for children more than 10 years of age. All measurements were repeated at least three months later in participants who presented with kidney abnormalities at the first screening. The main outcome parameter was persistent albuminuria or persistent GHF for more than three months.

Results: At enrollment, 234/585 (40.0%) participants presented with kidney abnormalities, among which 80/585 (13.7%) with albuminuria and 171/585 (29.2%) with hyperfiltration. From participants found with kidney abnormalities at the first screening, 176/234 (75.2%) were available for repeated screening: 56/176 (31.8%) presented with persistent kidney abnormalities and 120/176 (68.2%) had a regression of kidney abnormalities without any treatment. Out of 176 participants who benefited from repeated screening, 57 had baseline albuminuria and 130 had baseline GHF. Persistent albuminuria and persistent GHF were found in 38.6% (22/57) and 28.5% (37/130), respectively. Multivariate logistic regression revealed that APOL1 HRG was significantly associated with persistent albuminuria (OR 3.4, 95CI 1.1-10.7, p = 0.037), while male gender was significantly associated with persistent GHF (OR 2.1, 95CI 1.0-4.2, p = 0.042).

Conclusion: A significant proportion (almost 70.0%) of SCA children who had kidney abnormalities at the first measure, presented regression of these abnormalities without any reno-protective drugs. This result emphasizes the importance of repeating screening at least three months later to confirm CKD, as recommended by the KDIGO Guidelines. This strategy will reduce the need for unnecessary treatment, which represents a high financial burden in a resource-limited area.

#4427

USING REDUCED RANK REGRESSION TO INVESTIGATE THE RELATIONSHIP BETWEEN DIETARY PATTERNS AND ADULT KIDNEY FUNCTION IN THE GENERAL POPULATION

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Background and Aims: Chronic kidney disease (CKD) is a severe public health burden, characterized by a gradual loss of kidney function over time. Diet is a modifiable lifestyle-related risk factor for CKD. However, there is uncertainty about which specific dietary patterns (DPs) are more beneficial or detrimental in CKD prevention. We aimed at deriving DPs using an hybrid approach that combines a priori knowledge and data-driven methods to identify dietary factors that may affect kidney function in healthy and diseased subjects.

Method: We analysed data of 8686 adults participating in the population-based Cooperative Health Research In South Tyrol (CHRIS) study. Kidney function was multiply assessed by the estimated glomerular filtration rate (eGFR), based on serum creatinine, using the 2021 CKD-EPI equation, the urinary albumin-to-creatinine ratio (UACR), and a kidney disease questionnaire. Participants were split between those free of diagnosed kidney disease, hypertension or diabetes (Group1, n = 6133) and those diagnosed with any of the three conditions (Group2, n = 2553). Diet was assessed through the self-administered and validated GA2LEN food frequency questionnaire (FFQ). The individual consumption of each food group was converted into portions per week and adjusted for total energy intake. DPs were estimated using reduced rank regression (RRR), based on four FFQ-derived nutrient mediators (total daily dietary protein; potassium; sodium; and phosphorus intake) selected based on known effects on kidney health. Generalized cross-validation identified an optimal number of 3 DPs. Factor Loading (FL)-based scores, either as continuous or stratified into sex-stratified tertiles (T1-T2-T3), were included in multiple-adjusted linear regression models for eGFR and log(UACR).

Results: Group1 participants (53.4% females) were younger and presented better kidney health (median, Mdn age 39.7 years; Mdn eGFR 101.8 ml/min/1.73m², interquartile range, IQR 91.5-112.1; Mdn UACR 5.2 mg/g, IQR 3.5-8.8) than Group2 participants (Mdn age 57.2 years; Mdn eGFR 90.8 ml/min/1.73 m², IQR 80.4-100.3; Mdn UACR 6.5 mg/g, IQR 4.1-12). The identified DPs were (Figure 1): DP1, reflecting greater consumption of all nutrients; DP2, reflecting increased potassium and phosphorus intake and lower sodium and protein intake; and DP3, reflecting increased intake of protein and phosphorus and lower intake of potassium and sodium. The 3 DPs presented stable FLs across groups. In Group1, DP1 was negatively associated with eGFR (larger effect size in males) both as linear score and in the 3rd tertile (Figure 2); DP2 was positively associated with eGFR in males and with UACR both at low and high levels of the score, with heterogeneous effects between males and females; DP3 was positively associated with UACR overall in the 3rd tertile. In Group 2, we observed protective effects of diet on eGFR, especially at lower DP1 and DP3 levels, and at high levels of DP2 (Figure 2). Similar to Group1, also in Group2 DP2 was positively associated with UACR both at low and high level of the score, but not in males. In its 3rd tertile, DP3 was negatively associated with UACR in females.

Conclusion: Using RRR proved to be a valid approach to integrate a priori knowledge about nutrients in the estimation of kidney function-oriented DPs. Our results showed heterogeneous effects of the DPs across kidney outcomes, possibly reflecting specificity to kidney function or damage. In individuals affected by any kidney disease, hypertension or diabetes, the effects of DPs

Figure 1: DPs in Group1 (blue) and Group2 (orange), described by Factor Loadings (FLs) of the most characterizing food groups.

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on eGFR reflected possible benefits of specific diets, suggesting that disease-specific dietary interventions can be a fundamental and effective approach for disease control.

#5500
THE IMPACT OF CHRONIC KIDNEY DISEASE-ASSOCIATED PRURITUS RELIEF ON SKINDEX-10 DISEASE AND SOCIAL FUNCTIONING DOMAINS
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Background and Aims: Chronic kidney disease-associated pruritus (CKD-aP) is a serious condition that greatly impacts patients’ quality of life (QoL). Moderate-severe pruritus affects up to 47% of patients undergoing haemodialysis (HD) [1]. The aim of this analysis was to assess the impact of itch relief on the disease and social functioning domains of the Skindex-10 questionnaire in a post hoc analysis of the difelikefalin (DFK) Phase 3 studies in patients with CKD-aP undergoing HD.

Method: Patients with moderate-to-severe CKD-aP (mean Worst Itch Numerical Rating Scale [WI-NRS] score ≥4 [KALM-1] or ≥5 [Study 3105 and KALM-2]) undergoing HD were enrolled and randomised 1:1 to receive intravenous DFK 0.5 μg/kg or placebo (KALM-1 and -2) or open-label DFK (Study 3105) 3 times/week for 12 weeks. Data from all patients who completed the studies were included in the present analysis irrespective of study drug exposure; data were pooled for patients receiving DFK and placebo from the KALM studies. The 12-week change from baseline in the Skindex-10 questionnaire subdomains were assessed for disease (Q1–3) and social functioning (Q7–10). Change from baseline in the mood/emotional distress domain has previously been reported (Q4–6) [2].

Results: Skindex-10 scores were available for 914 patients (KALM studies: n = 720; Study 3105: n = 194). At Week 12, patients with a clinically relevant (WI-NRS ≥3-point) change (decrease) in itch (KALM: n = 305; 3105: n = 143) reported a relative mean (± standard error) corresponding improvement of 59.7% ± 2.0 (KALM) and 65.9% ± 2.6 (3105) from baseline in the disease domain of Skindex-10, compared with 18.4% ± 2.3 and 30.7% ± 4.4 of patients with <3-point WI-NRS improvement (KALM: n = 415; Figure A; 3105: n = 51; Figure B). In addition, a much greater improvement in QoL was reported for the social functioning domain for patients with ≥3-point WI-NRS improvement, compared with patients with <3-point improvement (66.2% ± 3.5 vs 11% ± 7.6 in the KALM studies; 75.5% ± 4.0 vs 49.4% ± 8.5 in Study 3105). Overall, the patients with ≥3-point WI-NRS change reported relative mean improvement from baseline ranging from 64% ± 2.3 to 70.2% ± 2.6 across the total Skindex-10 scale compared with 15.1% ± 4.8 to 35.4% ± 5.3 of patients with <3-point improvement at Week 12 across all studies.

Conclusion: In this post hoc analysis, patients with CKD-aP undergoing HD who reported a clinically meaningful reduction in itch intensity also achieved a substantially greater improvement in both the disease and social functioning domains of Skindex-10, as well as overall itch-related QoL.

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Figure 1: The relative mean (standard error) percentage change from baseline to Week 12 in Skindex-10 questionnaire scores for patients reporting ≥3-point vs <3-point improvement in in disease and social functioning domains in KALM studies (A) and Study 3105 (B).

REFERENCES

#6146

EARLY REFERRAL TO PRE-DIALYSIS NEPHROLOGICAL CARE ASSOCIATES WITH LOWER COVID-19 INCIDENCE IN PREVALENT DIALYSIS PATIENTS

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Background and Aims: Early referral to nephrological care associates with improved long-term survival and lower hospitalization rates after dialysis initiation. Despite the strong evidence for this beneficial effect of early referral to pre-dialysis nephrological care in dialysis patients, the effect on COVID-19 incidence and outcome has not yet been investigated.

Method: Patients in the current study were recruited from a cohort of 349 consecutive patients who initiated dialysis between 2015 and 2018 at a dialysis network in Romania. All patients alive at the start of the pandemic (March 2020 = baseline) were included in this retrospective cohort study. Follow-up ended July 2021. At each visit, patients were screened for 2019 Coronavirus Disease (COVID-19) symptoms and symptomatic patients underwent PCR testing. We studied the effect of pre-dialysis nephrological care in COVID-19 incidence, and outcome has not yet been investigated.

Results: In total, 224 patients were included. Of these, 89 were early referral patients. At dialysis initiation, they had higher hemoglobin (median (25-75%), 10.0 (9.4-10.8) g/dL vs. 8.5 (7.6-9.4) g/dL, p < 0.001), transferrin saturation (21.5 (16.8-25.3)% vs. 18.1 (13.4-23.5)%), p = 0.01), calcium (8.8 (8.3-9.1) mg/dL vs. 8.3 (7.8-8.8) mg/dL, p < 0.001), phosphate (5.9 (5.0-6.8) mg/dL vs. 4.8 (3.9-5.8) mg/dL, p < 0.001), and albumin (3.5 (3.2-4.2) g/dL vs. 3.5 (3.2-3.8) g/dL, p = 0.04), lower PTH (220 (136-357) pg/mL vs. 289 (148-510) pg/mL, p = 0.03), and initiated dialysis less often via a central dialysis catheter (40 (44.9%) vs. 132 (97.8%), p < 0.001). Age, sex, diabetes, and Charlson Comorbidity Index did not differ between groups. During the 16 months of follow-up, 82 patients (36.6%) developed COVID-19. Incidence of COVID-19 was higher in patients with diabetes (32 (46.4%) vs. 50 (32.4%), p = 0.04), while early referral was weakly associated with a lower COVID-19 incidence (26 (29.2%) vs. 56 (41.5%), p = 0.06). Logistic regression, correcting for differences between early and late referral and differences between patients with and without COVID-19, identified a lower risk for COVID-19 among early referral patients (Table 1). No difference in mortality was detected between patients with and without COVID-19 during follow-up (19 (23.2%) vs. 36 (25.4%), p = 0.7).

Table 1: Independent predictors of COVID-19 infection in prevalent dialysis patients.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Exp(B) (95% confidence interval)</th>
<th>Sig.</th>
</tr>
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<tbody>
<tr>
<td>Age (year)</td>
<td>1.000 (0.965-1.037)</td>
<td>0.99</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>0.646 (0.331-1.261)</td>
<td>0.2</td>
</tr>
<tr>
<td>Early referral before dialysis initiation</td>
<td>0.344 (0.132-0.896)</td>
<td>0.03</td>
</tr>
<tr>
<td>Dialysis vintage at baseline (month)</td>
<td>1.000 (0.958-1.043)</td>
<td>0.98</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>2.432 (0.990-5.976)</td>
<td>0.05</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>1.185 (0.927-1.514)</td>
<td>0.2</td>
</tr>
<tr>
<td>Intact parathyroid hormone (pg/mL)</td>
<td>1.001 (1.000-1.002)</td>
<td>0.2</td>
</tr>
<tr>
<td>Bicarbonate (mEq/L)</td>
<td>0.904 (0.813-1.007)</td>
<td>0.07</td>
</tr>
<tr>
<td>Phosphate (mg/dL)</td>
<td>0.978 (0.785-1.218)</td>
<td>0.8</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>0.906 (0.594-1.384)</td>
<td>0.6</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>0.779 (0.597-1.018)</td>
<td>0.07</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>0.977 (0.948-1.008)</td>
<td>0.1</td>
</tr>
<tr>
<td>Constant</td>
<td>242.810</td>
<td>0.06</td>
</tr>
</tbody>
</table>
Conclusion: Among prevalent dialysis patients, early referral to nephrological care before dialysis initiation was an independent predictor of lower COVID-19 incidence during a follow-up period of 16 month from the beginning of the pandemic.

#6431
THE DEVELOPMENT OF AN INTEGRATED COMMUNITY, CONSERVATIVE KIDNEY CARE AND PALLIATIVE-RENAL CARE SERVICE
Jawad Ahmed1, Lucia Birch 2, Matthew Dodd3, Donna Roberts3, Simon Harlin4 and Huda Mahmoud4
1Walsall Manor Hospital, Medicine, Walsall, United Kingdom, 2Walsall Together, Palliative Care, Walsall, United Kingdom, 3Walsall Together, Community Services, Walsall, United Kingdom and 4Walsall Manor Hospital, Nephrology Department, Walsall, United Kingdom

Background and Aims: Conservative kidney care is the chosen therapeutic strategy for approximately 6% of renal patients. It is estimated that a third of renal patients in the United Kingdom have a dedicated conservative kidney care service. Equally, other units manage this cohort of patients in general nephrology/low-clearance clinics or alternatively, discharge to community services. Walsall Together, is a collaborative initiative between community and speciality services, driven to provide multi-agency, patient-focused care. By combining specialist input and community resources, we aimed to optimally manage individuals on the conservative kidney care and palliative-renal pathways at home.

Method: Community, nephrology and palliative care teams devised a service for those individuals identified for conservative kidney care or individuals with renal disease requiring palliative care management. Two separate, yet linked services; the community, conservative care pathway feeding into the community, palliative renal pathway. Individuals suitable for community conservative care pathway were identified from routine nephrology inpatient and outpatient workstreams. Prior to a telephone consultation with a nephrologist, phlebotomy for routine bloods were performed at the GP surgery or at the patients home by the community phlebotomy service. Any alterations to medications would be performed directly by the community pharmacist. Symptoms were assessed using the integrated palliative outcome score (IPOS)-renal survey. The IPOS renal-survey asks individuals to rate symptom burden as the three most common symptoms that generated discomfort in the three days prior to taking the IPOS-renal survey. On detailed assessment; significant symptom burden was attributed to reduced mobility (82% scoring slightly to overwhelmingly), pain (65% scoring slightly to overwhelmingly) and bowel concerns (65% scoring slightly to overwhelmingly). Ictching affected a third of the cohort, scoring moderately to overwhelmingly. Importantly, as a result of the service, patients reported that either all or most renal-related problems were addressed. To date all patients who died while under the renal-palliative care service, died in their chosen place of death, and not in hospital.

Conclusion: The Walsall Together initiative has demonstrated that utilising conservative care and renal-palliative care pathway. 94% of patients felt that the community approach did not waste time waiting for appointments/treatments. 87% of patients felt that the community approach provided them with sufficient information to understand their healthcare condition and relevant management strategies. Patients reported pain, nausea and reduced appetite as the three most common symptoms that generated discomfort in the three days prior to taking the IPOS-renal survey. On detailed assessment; significant symptom burden was attributed to reduced mobility (82% scoring slightly to overwhelmingly), pain (65% scoring slightly to overwhelmingly) and bowel concerns (65% scoring slightly to overwhelmingly). Ictching affected a third of the cohort, scoring moderately to overwhelmingly. Importantly, as a result of the service, patients reported that either all or most renal-related problems were addressed. To date all patients who died while under the renal-palliative care service, died in their chosen place of death, and not in hospital.

Conclusion: The Walsall Together initiative has demonstrated that utilising a collaborative approach to managing complications of advanced kidney disease can result in the reduction of hospital admissions, face-to-face hospital outpatient appointments and time wasted attending healthcare appointments. Furthermore, the cooperative multi-speciality approach, has led to improve patient satisfaction and the attainment of patient healthcare goals.

REFERENCE

#3336
EFFECTS OF LIPID-LOWERING DRUGS ON IMPROVING KIDNEY FUNCTION: A DRUG TARGET MENDELIAN RANDOMIZATION STUDY
Schyler Bennett1, Venexia Walker2,3, Jie Zheng1, Ben Brumpton1, Kristian Hveem1, Anna Köttgen1,5, Bjorn Åsvold6,9, Tom Gaunt2,7 and Humaira Rasheed1,2
1Norwegian University of Science and Technology (NTNU), K.G. Jebsen Center for Genetic Epidemiology, Trondheim, Norway, 2University of Bristol, Medical Research Council Integrative Epidemiology Unit, Bristol, United Kingdom, 3Perelman School of Medicine at the University of Pennsylvania, Department of Surgery, Philadelphia, United States of America, 4Institute of Genetic Epidemiology, University of Freiburg, Department of Biometry, Epidemiology and Medical Bioinformatics, Freiburg, Germany, 5Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, United States of America, 6St. Olav’s University Hospital, Department of Endocrinology, Trondheim, Norway and 7University of Bristol, NIHR Biomedical Research Centre, Bristol, United Kingdom

Background and Aims: Chronic kidney disease (CKD) affects one in ten adults worldwide. CKD frequently co-occurs with cardiovascular diseases, hypertension, and diabetes. Despite this high prevalence, few specific therapies exist. Thus, using drug-target Mendelian randomization (MR), we investigated the existing treatments for cardiovascular diseases, hypertension, and diabetes as potential treatment options for improving kidney function.

Methods: We identified SNPs as genetic proxies for the effects of targets of statins, ezetimibe, and alirocumab/evolocumab (as hypercholesterolemia drugs); angiotensin-converting enzyme (ACE) inhibitors, β-blockers (BB), and calcium channel blockers (CCB: as antihypertensive drugs); and metformin (as an antidiabetic drug) on kidney function. Effects of these SNPs on exposures, including low-density lipoprotein cholesterol (LDL-C) for hypercholesterolemia drugs, systolic blood pressure (SBP) for antihypertensive drugs, and Hba1c for antidiabetic drug, were obtained from published genome wide association studies (GWASs) summary statistics. Similarly, SNP-outcome data for kidney related markers, including serum creatinine and serum cystatin C based estimated glomerular filtration rate (eGFRcrea and eGFRcys, respectively) and blood urea nitrogen (BUN), were obtained using the largest GWAS for these phenotypes. Two-sample MR analysis using the inverse variance weighted (IVW) method and additional sensitivity analyses including weighted median, weighted mode, and MR-Egger methods were carried out in R (version 4.2.1). The results are presented as standard deviation (SD) change in outcome per 1 SD change in exposure caused by the drug.

Results: Each 1 SD lowering in LDL-C caused by HMGGCR variants, proxying the effect of statins, was associated with higher serum creatinine and cystatin-C based eGFR of approximately 0.01 SD (eGFRcrea β = 0.012, 95% CI = 0.007-0.018, p = 0.00032; eGFRcys β = 0.012, 95% CI = 0.002-0.022, p = 0.017), and lower BUN of 0.010 SD (β = -0.010, 95% CI = -0.020-0.00020, p = 0.050) (Figure 1), with consistent findings from sensitivity methods and no bias due to pleiotropy (Pegger = 0.22-0.70). Findings for other lipid-lowering drugs including NPC1L1 (target of ezetimibe) and PCSK9 (target of alirocumab/evolocumab) remained inconclusive. Similarly, we found limited evidence for the causal role of genetically proxied antihypertensive or antidiabetic drugs in improving kidney function, though beta values were close to null (Figure 1).

Conclusion: The genetically proxied LDL-C lowering effect of HMGGCR variants is associated with improved kidney function, which is consistent with the reported causal association of LDL-C with kidney function in a previous trans-ethnic MR study (1). Limited evidence was found for antihypertensive and antidiabetic drugs. These results provide insights into potential drug target candidates for future trials to address the treatment of CKD and comorbidities.

Abstracts

i663
RENAL SAFETY OF FLOT REGIMEN FOR GASTROESOPHAGEAL CANCER

Francesco Trevisani1, Matteo Floris2, Andrea Angioi2, Nicole Liscia3, Alessandra Cinque4, Antonello Pani2, Marco Puzzoni2, Mario Scartozi3, Manuela Dettori6, Elena Mazza3 and Stefano Cascini4

1San Raffaele Scientific Institute, Urology, Milano, Italy; 2G. Brotzu Hospital, Nephrology, Cagliari, Italy; 3San Raffaele Scientific Institute, Oncology, Milano, Italy; 4San Raffaele Scientific Institute, Biorek, Milano, Italy; 5Policlinico Universitario, Oncology, Monserrato, Italy and 6G. Brotzu Hospital, Nephrology, Cagliari, Italy

Background and Aims: Currently, peri-operative docetaxel, oxaliplatin, leucovorin, and 5-fluorouracil (FLOT) chemotherapy is the gold standard treatment for patients with locally advanced gastric cancer (LAGC), who undergo peri-operative chemotherapy and surgery. The known nephrotoxicity of both docetaxel and oxaliplatin compounds may limit its application in CKD population. Nevertheless, limited evidence is available regarding the effects of FLOT regimen on renal function. In our analysis we evaluated the renal safety of FLOT regimen in LAGC population.

Method: Retrospective data on patient with resectable gastric cancer in four tertiary referral hospital between January 2018 to January 2022 have been analyzed. Patient have been treated with docetaxel (60 mg/m2), oxaliplatin (85 mg/m2), leucovorin (200 mg/m2), and 5-fluorouracil (2,600 mg/m2 as a 24 hr infusion), all given on day 1 and administered every 2 weeks in 4 administrations before surgery. Serum creatinine, hemoglobin, lymphocytes and CKD-EPI eGFR were detected at baseline and before each cycle. AKI and CKD onset/prevalence were determined according to K-DIGO criteria.

Results: A consecutive cohort of 90 patients was enrolled. At baseline CKD was present in 16 pts (21.9%). Median eGFR was 84.9 ml/min. In terms of eGFR decay and CKD onset during the treatment cycle, the result of ANOVA indicated no significant differences or relationship with FLOT; Wilks’ Lambda = 0.94, p = 0.354 (Table 1 and Figure 1). AKI incidence was very low with one episode of stage 2 AKI (0.7%) between the 2nd and the 4th treatment cycle. New onset anemia between the 1st and the 2nd cycle was the only significant adverse event observed (p = 0.003).

Conclusion: According to our results, the pre-operative FLOT regimen seems to have a negligible impact on renal function with very low rate of renal toxicity suggesting the possibility to extend its use even in patient with advanced CKD.

Table 1: Baseline characteristics of the 89 patients of the cohort.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>89 (58.0 – 71.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - years (Median/ Interquartile range)</td>
<td>64.2</td>
</tr>
<tr>
<td>Female sex – no. (%)</td>
<td>32 (35.9)</td>
</tr>
<tr>
<td>Diabetes – no. (%)</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Hypertension – no. (%)</td>
<td>30 (33.6)</td>
</tr>
<tr>
<td>Smoker – no. (%)</td>
<td>20 (22.4)</td>
</tr>
<tr>
<td>Alcohol – no. (%)</td>
<td>6 (6.7)</td>
</tr>
<tr>
<td>eGFR CKD-EPI (Median/ Interquartile range)</td>
<td>84.9 (71.9 – 97.2)</td>
</tr>
<tr>
<td>eGFR &lt; 90 and ≥60 ml/min/1.73 m2</td>
<td>37 (41.4)</td>
</tr>
<tr>
<td>eGFR &lt; 60 ml/min/1.73 m2</td>
<td>7 (7.8)</td>
</tr>
<tr>
<td>Cancer site – no. (%)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Angulus</td>
<td>15 (16.8)</td>
</tr>
<tr>
<td>Antrum</td>
<td>23 (25.3)</td>
</tr>
<tr>
<td>Cardias</td>
<td>11 (12.3)</td>
</tr>
<tr>
<td>Gastric body</td>
<td>8 (8.9)</td>
</tr>
<tr>
<td>Distal esophagus</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Medium esophagus</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>Fundus</td>
<td>14 (15.4)</td>
</tr>
<tr>
<td>Gastro-esophagus junction</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Pylorus</td>
<td>5 (5.6)</td>
</tr>
<tr>
<td>Prior Cancer – no. (%)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Prior AKI on CT – no. (%)</td>
<td>12 (13.2)</td>
</tr>
<tr>
<td>RAAS inhibition – no. (%)</td>
<td>8 (8.9)</td>
</tr>
<tr>
<td>Beta-blockers – no. (%)</td>
<td>8 (8.9)</td>
</tr>
<tr>
<td>Calcium antagonists – no. (%)</td>
<td>8 (8.9)</td>
</tr>
<tr>
<td>Diuretics – no. (%)</td>
<td>6 (6.6)</td>
</tr>
<tr>
<td>Acetylsalicylic acid – no. (%)</td>
<td>8 (8.9)</td>
</tr>
<tr>
<td>Oral antidiabetics – no. (%)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>Proton pump inhibitors – no. (%)</td>
<td>40 (44)</td>
</tr>
<tr>
<td>Nutritional inhibitors – no. (%)</td>
<td>11 (12.3)</td>
</tr>
</tbody>
</table>
Efficacy and Safety of Sacubitril/Valsartan in Patients with Stage 3B-5 CKD and Hypertension

Qin Zhou, Wenjuan Yu, Xiaofei Shao, Qin Liu, Honglei Wang, Junzhe Chen and Ying Tang

The Third Affiliated hospital of Southern Medical University, Department of Nephrology, Guangzhou, P.R. China

Background and Aims: Sacubitril/valsartan (SV) plays a key role in improving left ventricular remodeling and prognosis in patients with heart failure. However, its effects on kidney function in people with moderate to severe chronic kidney disease (CKD3b-5) are unknown. The present study was designed to assess the efficacy and safety of sacubitril-valsartan in patients with stage 3b-5 CKD and hypertension.

Method: In this randomized, double-blind, 3-month trial, patients with stage 3b-5 CKD and hypertension were randomly assigned to sacubitril/valsartan treatment group (n = 44, the doses of SV were up-titrated to sacubitril/valsartan 400 mg), and conventional antihypertensive treatment group (n = 40). The primary outcome was reduction in GFR from baseline at week 12.

Results: In total, 44 participants were assigned to sacubitril/valsartan group and 40 to control group (conventional antihypertensive group). Baseline measured GFR was 29.94±11.83, 27.86±10.14 mL/min/1.73 m², respectively. There was no difference in measured GFR (P = 0.064). At week 12, there was a reduction in measured GFR in control group: 27.86±9.15 versus 22.03±11.41, but there was no significant difference (P = 0.155). Sacubitril/valsartan could improve eGFR: 29.94±11.83 versus 32.05±14.57 (P = 0.018). We also observed that, compared with control group, sacubitril/valsartan decreased albuminuria: reductions in urinary albumin:creatinine ratio (ACR) in sacubitril/valsartan group was 89.5mg/g and reductions in urinary ACR in control group was -44.55mg/g. At week 12, Sacubitril/valsartan provided a significantly greater reduction in office mean sitting (ms) systolic BP (msSBP) than control group (20.75mmHg vs 12.88mmHg, P = 0.046). There was no serious adverse events in both groups. The incidence of hyperkalemia (potassium ≥ 5.5 mmol/L) was 4.5% in SV group and 7.5% in control group.

Conclusion: The present data suggested that, in patients with stage 3b-5 CKD and hypertension, Sacubitril-valsartan could improve kidney function and decrease albuminuria, and was generally safe and well tolerated.
Figure 2: ACR and BNP of patients before and after initiating sacubitril-valsartan treatment and conventional treatment: A: BNP; B: ACR.

Table 1. Patients demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sacubitril/valsartan n = 44</th>
<th>Control n=40</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (years)</td>
<td>60.39±13.95</td>
<td>58.33±15.31</td>
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</tr>
<tr>
<td>SEX</td>
<td></td>
<td></td>
<td>0.883</td>
</tr>
<tr>
<td>Male(n,%)</td>
<td>26(44, 59.1%)</td>
<td>22(40, 55%)</td>
<td></td>
</tr>
<tr>
<td>Female(n %)</td>
<td>18(44, 40.9%)</td>
<td>18(40, 45%)</td>
<td></td>
</tr>
<tr>
<td>CAUSES OF ESKD</td>
<td></td>
<td></td>
<td>0.640</td>
</tr>
<tr>
<td>Chronic glomerulonephritis</td>
<td>9(20.5%)</td>
<td>12 (30%)</td>
<td></td>
</tr>
<tr>
<td>Diabetic kidney disease</td>
<td>6(15.6%)</td>
<td>5 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>Hypertensive nephropathy</td>
<td>3(6.8%)</td>
<td>1 (2.5%)</td>
<td></td>
</tr>
<tr>
<td>Obstructive nephropathy</td>
<td>1(2.3%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>25 (56.8%)</td>
<td>22 (55%)</td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>152.70±21.66</td>
<td>153.35±13.62</td>
<td>0.794</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>88.82±14.05</td>
<td>89.25±12.44</td>
<td>0.882</td>
</tr>
<tr>
<td>ACR (mg/L)</td>
<td>932.25(251.72-2816.15)</td>
<td>808.7(337.8-2842.28)</td>
<td>0.629</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>12.10±6.14</td>
<td>15.17±5.81</td>
<td>0.021</td>
</tr>
<tr>
<td>SCR (mg/dL)</td>
<td>216.98±102.32</td>
<td>259.23±105.89</td>
<td>0.067</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m²)</td>
<td>29.94±11.83</td>
<td>27.86±10.14</td>
<td>0.064</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>4.13±0.62</td>
<td>4.16±0.52</td>
<td>0.852</td>
</tr>
<tr>
<td>BNP (ng/L)</td>
<td>326.4(95.91-711)</td>
<td>395.6(259.05-609.53)</td>
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</tr>
<tr>
<td>ALT (u/L)</td>
<td>18.23±13.45</td>
<td>19.85±14.71</td>
<td>0.599</td>
</tr>
<tr>
<td>AST (u/L)</td>
<td>21.25±6.97</td>
<td>21.33±11.44</td>
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</tr>
<tr>
<td>CKD3b</td>
<td>20(45.5%)</td>
<td>16(40%)</td>
<td></td>
</tr>
<tr>
<td>CKD4</td>
<td>20(45.5%)</td>
<td>19(47.5%)</td>
<td></td>
</tr>
<tr>
<td>CKD5</td>
<td>4(9.1%)</td>
<td>5(13.8%)</td>
<td></td>
</tr>
<tr>
<td>Treatment-no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>23(52.3%)</td>
<td>35(87.5%)</td>
<td></td>
</tr>
<tr>
<td>Diuretic agent</td>
<td>3(6.8%)</td>
<td>2(5%)</td>
<td></td>
</tr>
<tr>
<td>Beta- blocker</td>
<td>8(18.2%)</td>
<td>11(27.5%)</td>
<td></td>
</tr>
<tr>
<td>Alpha- blocker</td>
<td>4(9%)</td>
<td>3(7.5%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Comparisons of the characteristics of patients before and after initiating sacubitril-valsartan with observation period of 3 months.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Sacubitril/valsartan n = 44</th>
<th>After Sacubitril/valsartan n = 44</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>152.70±21.66</td>
<td>131.95±16.89</td>
<td>0.000</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>88.82±14.05</td>
<td>72.72±12.80</td>
<td>0.000</td>
</tr>
<tr>
<td>ACR (mg/g)</td>
<td>932.25(251.72-2816.15)</td>
<td>787.75(154.18-2454.05)</td>
<td>0.050</td>
</tr>
<tr>
<td>BUN (mmol/L)</td>
<td>12.10±6.14</td>
<td>13.19±8.47</td>
<td>0.083</td>
</tr>
<tr>
<td>SCR (umol/L)</td>
<td>216.98±102.32</td>
<td>219.25±118.56</td>
<td>0.695</td>
</tr>
<tr>
<td>eGFR (ml/min)</td>
<td>29.94±11.83</td>
<td>32.05±14.57</td>
<td>0.018</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.13±0.62</td>
<td>4.32±0.62</td>
<td>0.018</td>
</tr>
<tr>
<td>BNP (pg/ml)</td>
<td>326.4(95.91-711)</td>
<td>223.65(89.38-503.93)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Table 3: Comparisons of the characteristics of patients before and after initiating conventional treatment with observation period of 3 months.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before n = 40</th>
<th>After n = 40</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>153.75±13.62</td>
<td>140.88±13.62</td>
<td>0.01</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>89.25±12.44</td>
<td>80.25±12.34</td>
<td>0.000</td>
</tr>
<tr>
<td>ACR</td>
<td>808.7(337.8-2842.28)</td>
<td>1248.9(438.3-2859.1)</td>
<td>0.252</td>
</tr>
<tr>
<td>BUN</td>
<td>15.17±5.81</td>
<td>16.77±7.28</td>
<td>0.139</td>
</tr>
<tr>
<td>SCR</td>
<td>259.23±105.89</td>
<td>289.65±129.50</td>
<td>0.09</td>
</tr>
<tr>
<td>eGFR</td>
<td>27.86±9.15</td>
<td>22.03±11.41</td>
<td>0.155</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.16±0.52</td>
<td>4.43±0.58</td>
<td>0.012</td>
</tr>
<tr>
<td>BNP</td>
<td>395.6(259.05-609.53)</td>
<td>287.4(146.4-663.3)</td>
<td>0.122</td>
</tr>
</tbody>
</table>

Table 4: Incidence of AEs

<table>
<thead>
<tr>
<th></th>
<th>Sacubitril/valsartan group n=44</th>
<th>Control group N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hyperkalaemia</td>
<td>2 (4.5%)</td>
<td>3 (7.5%)</td>
</tr>
<tr>
<td>Angioedema</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Deterioration of renal function</td>
<td>2 (4.5%)</td>
<td>4 (17.2%)</td>
</tr>
</tbody>
</table>
EFFECTS OF SODIUM-GLUCOSE CO-TRANSPORTER 2 INHIBITORS ON CARDIOVASCULAR MORTALITY IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: In studies of patients with chronic kidney disease (CKD), recommended nephroprotective therapy with ACE-inhibitors or ARBs has not been shown to reduce cardiovascular (CV) events or mortality. Sodium-glucose co-transporter 2 (SGLT-2) inhibitors reduce cardiovascular events and death in patients with diabetes and established CV disease; evidence from studies in populations with CKD has been inconsistent. The aim of this meta-analysis was to evaluate the effect of SGLT-2 inhibitors on cardiovascular (CV) mortality in patients with CKD.

Method: Studies were identified by search in major electronic databases (PubMed/MEDLINE, Scopus, Cochrane Library and Web of Science) (PROSPERO ID: CRD42022382863). We included randomized controlled trials assessing the effect of SGLT-2 inhibitors on the primary outcome, time to cardiovascular death, in patients with CKD at baseline. Secondary outcomes included all-cause mortality and major adverse cardiac events (MACE).

Results: Eleven studies with 83,203 participants with CKD were eligible for inclusion in the meta-analysis. Treatment with SGLT-2 inhibitors, compared to placebo, reduced the risk of CV death by 14% (hazard ratio [HR] 0.86; 95%CI 0.79-0.94), of all-cause death by 15% (HR 0.85; 95%CI 0.79-0.91) and of MACE by 13% (HR 0.87; 95%CI 0.81-0.93). A consistent treatment effect on the primary outcome was observed with all SGLT-2 inhibitors (canagliflozin: HR 0.84; 95%CI 0.69-1.02, dapagliflozin: HR 0.89; 95%CI 0.78-1.01, empagliflozin: HR 0.82; 95%CI 0.69-0.97, tofagliflozin: HR 0.90; 95%CI 0.73-1.12) studied (p-subgroup differences = 0.85). Sensitivity analysis pooling data from studies including only diabetic patients with CKD yielded similar results (HR 0.86; 95%CI 0.77-0.97).

Conclusion: Treatment with SGLT-2 inhibitors led to a significant reduction in the risk for CV and all-cause mortality in CKD patients. These findings support the use of these agents also for protection against cardiovascular events and death in CKD.

POTASSIUM LEVELS AND EGFR DO NOT PREDICT SEVERE HYPERKALEMIA FOLLOWING SPIRONOLACTONE INTRODUCTION IN PATIENTS WITH CKD AT HIGH RISK OF HYPERKALEMIA

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Background and Aims: Mineralocorticoid receptor antagonists (MRA) reduce blood pressure, albuminuria and the rate of disease progression in patients with chronic kidney disease (CKD) and albuminuria. Despite these apparent benefits, only a very small fraction of patients with CKD are treated with an MRA. This may in part be due to the fear of hyperkalemia (HK), which in the most severe cases can cause life-threatening arrhythmias. Indeed, international guidelines and previous studies have excluded patients believed to be at high risk of severe HK from treatment with MRA including patients with pre-existing high serum potassium. To examine if the risk of HK can in fact be predicted by baseline potassium levels or eGFR, we performed a clinical study testing the effect of introducing spironolactone on plasma potassium (P-K) levels in closely monitored, high-risk patients excluded from other studies. Secondly, we analyzed the effect of spironolactone on eGFR and albuminuria.

Method: We included patients with eGFR 25-60 ml/min/1.73 m² on maximal tolerated RAAS-blockade (ACEi or ARB) and a history of at least two HK-episodes (P-K > 4.5 mmol/l) within 24 months prior to inclusion. Following dietary counselling on avoidance of potassium-rich foods, spironolactone was initiated at 25 mg daily. If tolerated as defined by a decline in eGFR < 30%, a P-K ≤ 5.5 mmol/l and the absence of severe hypotension, the dose was increased to 50 mg after two weeks. Total follow-up was four weeks measuring P-K, eGFR, blood pressure and spot urine albumin creatinine ratio. Results from maximal tolerated dose were compared to baseline using paired t-test. In a post-hoc analysis, patients were grouped based on the occurrence of severe HK (P-K > 5.5 mmol/l) or not, and baseline characteristics and the change from baseline to maximal dose were compared using unpaired t-test. Linear regression model was used to test the association between baseline P-K vs. P-K at maximal dose of spironolactone and the change in P-K from baseline to maximal dose of spironolactone vs. baseline eGFR.

Results: Fifty-eight patients were included with a mean age of 65 years. Forty-seven were males and 23 had diabetes. Forty-eight patients reached a spironolactone dose of 50 mg. Following spironolactone introduction, mean eGFR declined from 39 at baseline to 34 ml/min/1.73 m² (p < 0.001) and albuminuria was reduced from a median of 1276 mg/g to 654 mg/g (49%; 95% CI: 44 – 54%) with no significant change in blood pressure. Mean P-K increased 0.5 mmol/l (95% CI 0.3 – 0.7 mmol/l) from 4.70 vs 4.67 mmol/L (p = 0.83 and 36.2 vs. 40.1 ml/min/1.73 m², p = 0.13). Furthermore, baseline P-K did not correlate with P-K at maximum spironolactone dose (Figure 1) and the change in P-K did not significantly correlate with baseline eGFR (Figure 2).

Conclusion: Short-term treatment with spironolactone in patients with CKD at high risk of HK leads to similar reductions in albuminuria and eGFR when compared with low-risk cohorts. With dietary counseling, 30% of patients will develop severe HK within 4 weeks. Importantly and contrary to common belief, neither baseline P-K levels nor baseline eGFR were associated with the development of severe HK. Thus, excluding patients from MRA treatment based solely on eGFR and P-K levels is not appropriate. Instead, we believe an empirical approach based on dietary counseling and close monitoring of P-K should be used.
Figure 1: Scatterplot of P-K at maximal dose of spironolactone vs. baseline. Best fitted line is plotted. $R^2$ and $P$-values are from linear regression model.

Figure 2: Scatterplot of the change in P-K from baseline to maximal dose of spironolactone vs. baseline eGFR. Best fitted line is plotted. $R^2$ and $P$-values are from linear regression model.
PATIENT ACTIVATION STATUS AND PATIENT PERCEIVED FUNCTION IMPAIRMENT IN CKD: A ROUTE TO OPTIMISING LIFE PARTICIPATION THROUGH ENHANCED SELF-MANAGEMENT?

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Background and Aims: Chronic kidney disease (CKD), even at earlier stages where kidney replacement therapy is not required, is associated with significant health and symptom burdens which negatively impact on an individual’s functional status and ability to fully engage with work, leisure, and social activities. Life participation can be maximized with optimal day-to-day management of CKD. A strong partnership between the healthcare team and patient is required to support effective self-management. Central to this partnership is patient activation, defined as the knowledge, skills, and confidence to manage one’s own health. Individuals who are highly activated take an active role in their health, whilst those with low activated have a more passive role. Higher activation is associated with better clinical outcomes. As part of a wider survey in people living with non-dialysis CKD (ND-CKD), we explored the relationship between patient activation and perceived functional impairment as a result of CKD.

Method: 14 hospital sites across England invited patients with ND-CKD to complete a survey on health and lifestyle factors including demographic and clinical information, the SF-12 health-related quality of life (QoL) questionnaire, Chalder Fatigue Scale, Patient Activation Measure (PAM-13), and Work and Social Adjustment Scale (WSAS). Participants were classified as having ‘low’ or ‘high’ activation based on their PAM-13 level (Levels 1&2 ‘low’; 3&4 ‘high’). Higher WSAS scores indicated greater perceived functional impairment due to CKD. To compare perceived impairment in WSAS domains between low and high activated participants, Mann-Whitney tests was conducted. To determine the relationship between participant characteristics (i.e., age, gender, ethnicity, eGFR, patient activation, fatigue, physical and mental QoL) and WSAS score, linear regression was performed.

Results: 828 ND-CKD patients completed the survey [mean age 67.9 (±13.8) years, 60% (n = 501) male, 92% White British (n = 771), eGFR 33.1 (±19.7) ml/min/1.73m², total number of additional comorbidities 2.0 (±1.5)], 64% (n = 529) of participants were classified as having ‘low’ activation. The mean WSAS score was 7.8 (±9.9) indicating mild functional impairment. Both high and low PAM groups perceived social and leisure activities (with other people e.g., outings/dating/parties) to be their most impaired functional activities, and close relationships with others as least impaired. Low activated participants perceived greater impairment on work (P = 0.035), home management (P <0.001), other social activities (P =0.001), leisure activities (P =0.001) and close relationships (P = <0.001) as a result of their CKD compared to those with higher activation. Individuals who perceived greater functional impairments were younger (P <0.001), had lower levels of activation (P = 0.036), poorer physical (P <0.001) and mental (P = 0.043) QoL, and greater levels of fatigue (P = 0.001).

Conclusion: People with lower patient activation perceived greater functional impairment to work, leisure, and social activities as a result of their CKD. Younger people may have greater expectations as to what they can functionally achieve and the marked impact in comparison to their peers without CKD may be greater and more prominent. Conversely, older individuals may be more likely to attribute functional impairments to other age-associated comorbidities or to the effects of aging itself than to CKD. Interventions designed to increase patient activation and improve psychosocial adjustment have the potential to help individuals manage their CKD and reduce the perceived impairment on life participation.

USE OF SUPERVISED DEEP LEARNING ALGORITHM TO PREDICT RISK OF RENAL REPLACEMENT THERAPY (RRT) IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD)

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Background and Aims: Chronic kidney disease (CKD) is one of the most common causes of mortality, affecting around 10% adults worldwide [1]. Although statistical models for predicting risk of renal replacement therapy (RRT) have been developed for a decade [2], referral of patients with CKD to nephrology service is often based on clinical experience of primary care physicians. The use of deep learning algorithms (DLAs) allow clinicians to capture complex, multidimensional, non-linear relationships instead of relying on linear relationships between independent variables and outcome. Our study aims to develop a DLA that has at least non-inferior performance compared to the Kidney Failure Risk Equation (KFRE), which is a well-established and validated risk prediction tool [3].

Method: This is a retrospective cohort study carried out in 3 acute hospitals in Hong Kong providing a total of 3000 beds from Jan 1, 2009 to Mar 31, 2022. All patients aged > 18 with an estimated glomerular filtration rate (eGFR) <30 ml/min/1.73 m² according to the CKD-EPI formula, who attended follow-up for at least 3 months in nephrology clinic of the 3 hospitals, were recruited. Those who were on chronic RRT, received renal transplantation or had an eGFR<15 ml/min/1.73 m² before referral were excluded. Supervised DLAs of different structures and their combinations were created and trained. Data in the test set were fed into models to predict the risk of requiring RRT in 2 years and 5 years. Predictive performance of these models were compared with that of KFRE [3].

Results: 4992 patients were recruited in the study. Data of 499 patients were isolated as test set and were not used for model training. 1576 patients progressed to stage 5 CKD during their follow-up, and 989 patients required initiation of RRT during the study timeframe. When compared with KFRE (4-variable: ROC-AUC = 0.84, 95%CI:0.835-0.852; 8-variable: ROC-AUC = 0.84, 95%CI:0.830-0.847), almost all DLAs showed statistically significant superior robustness in predicting the risk of requiring RRT (Figure 1). No significant difference was found between performance of DLAs combining different neural network layers and those with single structures (CNN+LSTM+ANN layers ROC-AUC = 0.90, 95%CI:0.896-0.902; CNN ROC-AUC = 0.91, 95%CI:0.907-0.914) (Table 1).

Conclusion: The use of DLAs provided better prediction in the risk of requiring RRT when compared with KFRE.
Table 1: Evaluation of DLAs and KFRE.

<table>
<thead>
<tr>
<th>Method</th>
<th>ROC AUC</th>
<th>F1 score</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNN</td>
<td>0.91 (0.907 - 0.914)</td>
<td>0.79 (0.781 - 0.795)</td>
<td>0.47 (0.465 - 0.474)</td>
<td>0.97 (0.973 - 0.975)</td>
<td>0.9 (0.895 - 0.906)</td>
<td>0.79 (0.784 - 0.787)</td>
</tr>
<tr>
<td>CNN + LSTM + ANN</td>
<td>0.90 (0.896 - 0.902)</td>
<td>0.76 (0.758 - 0.769)</td>
<td>0.74 (0.733 - 0.744)</td>
<td>0.88 (0.879 - 0.885)</td>
<td>0.76 (0.752 - 0.764)</td>
<td>0.87 (0.868 - 0.874)</td>
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<tr>
<td>ANN</td>
<td>0.88 (0.876 - 0.882)</td>
<td>0.76 (0.756 - 0.767)</td>
<td>0.71 (0.706 - 0.719)</td>
<td>0.87 (0.870 - 0.876)</td>
<td>0.74 (0.732 - 0.743)</td>
<td>0.86 (0.856 - 0.862)</td>
</tr>
<tr>
<td>ConvLSTM + ANN</td>
<td>0.88 (0.875 - 0.881)</td>
<td>0.76 (0.755 - 0.763)</td>
<td>0.71 (0.707 - 0.715)</td>
<td>0.87 (0.870 - 0.874)</td>
<td>0.73 (0.732 - 0.740)</td>
<td>0.86 (0.856 - 0.860)</td>
</tr>
<tr>
<td>LSTM</td>
<td>0.85 (0.844 - 0.852)</td>
<td>0.68 (0.673 - 0.684)</td>
<td>0.50 (0.493 - 0.505)</td>
<td>0.88 (0.875 - 0.881)</td>
<td>0.67 (0.664 - 0.679)</td>
<td>0.78 (0.776 - 0.781)</td>
</tr>
<tr>
<td>KFRE (4 variable)</td>
<td>0.84 (0.835 - 0.852)</td>
<td>0.32 (0.313 - 0.319)</td>
<td>0.40 (0.395 - 0.405)</td>
<td>0.75 (0.747 - 0.754)</td>
<td>0.42 (0.410 - 0.429)</td>
<td>0.88 (0.870 - 0.882)</td>
</tr>
<tr>
<td>KFRE (8 variable)</td>
<td>0.84 (0.830 - 0.847)</td>
<td>0.40 (0.394 - 0.406)</td>
<td>0.40 (0.395 - 0.405)</td>
<td>0.75 (0.747 - 0.754)</td>
<td>0.42 (0.410 - 0.429)</td>
<td>0.88 (0.870 - 0.882)</td>
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Figure 1: ROC curve of different DLAs and KFRE.

#3659
KIDNEY FAILURE MANAGEMENT IN THE ELDERLY: A PRELIMINARY SURVIVAL ANALYSIS
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Background and Aims: Dialysis treatment (DT) is the most common approach for patients with kidney failure. However, this may not be optimal for geriatric individuals, as more than half of elderly patients who initiate DT die within the first year. As a result, current guidelines advocate for presenting comprehensive conservative management (CM) as an alternative option for vulnerable patients and their families. A recent meta-analysis (2022) revealed that DT had a median survival time of 20-67 months, compared to 6-31
months for CM, indicating that individuals who opt for DT may have higher survival benefits. This distinction, however, disappears in +80 y/o patients, suggesting that both therapies may yield similar outcomes in this population.

The efficacy of CM, however, remains poorly recognized due to the difficulty in comparing the treatments and the heterogeneous nature of the studies conducted. Therefore, our study aimed to investigate and compare the survival of the elderly who elected to undergo either conservative therapy or dialysis.

**Method:** We present a preliminary analysis of a prospective observational study conducted across 3 Nephrology Units (Veneto, Italy). We enrolled 117 patients in the pre-dialysis or CM clinics, meeting the eligibility criteria: ≥75 y/o, eGFR >15 ml/min/1.73 m² (CKD-EPI formula), and had not already undergone DT or CM (personalized pharmacological therapy combined with a low-protein diet). At baseline, socio-demographic information, patient comorbidities, and blood and urine tests were collected through medical records and interviews. Additionally, the SF-36 questionnaire, the Barthel questionnaire, and the Mini-Mental State Examination assessed the quality of life, functional status, and global cognitive functioning.

Survival was evaluated at 3 and 9 months after follow-up initiation, defined as the date of the first dialysis session or when the eGFR dropped below 15 ml/min/1.73 m² (CKD-EPI formula), and had not already undergone DT or CM (personalized pharmacological therapy combined with a low-protein diet). At baseline, socio-demographic information, patient comorbidities, and blood and urine tests were collected through medical records and interviews. Additionally, the SF-36 questionnaire, the Barthel questionnaire, and the Mini-Mental State Examination assessed the quality of life, functional status, and global cognitive functioning. Survival was evaluated at 3 and 9 months after follow-up initiation, defined as the date of the first dialysis session or when the eGFR dropped below 10 ml/min/1.73 m² in CM patients. The follow-up ended when patients reached the 9th month, died from any cause, switched treatments, discontinued medical follow-up, dropped out of the study voluntarily, or at the end of the project. To determine if any across-group differences existed at the baseline, non-parametric tests were used for continuous variables and the chi-square test for categorical variables. Kaplan-Meier curve, Log Rank Test and Cox regression were performed for survival analysis.

**Results:** Of the 117 enrolled patients, 64 initiated the follow-up, 47 (59.6% M) in CM, and 17 (64.7% M) in DT. The patients in CM were older than those in DT (p = 0.028), with a median age of 82.5 (75.4-91.7) compared to 78.9 (75.6-87.9). At baseline, there were other statistically significant differences (p < 0.05) in median levels of BUN, creatinine, PTH, haemoglobin, and total cholesterol.

Comorbidities were similar in both groups. During the follow-up, 11 patients died (17.2%), 10 in CM (21.3%) and 1 in DT (5.9%). One patient in CM had an unavailable death date and was, therefore, excluded from further analysis. Kaplan-Meier curves and Log Rank Test revealed no significant difference in survival (p = 0.25). The median survival time was undefined, as over 50% of subjects in both groups did not experience the event during follow-up. In CM, unadjusted survival rates at 3 and 9 months were 91.3% and 78.2%, respectively. The effect of the therapies resulted in not significant after adjusting for important prognostic covariates.

**Conclusion:** In this study, we found that middle-term survival in the elderly is comparable to DT and CM. Despite limitations, these results provide valuable information for clinical decision-making. Our results suggest that well-organized CM can be a reasonable option for elderly patients with kidney failure.

#4063

**APELIN INCREASES FOREARM BLOOD FLOW IN CHRONIC KIDNEY DISEASE**

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**Background and Aims:** Chronic kidney disease (CKD) affects 1 in 10 people and cardiovascular disease is its commonest complication. Despite current standard of care, many patients continue to progress to kidney failure and/or die of cardiovascular disease. Thus, there is an urgent unmet need for new treatments that slow kidney function decline and offer broad cardiovascular protection. The apelin system, comprising the apelin receptor and its two endogenous ligands apelin and elabela, is an attractive therapeutic target for CKD. Apelin is an endothelium-dependent vasodilator and a potent inotrope. Clinical studies show that apelin improves endothelial function in health and heart failure, and pre-clinical studies in models of kidney disease find apelin offers renoprotection. At present, apelin has not been studied in patients with CKD. The aims of this study were to examine the local vascular actions of apelin in CKD.

**Method:** Participants with stable, non-diabetic CKD and age- and sex-matched healthy volunteers were recruited to a prospective, randomised, placebo-controlled study. Blood pressure and arterial stiffness (measured using pulse wave velocity) were assessed at baseline. Endothelial function was examined using gold-standard venous occlusion plethysmography. Forearm vasodilation was measured in response to incremental intra-arterial doses of acetylcholine (7.5, 15 and 30 μg/min, used to assess endothelium-dependent vasodilatation), sodium nitroprusside (1, 2 and 4 μg/min, used to assess endothelium-independent vasodilatation), and pyroglutamated apelin-13 ([Pyr¹]apelin-13; 0.3, 1, 3, 10, 30 and 100 nmol/min). Circulating tissue plasmogen activator (tPA) and plasmogen activator inhibitor-1 (PAI-1) were assessed as measures of endogenous fibrinolysis.

**Results:** Fifteen patients with CKD (mean age 55±4 years; 53% male) and 15 healthy volunteers (mean age 51±3 years; 67% male) completed the study. In comparison to healthy volunteers, patients with CKD had a higher blood pressure (mean arterial pressure: 102 mmHg versus 93 mmHg, p < 0.05) and increased pulse wave velocity (7.5±2.2 m/s versus 6.0±0.9 m/s, p < 0.01). Similar dose-dependent vasodilatation to acetylcholine and sodium nitroprusside was seen in both groups. [Pyr¹]apelin-13 increased forearm blood flow by a maximum of ~30% in both health and CKD (p < 0.01 compared to baseline for both) (Figure 1). This response appeared to be dose-dependent. Net tPA antigen release increased 20-70 fold in response to [Pyr¹]apelin-13 in both health and CKD, with a trend to a greater release in CKD. There

**Figure 1:** Kaplan-Meier curve showing the estimated survival probability of patients following DT and CM during the 9-month follow-up.
was no change in PAI-1. No relationship was seen between the response to [Pyr1]apelin-13 and kidney function.

**Conclusion:** Apelin promotes vasodilatation in optimally managed patients with CKD and may regulate endogenous fibrinolysis. If this effect were maintained in the long-term with systemic apelin treatment, it would be expected to reduce cardiovascular risk. Systemic studies are now justified to investigate the haemodynamic and renal effects of apelin in these patients.

**#5621**

**BENEFICIAL EFFECTS OF CHRONIC INTRADIALYTIC EXERCISE TRAINING ON HEMODIALYSIS-INDUCED-MYOCARDIAL STUNNING**

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1 Avignon University, UPR4278, Laboratoire de physiologie expérimentale cardiovasculaire, Avignon, France, 2 Fondation Charles Mion – AIDER Santé, France, 3 Grabels, France, 4 CHU Nîmes, France, Nîmes, France, 5 ATIR Avignon, France, Avignon, France, 6 CHRU Montpellier, Montpellier, France and 7 University of Limoges, Laboratory HAVAEEA-6310, Limoges, France

**Background and Aims:** Hemodialysis (HD) induces left ventricular (LV) segmental regional wall motion abnormalities (RWMAs) due to hypoperfusion, leading to acute LV transient dysfunction, well known as myocardial stunning. Repeated episodes of HD-related myocardial stunning contribute directly to the development of heart failure and increased mortality in patients receiving HD (Burton et al., 2009). Exercise training exert pleiotropic favorable effects on the cardiovascular system. No study has however investigated its impact on the kinetics of regional myocardial function during HD. This study aims to evaluate the effect of intradialytic exercise (IDE) on RWMAs compared with standard care.

**Method:** This was a prospective, open-label, two-center trial (clinicaltrials.gov NCT04697459) with two parallel groups: 31 patients (ENT) undergoing a 4-month IDE program (30min of cycling + 30min of resistance training starting 30 min after HD onset) and 21 patients continuing usual care (CTRL). Untrained adults, aged 20-79 years, undertaking maintenance HD for >3 months were eligible to participate. Exclusion criteria were poor echogenicity, contraindication to exercise, orthopedic complications, severe heart (ischemic, valvular, ...), vascular or respiratory diseases, ejection fraction <45% and body mass index >35. Longitudinal strain (LS) using speckle-tracking echocardiography were measured during a standard HD session, just before HD onset (HD_{T0}) and at peak stress of HD (30 min before HD-ending, HD_{Peak}). The same procedure was used before and after 4-months of IDE or usual care. LS from a 18 LV segment model were used to assess the presence of HD-induced RWMAs, defined as ≥20% reduction in LS at peak stress compared to baseline. A generalized linear mixed model (Poisson model) was used to analyze the effect of IDE on RWMAs.

**Results:** After 4 months of IDE, we observed a significant reduction of RWMAs at HD_{Peak} (mean before: 6.09±3.16; point estimate: -0.05, 95% CI: -1.45/-1.54, p = 0.06). There was also evidence that IDE program significantly attenuated the decline of global LS observed during HD (mean before: 20.21±3.19 vs after: 4.55±2.26; point estimate: -1.48, 95% confident interval CI: -0.39/-2.57, p = 0.03), whereas its occurrence remained unchanged in CTRL (mean before: 6.14±3.51 vs after: 6.09±3.16; point estimate: -0.05, 95% CI: 1.45/-1.54, p = 0.96). There was also evidence that IDE program significantly attenuated the decline of global LS observed during HD (mean before: 2.11±2.39% vs after: 1.10±1.95%; point estimate: -1.01%, 95% CI: -1.86/-0.13, p = 0.02) compared to the similar impairment in CTRL (before: 1.60±2.30% vs after: 1.79±2.08%; point estimate: +0.18%, 95% CI: +1.20/-0.85 p = 0.72).

**Conclusion:** There is clear evidence that chronic IDE is cardioprotective. Identifying the underlying mechanisms responsible for exercise-induced cardioprotection was beyond the scope of our study, but we can reasonably assume that structural and/or functional changes in the coronary arteries, especially in microcirculatory territories (i.e. increased collateral circulation due to angiogenesis/arteriogenesis, improved endothelial function, reduced blood viscosity) and/or intrinsic changes in the cardiac myocyte (reduced fibrosis, enhanced calcium handling/sensitivity, altered mitochondrial turnover and phenotype), related among others to reduced oxidative stress and/or inflammation, might play a role (Powers et al 2014). Whether our results translate to longer-term reduction in clinical outcomes and cardiovascular mortality in end-stage renal disease patients require further studies.
SCREENING AND DIAGNOSIS STRATEGY FOR FABRY DISEASE IN TAIWANESE PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background and Aims: Fabry disease (FD) is not uncommon in patients with chronic kidney disease (CKD) who are on dialysis or have stroke at a young age, left ventricular hypertrophy (LVH) or hypertrophic obstructive cardiomyopathy (HOCM). However, FD is easily overlooked by physicians due to the heterogeneity of clinical manifestations. Therefore, an expert consensus meeting was held to establish a screening algorithm for FD in patients with CKD.

Method: The first meeting was held in Taiwan in August 2022. The screening criteria for FD with respect to age, sex, family history, cardiac involvement and signs and symptoms were discussed. The findings of meeting and the consensus opinion of the expert group were summarized.

Results: The screening algorithm was shown in Figure 1. It is recommended to screen for FD regardless of age. Screening for FD is recommended for CKD patients with family history of FD, stroke at young age (<55 years) or typical signs and symptoms including angiokeratoma, hypohidrosis, neuropathic pain, heat/cold and exercise intolerance, hearing loss and cornea verticillata. If CKD patients have one of the cardiac symptoms including dyspnea, palpitation and chest pain, it is recommended to check the cardiac-related red flags including LVH and HOCM using echocardiogram, short PQ interval, atrioventricular block and prolonged QRS interval using electrocardiogram, and low native T1 and posterolateral late gadolinium enhancement using magnetic resonance imaging. If cardiac-related red flags are present, screening for FD is recommended. Screening can also be performed in patients with CKD who do not have any typical symptoms but have a high suspicion of FD. In males, screening can be performed by measuring α-galactosidase A enzyme activity. If the enzyme activity is reduced or absent, assessment of globotriaosylsphingosine (lyso-Gb3) levels in plasma and genetic analysis are recommended. In female, assessment of lyso-Gb3 levels in plasma and genetic analysis are recommended.

Conclusion: FD is an underrecognized and not so rare disease. Physicians should maintain a skeptical attitude in clinical practice in order to make diagnosis in time and help patients and their entire families avoid life-threatening diseases at a young age. There are still more issues to be addressed, including whether to inform patients of the screening results, how to interact and communicate with patients, etc.

Figure 1: Proposed flowchart for diagnosis of Fabry disease in patients with chronic kidney disease. HOCM, hypertrophic obstructive cardiomyopathy; lyso-Gb3, globotriaosylsphingosine; LVH, left ventricular hypertrophy.
C3 GLOMERULOPATHY CURRENT THERAPY AND REAL-WORLD MANAGEMENT - INTERIM RESULTS FROM A MULTI-COUNTRY STUDY

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Background and Aims: C3 glomerulopathy (C3G) is a rare form of glomerulonephritis, with an estimated incidence of 1–2 per million per year. C3G is associated with a high risk of disease progression with approximately 50% of patients reaching kidney failure within 10 years of diagnosis. No treatments have been proven effective through randomized controlled trials. KDIGO glomerular disease guidelines recommend treating with renin-angiotensin-aldosterone system inhibitors (RAASi) to reduce blood pressure and proteinuria, and, in select patients, utilization of immunosuppressants such as mycophenolate mofetil and corticosteroids. Newer agents, such as eculizumab, are also sometimes used off-label. The aim of this analysis was to better understand the current management of C3G in the US, Europe, and Asia.

Method: An analysis was conducted using interim data from the Adelphi C3G Disease Specific Programme (DSP), a cross-sectional survey of C3G-treated nephrologists in US, EU5 (France, Germany, Italy, Spain, UK), China and Japan (study ongoing since August 2022; interim analysis based on data until November). Nephrologists completed structured forms administered via online links for consecutive patients presenting with C3G. Forms included information on current and most recent therapy.

Results: In this interim analysis, 88 nephrologists had completed records for 277 patients, including 95 in US, 120 in EU5, 39 in China and 23 in Japan. Median patient age at time of the survey was 44, and 60% were male. 80% had C3 glomerulonephritis (C3GN) and 19% had dense deposit disease (DDD). At the time of the survey, 82% out of 277 patients were receiving treatment. The majority (69%) of 228 treated patients were receiving RAASi, 27% were receiving mycophenolate mofetil/mycophenolate sodium, 48% corticosteroids, and biologics were used in almost a third of patients. At the time of the survey, mean proteinuria was 2.1 g/day, with 60% of patients having proteinuria ≥ 1 g/day (Table 1).

Conclusion: C3G is a rapidly progressing glomerulonephritis for which there is no approved therapy. Most patients in this real-world study were receiving treatment, with both conventional immunosuppressants and biologics frequently added to RAASi. Despite this, proteinuria remained high, with the majority of patients having proteinuria ≥ 1 g/day. This highlights the need for novel therapies to actively treat C3G.

Table 1: Current therapy and proteinuria levels by region.

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>US</th>
<th>EU5</th>
<th>China</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base (All patients)</td>
<td>n = 277</td>
<td>n = 95</td>
<td>n = 120</td>
<td>n = 39</td>
<td>n = 23</td>
</tr>
<tr>
<td>Currently on therapy</td>
<td>228 (82%)</td>
<td>75 (79%)</td>
<td>98 (82%)</td>
<td>37 (95%)</td>
<td>18 (78%)</td>
</tr>
<tr>
<td>No, but have been in the past</td>
<td>26 (9%)</td>
<td>10 (11%)</td>
<td>13 (11%)</td>
<td>0 (0%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Never received any therapy</td>
<td>23 (8%)</td>
<td>10 (11%)</td>
<td>9 (8%)</td>
<td>2 (5%)</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Current treatment</td>
<td>n = 228</td>
<td>n = 75</td>
<td>n = 98</td>
<td>n = 37</td>
<td>n = 18</td>
</tr>
<tr>
<td>ACEi and/or ARB</td>
<td>158 (69%)</td>
<td>45 (60%)</td>
<td>72 (73%)</td>
<td>28 (76%)</td>
<td>13 (72%)</td>
</tr>
<tr>
<td>ARB</td>
<td>85 (37%)</td>
<td>20 (27%)</td>
<td>30 (31%)</td>
<td>22 (59%)</td>
<td>13 (72%)</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>78 (34%)</td>
<td>25 (33%)</td>
<td>45 (46%)</td>
<td>8 (22%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Immunosuppressant</td>
<td>174 (76%)</td>
<td>63 (84%)</td>
<td>76 (78%)</td>
<td>27 (73%)</td>
<td>8 (44%)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>109 (48%)</td>
<td>35 (47%)</td>
<td>43 (44%)</td>
<td>23 (62%)</td>
<td>8 (44%)</td>
</tr>
<tr>
<td>Non-steroidal immunosuppressants</td>
<td>75 (33%)</td>
<td>23 (31%)</td>
<td>41 (42%)</td>
<td>8 (22%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>Mycophenolate mofetil/ mycophenolate sodium</td>
<td>61 (27%)</td>
<td>21 (28%)</td>
<td>34 (35%)</td>
<td>3 (8%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>Biologics</td>
<td>71 (31%)</td>
<td>29 (39%)</td>
<td>31 (32%)</td>
<td>11 (30%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Eculizumab</td>
<td>40 (18%)</td>
<td>13 (17%)</td>
<td>22 (22%)</td>
<td>5 (14%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Proteinuria at time of survey</td>
<td>n = 235</td>
<td>n = 66</td>
<td>n = 110</td>
<td>n = 36</td>
<td>n = 23</td>
</tr>
<tr>
<td>≥ 1 g/24hr</td>
<td>141 (60%)</td>
<td>43 (65%)</td>
<td>65 (59%)</td>
<td>25 (69%)</td>
<td>8 (35%)</td>
</tr>
<tr>
<td>Mean</td>
<td>2.1</td>
<td>1.9</td>
<td>2.1</td>
<td>3.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>2.8</td>
<td>2.3</td>
<td>2.8</td>
<td>4</td>
<td>0.9</td>
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</tbody>
</table>
REAL WORLD EVALUATION OF SGLT2 INHIBITORS IN PATIENTS WITH DIABETIC NEPHROPATHY AND HEART FAILURE: THE EFFECT ON THE DIASTOLIC DYSFUNCTION

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Background and Aims: In patients with diabetes mellitus and diabetic nephropathy, a high incidence of left ventricular diastolic dysfunction has been reported by various studies. The objective of this study was to the real world evaluation of the impact of sodium glucose cotransporter type 2 (SGLT2) inhibitors on left ventricular (LV) diastolic function of type 2 diabetes mellitus (T2DM) patients with diabetic nephropathy and heart failure (HF).

Method: We studied patients with Diabetes Mellitus type 2, diabetic nephropathy (eGFR > 30 ml/min/1.73 m²) and stable (at least for 3 months) Heart Failure with reduced ejection fraction. We excluded patients treated with SGLT2 before the study initiation. Laboratory and Echocardiographic studies (Left Ventricular Ejection Fraction LVEF%, the ratio (E/A), Early diastolic velocity (Em), LV mass index (LVMI)), were performed in all patients at baseline and after 12 months of treatment with dapagliflozin 10 mg/day.

Results: 67 patients were included (38/29 M/F, age 68 ± 14.2 years), with eGFR 72.5 ± 9.2 ml/min/1.72 m²) at baseline. Mean duration of diabetes was 14.2 ± 7.9 years, and mean HbA1c was 7.9 ± 1.1%. There was a significant increase of LVEF (38.5 ± 8.1% to 43.7 ± 7.4%; p = 0.02). LV Mass Index was decreased from 78 g/m² to 67 g/m² (p = 0.01) and there was a significant decrease in E/e′ (11.8 to 9.6 cm/s (p = 0.01). Urinary albumin excretion rate at baseline was 526 ± 233 mg/24H and there was a reduction of 32% at the end of the follow up. Multiple regression analysis showed that reduction in albuminuria was an independent predictive factor for E/e′ changes.

Conclusion: Data from this study showed LV diastolic function as assessed in terms of E/e′ and LVMI had significantly improved 12 months after the initiation of dapagliflozin. Reduction of albuminuria by SGLT2i, is an independent predictive factor for improvement of LV function.

A NETWORK META-ANALYSIS COMPARING INTENSIVE GLYCEMIC CONTROL AND SGLT-2 INHIBITORS IN PREVENTING RENAL OUTCOMES

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Background and Aims: Type 2 diabetes (T2D) is one of the prominent causes for chronic kidney disease (CKD) leading to end-stage renal failure. Traditionally, prevention and retardation of CKD was attempted with effective glycemic and blood pressure control. In recent times sodium glucose co-transporter 2 inhibitors (SGLT-2is), glucagon-like peptide 1 receptor agonists (GLP1-RA), and non-steroidal mineralocorticoid receptor (MRA) inhibitors have proved to be excellent agents in preventing cardio-renal outcomes in patients with T2D, independent of baseline glucose control. SGLT-2is rank the highest in recent network meta-analysis-based scoring. We conducted this network meta-analysis to explore the ranking of intensive glucose therapy in comparison to SGLT-2is, to better understand the present position of the traditional approach and its relevance.

Method: A database search was conducted using the Cochrane library to identify relevant citations. Analysis was conducted using RStudio (2022.07.1, Build 554). Using progression of macroalbuminuria and end-stage kidney disease (ESKD) as the outcomes of interest, scoring was performed comparing intensive glycemic control (IGC) and SGLT-2is. Using a frequentist approach P-score was conducted and corroborated using the Surface Under the Cumulative Ranking (SUCRA) using Bayesian network meta-analysis.

Results: A pooled population of 62,742 patients from twelve citations were included for analysis. The Cochrane risk of bias was used to assess quality of the studies. IGC scored higher than SGLT-2ias as far as retardation of progression of macroalbuminuria was concerned while using both the P-score (0.99 Vs 0.50) as well as the SUCRA (0.97 Vs 0.52). A similar trend was also observed with ESRD as the end point with both the P-score (0.84 Vs 0.65) and the SUCRA (0.81 Vs 0.68) rankings favoring IGC (Fig. 1).

Conclusion: The importance of achieving glycemic targets should be emphasized in recommendations in the same footing as the choice of individual reno-protective agents.
Background and Aims: ADPKD is the most prevalent genetic kidney disease. Tolvaptan is the first proven disease-modifying therapy, but is associated with aquaretic side effects, frequently leading to treatment discontinuation. Therefore, identifying factors, which can ameliorate the aquaretic side effects and facilitate therapy is crucial. Previous data reported 24-h-osmolar excretion in urine or GFR as the main determinants of urine volume on tolvaptan but included only few patients. This study’s objective was to prospectively examine the 24-hour urine volume and urine osmolality during the up-dosing phase of tolvaptan in a cohort with a moderate sample size and different subgroups in order to identify modifiable and non-modifiable factors for urine volume increase. Finally, quality of life (QoL) during tolvaptan treatment was investigated in relation to urine volume since these data are scarce thus far and provide crucial insights into the therapy burden.

Method: Analysis of 24-h urine collection at baseline and at least once on tolvaptan was carried out for 75 patients (complete cohort). For 35 patients (longitudinal cohort) urine collections were available for baseline and all three tolvaptan doses (45/15 mg, 60/30 mg and 90/30 mg). All patients are participants of the German AD(H)PKD registry. Sodium, protein and potassium intake were calculated from excretion in 24h-urine and QoL was assessed by the Short Form-12 (SF-12) questionnaire. Statistical analyses were computed using R statistical software. A p-value of ≤ 0.05 was regarded as significant.

Results: The mean age of the patients in the complete cohort was 41.3 ± 10.7 (range 18-64 years) with a mean eGFR of 67.3 ± 27.2 ml/min/1.73m² and was similar to the longitudinal cohort with a mean age of 41.8 ± 10.1 (23-64 years) and eGFR of 69.4 ± 27.5ml/min/1.73m². A significant increase (p< 0.0001) in 24-hour urine volume (138%) occurred only immediately after therapy initiation with no further significant increase during up-dosing in the complete and longitudinal cohort. In line with this 24-hour osmolality decreased (57%) significantly (p< 0.0001) only after beginning of treatment and remained almost unchanged after up-dosing. Total solutes, protein and sodium intake showed non-significant changes across all doses. There were no significant differences in urine volume between gender, age classes (<45 vs. >45 years), or Mayo class when examining the various subgroups. Considering modifiable factors, 24-hour urine volume was positively correlated with eGFR on tolvaptan reaching significance on 45/15 mg (p = 0.013) and 90/30 mg (p = 0.027). Patients <45 years and patients with an eGFR ≥ 60 ml/min/1.73m² experienced a significantly higher relative urine volume increase at the beginning (p = 0.0332 vs. ≥45 years and p = 0.0097 vs eGFR < 60 ml/min/1.73m²) in the complete cohort. In multivariable linear regression analyses containing modifiable and non-modifiable covariates only sodium intake had a significant impact in tolvaptan-naive patients (p = 0.0064), while on tolvaptan age (p = 0.008) and weight (p = 0.0190) became significant together with sodium intake (p = 0.008) and potassium intake (p = 0.0040). Across the three tolvaptan doses no significant differences between the number of patients reaching pre-defined osmolality goals (< 250 mosmol/kg for spontaneous urine and < 150 mosmol/kg for 24-hour) could be detected. Before and after tolvaptan treatment, neither the mental nor physical QoL changed significantly.

Conclusion: Our study showed that the significant rise in urine volume occurs immediately after therapy initiation with only minor and non-significant increases upon further up-dosing. Urine osmolality decreases significantly directly after start of tolvaptan and remains constant with most patients achieving adequate suppression of urine osmolality. Patient counseling should consider that younger patients and patients with better eGFR might experience stronger urine volume increase at the beginning and advising to reduce salt and potassium intake can ameliorate aquaretic side effects. Tolvaptan treatment showed no negative impact on QoL but further investigations in larger cohorts are needed.
MAINTAINING PHYSICAL ACTIVITY IN PATIENTS THROUGH INTRADIALYTIC VIRTUAL REALITY EXERCISE INTERVENTION: THE REVID STUDY

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Background and Aims: People suffering from Chronic kidney disease (CKD) have lower levels of physical activity than their healthy counterparts. The lower level of physical activity is associated with impaired physical function in people undertaking hemodialysis. The COVID-19 pandemic has worsened the physical activity level of this cohort. Intradialysis exercise programs have a positive impact on many functional variables, but despite these proven benefits exercise interventions are scarce in clinical practice. Our group is implementing strategies to increase clinical applicability of exercise programs. Virtual reality (VR) intradialysis programs improve function of patients. The main aim of this study was to analyze the impact of an intradialytic non-immersive VR exercise program on physical activity level of people undertaking hemodialysis treatment.

Methods: A randomized trial (the REVID study) included two groups of patients, exercising at different times during the dialysis session for up to 12 months. The present study includes participants from the REVID study who, once the study finished, continued exercising at their preferred time during the hemodialysis treatment, with the only support of the health professionals at the HD unit. Adherence to the exercise program was measured as a percentage (number of sessions attended divided by the number of sessions offered). The physical activity level was evaluated using the Human Activity Profile (HAP) questionnaire. The HAP scale is self-administered and is a list of 94 daily activities; the maximal activity score (MAS) and adjusted activity score (AAS) were calculated in this evaluation. Depending on the outcome of the HAP, patients were classified as having physical activity levels that were “impaired” (<53 points), “moderately active” (33–74 points), or “active” (>74 points). These patients had been exercising The intradialytic exercise consisted of a non-immersive VR game called ‘Treasure Hunt’ in which the participant try to catch targets and avoid obstacles by moving their lower limbs (hip flexion, abduction and adduction, and knee flexion and extension). The difficulty level of the game was graduated according to the characteristics of each player and the participants were allowed to change their legs during the game at their convenience. The impact of the program on physical activity level was analyzed with a non-parametric test for paired samples (p < 0.05).

Results: This study included 11 participants, mean age 71.6 (13.9) years, 9 males, median dialysis vintage 18 months (10 to 50 interquartile range), and Charlson index 6.3 (2.2). The AAS at the baseline of the REVID study was 58.7 (58–72 interquartile range). The median time that participants exercised in the REVID study was 12 months (6 to 18 months interquartile range). After 3 months of the present study, when they exercised at any time during dialysis, they maintained their physical activity level, from a median AAS of 69 (interquartile range 52–71), to a Median of 70 (interquartile range 41–74). The changes were non-significant. The main adherence to the exercise sessions was 54.6 (11.7%).

Conclusion: This study suggests that an intradialysis virtual reality exercise program maintains the physical activity level of elderly patients undertaking HD. Most of the participants in this long-term intervention were male and moderately active. Future interventions should include an ‘exercise champion’ professionals in the units to recruit women and less conditioned participants, and to achieve higher adherence rates.

EFFECT OF BROCCOLI SPROUT EXTRACT IN PATIENTS WITH TYPE 2 DIABETES AND CHRONIC KIDNEY DISEASE (INITIATE) - DESIGN AND BASELINE DATA

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Background and Aims: In advanced stages of chronic kidney disease (CKD) some glucose-lowering agents, such as metformin, cannot be prescribed to patients with type 2 diabetes (T2D) due to the risk of accumulation and adverse events. Foods with bioactive components, “functional food”, can be an alternative to mitigate the metabolic disturbances in these patients. Previous research on experimental animals and patients with T2D has shown that sulforaphane, present in broccoli sprouts, improves insulin sensitivity and glucose control. We hypothesize that sulforaphane ingested as a broccoli sprout extract (BSE) can improve glucose control in patients with T2D and CKD.

Method: This is an ongoing multicentre randomized double-blinded controlled trial with glucose control as the primary outcome. Glucose control is evaluated by fasting serum glucose, serum insulin in all patients, and oral glucose tolerance test (OGTT) in patients not on insulin treatment. Moreover, as a secondary aim, we investigate the role of BSE in improving other signs of metabolic alterations, including oxidative stress, proteinuria, inflammation and production of uremic toxins from the gut microbiota.

Patients: Adult patients with T2D and CKD (eGFR 15–45 ml/min/1.73m²) are included and randomized 1:1 to receive BSE or placebo. Both groups are followed for 20 weeks. The first 12 weeks, patients receive BSE or placebo and are then followed for 8 weeks. Patients randomized to BSE receive an increasing dose of sulforaphane administered as BSE (Lamtämnes®) starting with 50 μmmol/day in week 0–4; 100 μmmol/day in week 5–8 and 150 μmmol/day in week 9–12. The placebo consists of maltodextrin sprayed with copper-chlorophyllin. Blood and urine laboratory measurements and OGTT is performed at week 0, 12 and 20. Randomization is done using a computer-based block randomization algorithm. The protocol is registered at clinicaltrials.gov (NCT049858854).

Results: 98 patients with T2D and CKD from 12 centers in Sweden were included and the recruiting phase has now been finalized but the follow up phase is still ongoing. We here present baseline characteristics of all study participants (Table 1). Median age is 75 years and a minority are women. Mean eGFR corresponds to CKD stage 4 and there are large variations in albumin/creatinine ratios. Most participants are on a combination of oral glucose-lowering agents and insulin. A history of cardiovascular disease is common, and 21% had a previously had myocardial infarction.

Conclusion: We are currently conducting a randomized clinical trial testing if BSE can be used as an alternative or add-on to improve glucose control in patients with T2D and CKD stages 3–4 type and to see if this ‘high risk’ patient group could benefit from treatment with BSE.

Table 1: Baseline characteristics of patients with type 2 diabetes and chronic kidney disease in the INITIATE trial (n = 98).

| Overall | Age, years, median (IQR) | 75 (70–78) |
| Sex, % (women) | 30 (31%) |
| Body mass index, kg/m², mean (SD) | 30.6 (4.9) |
| eGFR, ml/min/1.73 m², mean (SD) | 28 (7) |
| Urine albumin-to-creatinine ratio (UACR), mg/mmol, median (IQR) | 20.7 (4.9–78.5) |
| HbA1c, mmol/mol, mean (SD) | 56.6 (13.7) |
| Oral glucose-lowering medication, % (mean) | 73 (74%) |
| Insulin treatment, % (mean) | 63 (64%) |
| OGTT performed, % (mean) | 22 (22%) |
| Comorbidities, % (mean) | 21 (21%) |
| Myocardial infarction (MI) | 9 (9%) |
| Stroke | 7 (7%) |
| Atrial fibrillation (AF) | 20 (20%) |

Abbreviations: eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation; OGTT, oral glucose tolerance test.
CLINICALLY MEANINGFUL IMPROVEMENT IN QUALITY OF LIFE ACCOMPANIES ITCH RELIEF IN PATIENTS WITH CHRONIC KIDNEY DISEASE ASSOCIATED PRURITUS

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1Robert-Bosch-Krankenhaus, Stuttgart, Germany, 2CSL Vifor, Zurich, Switzerland, 3Cara Therapeutics, United States of America and 4University Clinic of the RWTH Aachen, Division of Nephrology and Rheumatology, Germany

Background and Aims: The impairing effect of chronic kidney disease-associated pruritus (CKD-aP) on the quality of life (QoL) of patients undergoing haemodialysis (HD) is well-established. The aim of this post-hoc analysis was to assess the impact of itch relief on QoL, as measured by the 5-Ditchscale,inpatientswithCKD-aPenrolledinthePhase3KALM-1and-2 clinicaltrials.Thisstudyalsoaimedtoconfirmtheuseof ≥5-pointreductionin 5-D itch scale total score as a threshold for clinically meaningful improvement in itch-related QoL, by comparing to notable improvement on the Patients’ Global Impression of Change (PGI-C) scale.

Method: Data were pooled from 851 patients with moderate-to-severe CKD-aP undergoing HD in the KALM-1 and -2 trials testing difelikefalin vs placebo. Sustained responders were defined as patients who achieved a ≥3-point improvement in the weekly mean 24-hour Worst Itching Intensity Numerical Rating Scale [WI-NRS] score at Week 12 of the study, whereas non-sustained responders were defined as patients that reported a ≥3-point improvement in any week of the study but not at Week 12. Improvements in QoL, as measured by the mean change in 5-D itch scale total score from baseline to Week 12, were compared in sustained responders vs non-sustained responders. Data were analysed by ANCOVA multiple imputation, with a missing-at-random assumption. The mean change in 5-D itch scale total score was analysed in relation to patients’ reporting on the five categories of the PGI-C scale.

Results: In pooled analysis, 305 patients undergoing HD with CKD-aP qualified as sustained responders, whereas 128 patients were non-responders. Reduction in 5-D itch scale total score over 12 weeks was significantly higher in sustained responders compared with non-sustained responders (least squares [LS] mean ±standard error; –7.1±0.2 vs –4.0±0.3, LS mean difference –3.0±0.3, p<0.001) (Figure 1). Greater reductions in 5-D itch scale total score were observed in patients reporting more substantial improvements in PGI-C. Specifically, patients reporting much, or very much, improvement in PGI-C score ≥5-point reduction on the 5-D itch scale (mean ±standard error; –5.3±0.2 and –8.2±0.3, respectively) (Figure 2).

Conclusion: This study observed a greater improvement in QoL, as measured by the 5-D itch scale total score, in patients with CKD-aP who reported a clinically meaningful reduction in itch, as measured by WI-NRS, at Week 12. These results also support the use of ≥5-point reduction in the 5-D itch scale total score as a threshold for clinically meaningful improvement in the QoL of patients with CKD-aP. As only sustained responders exceeded this threshold, these data suggest that continued treatment of itch may be necessary to maximally improve QoL in these patients.

Figure 1: Change from baseline to Week 12 in 5-D itch scale total score in sustained responders and non-sustained responders. ANCOVA analysis multiple imputation, with missing-at-random assumption. Responders were defined as patients who reported a ≥3-point improvement in WI-NRS score at the 12-week time point. Non-responders were defined as patients who no longer achieved ≥3-point improvement in WI-NRS score at the 12-week time point, despite achieving at least one weekly ≥3-point improvement in WI-NRS score earlier in the study period. LS, least squares; SE, standard error; WI-NRS, Worst Itch Numerical Rating Scale.
HEALTHY PLANT-BASED DIET IN CHRONIC KIDNEY DISEASE THROUGH USE OF SODIUM ZIRCONIUM CYCLOSILICATE (HELPFUL TRIAL): RESULTS OF DIETARY INTAKE

Torsten Sallstrom1, Olof Heimbürger 2, Charlotta Rubin3, Awa Danielsson4, Gerd Faxen Irving5, Bengt Lindholm6, Peter Stenvinkel6 and Carla Maria Avesani6

1Nyköping Hospital, Department of Dietetics, Nyköping, Sweden, 2Karolinska Institutet, Department of Clinical Science Intervention and Technology, Stockholm, Sweden, 3Karolinska University Hospital, Medical Unit Clinical Nutrition, Stockholm, Sweden, 4Karolinska University Hospital, Medical Unit Nephrology, Stockholm, Sweden, 5Karolinska Institutet, Department of Neurobiology, Care Sciences and Society, Stockholm, Sweden and 6Karolinska Institutet, Department of Clinical Science, Technology and Intervention, Stockholm, Sweden

Background and Aims: The dietary restriction of healthy food sources of potassium (K) counselled to patients with chronic kidney disease (CKD) and hyperkalemia (HK) contributes to a diet with poor dietary quality. The K lowering medication sodium zirconium cyclosilicate (SZC) has the potential to treat HK, thereby allowing a healthy plant-based diet (PBD). We designed a clinical trial to explore the safety and feasibility of prescribing a healthy PBD to CKD patients with HK with the concomitant use of SZC.

Method: The HELPFUL trial is an ongoing single-arm study with CKD stage 4-5 patients not on dialysis and with plasma K (pK) between 5.1-6.5 mmol/L at inclusion. Patients are followed for six weeks. In the first three weeks, SZC is prescribed to normalize pK while patients ingest a low protein diet with low K content. In the subsequent three weeks, a healthy PBD with a target K intake of 3700mg/day is prescribed while maintaining the use of SZC. A food basket with PBD is delivered to participants weekly. A weekly monitoring of pK and titration of SZC to keep normokalemia is performed. Two dietary quality scores were calculated using the 24-hour food record (24h-FR) at baseline, week three and six. The first index is the Swedish version of Nutrient rich food index (S-NRF11.3) that measures the density of 11 beneficial nutrients (fiber, folate, iron, calcium, potassium, protein and vitamins A, C, D and E) and three non-beneficial nutrients (saturated fat, sodium and added sugars). The second index is the mean adequacy ratio (MAR) with the average intake of the same 11 beneficial nutrients as a proportion of the recommended daily intake (RDI). Data was analyzed by repeated measures-ANOVA or by Friedman test for related samples, as appropriate. Registered at www.clinicaltrials.gov (identifier NCT04207203).

Results: 22 patients were included; 59±13 years; 13 men, eGFR 18±4 mL/min/1.73m² (Table 1). The total intake of energy, fibre, folate and K increased significantly in week 6. Nutrient density did not change, but the MAR-score increased significantly. The intake of servings of fruits, vegetables and nuts increased significantly throughout the PBD. Regarding animal protein, there was a tendency to decrease the intake of servings of red meat and a significant increase in poultry and fish. The mean pK normalized in week three and six. After the start of PBD, three patients (13.6%) had pK between 5.1-5.3 mmol/L.

Conclusion: The strategy of PBD food baskets with concomitant use of SZC improved the dietary quality and increased the intake of servings of healthy foods. The K intake increased but not to target value. The pK was kept within normal values for most patients.

Table 1:

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 3</th>
<th>Week 6</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake, kcal</td>
<td>1738±479</td>
<td>1696±507</td>
<td>1995±688</td>
<td>0.01</td>
</tr>
<tr>
<td>Fibre intake, g</td>
<td>21±7</td>
<td>20±7</td>
<td>25±11</td>
<td>0.01</td>
</tr>
<tr>
<td>Folate intake, µg</td>
<td>228±74</td>
<td>213±75</td>
<td>273±108</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Potassium intake, mg</td>
<td>2655±777</td>
<td>2333±768</td>
<td>2840±927</td>
<td>0.03</td>
</tr>
<tr>
<td>Protein intake, g/kg IBW</td>
<td>0.9±0.3</td>
<td>0.8±0.2</td>
<td>0.9±0.2</td>
<td>0.30</td>
</tr>
<tr>
<td>S-NRF11.3</td>
<td>37±13</td>
<td>37±14</td>
<td>41±16</td>
<td>0.50</td>
</tr>
<tr>
<td>MAR-11, %</td>
<td>75±12</td>
<td>72±11</td>
<td>79±16</td>
<td>0.03</td>
</tr>
<tr>
<td>Fruits*/day</td>
<td>1.5(1.2;3)</td>
<td>1.3(1.2)</td>
<td>3.2(3.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vegetables*/day</td>
<td>1(0.6;2)</td>
<td>1.1(1.2)</td>
<td>2(1.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Nuts*/week</td>
<td>0.3(0.7)</td>
<td>0(0.7)</td>
<td>13(7.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Whole grains*/week</td>
<td>14(6.20)</td>
<td>12(3.17)</td>
<td>14(8.19)</td>
<td>0.42</td>
</tr>
<tr>
<td>Red meat*/week</td>
<td>1.1(0.8;2.1)</td>
<td>1.8(1.3;1)</td>
<td>1(0.2;2.3)</td>
<td>0.062</td>
</tr>
<tr>
<td>Poultry*/week</td>
<td>1(0.5;2)</td>
<td>1.3(1.3)</td>
<td>2(1.3)</td>
<td>0.049</td>
</tr>
<tr>
<td>Fish*/week</td>
<td>1.3(0.9;3)</td>
<td>1.5(2.1;1)</td>
<td>2.8(1.8;3.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Plasma K, mmol/L</td>
<td>5.5±0.3</td>
<td>4.7±0.4</td>
<td>4.8±0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HK (pK&gt;5&lt;6.5 mmol/L), n; %</td>
<td>22;100</td>
<td>4;18</td>
<td>3;14</td>
<td>–</td>
</tr>
</tbody>
</table>

Data described as mean ± standard deviation or median and interquartile range. *Servings; IBW: ideal body weight.
THE EFFECT OF CHRONIC KIDNEY DISEASE IN CONTRAST-ENHANCED ULTRASONOGRAPHY WITH ARRIVAL TIME PARAMETRIC IMAGING

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Background and Aims: CEUS is a reliable method to diagnose ischemic renal pathologies such as infarction, identify renal abscesses, discriminate between renal tumors and anatomical variants, describe complex cyst lesions, and monitor non-surgical renal lesions. Few studies explore the relationship between CEUS and the diagnosis or progression of CKD. The aim of this study was to evaluate the relationship between contrast-enhanced ultrasonography with arrival time parametric imaging (CEUS-PAT) and CKD.

Method: We prospectively evaluated 64 subjects (37 liver cirrhosis patients and 27 healthy volunteers) using CEUS-PAT to detect if the presence of CKD influences the arrival time of the contrast in the kidney. CKD was defined according to KDIGO 2021 guidelines. Ultrasonography was performed using the LOGIQ E9 (GE Healthcare, Chalfont St.Giles-UK) system, probe C1-6. CEUS was performed on each subject using SonoVue (Bracco SpA, Milan, Italy) as a contrast agent (1/2 of a vial). A 2.5 mL contrast substance followed by a 5 mL normal saline solution was infused in the cubital vein. A ratio between the arrival time of the substance in the kidney and liver was calculated. Subjects were in fasting conditions for at least 12 h. Laboratory data were extracted from the patient’s GP file. The study was conducted between January - December 2018. All patients provided their informed consent for the procedures.

Results: The study included 64 subjects, mean age of 58.98 ± 8.90 years, predominantly male gender (56.3%). Of the 64 patients, 13 (20.3%) had chronic kidney disease. All patients with chronic kidney disease had liver cirrhosis. When comparing the two groups, with and without CKD, there was a significant difference between the ratio of the arrival time of the contrast agent into the kidney and liver, 0.85 ± 0.09 vs 0.65 ± 0.19, p = 0.0005. The factors associated with kidney disease were liver steatosis (p<0.0001), age over 60 years (p = 0.01) and low albumin (p<0.0001).

Conclusion: Our study indicated that the presence of CKD influences the contrast agent arrival time in the kidney. Further studies are needed to establish the predictive significance of CEUS-PAT data in CKD patients.

THE EFFECTS AND MECHANISM OF BRAIN-TARGETING DRUG-LOADED EXOSOMES ON ADRIAMYCIN NEPHROPATHY MODEL

Lishan Tan1,2, Guang Yang1,2, Zheng Fengping2, Zhiwei Lai1,2,3, Sanmu Li2 and Zibo Xiong3

1 P.R. China, 2 Peking University Shenzhen Hospital, Nephrology, Shenzhen, P.R. China and 3 Nephrology, Shenzhen, P.R. China

Background and Aims: Chronic kidney disease (CKD) is a common clinical syndrome, and the current clinical efficacy is still limited. Our previous study confirmed that a small amount of losartan injected into the central lateral ventricle can effectively protect the kidneys, but the route of administration limits its clinical application. As a drug carrier, exosomes have several advantages and are expected to support drug delivery. Therefore, this study aims to develop a brain-targeting exosome complex to provide a new idea for the treatment of CKD.

Method: In this study, the brain-targeting exosome complex (ExoACP) was synthesized by co-cultivation. The markers of ExoACP were detected by immunoblotting. The structure and particle size distribution were observed by TEM and NTA. Angiotensin II receptor antagonist losartan (ExoACP@Los) was loaded on ExoACP by electroporation. The mice of Adriamycin (ADR)-induced nephropathy were divided into 5 groups: Control, ADR, ADR + Los (IG), ADR + ExoACP (lv.), ADR + ExoACP@Los (lv.). Corresponding treatment was given every other day from the 3rd week after modeling, and all mice were sacrificed at the 5th week, serum and renal tissue was collected for the following experiments.

Results: This study found that the exosome markers of ExoACP were highly expressed. The Exo and Ang-CP06-Exo were disc-like structures, and the size of the latter was larger than that of the former, suggesting that ExoACP was successfully modified on the surface of Exo. The modification efficiency of ExoACP on Exo was as high as 96.1%. Compared with free Exo, the distribution of ExoACP in brain was increased. Blood biochemical results showed that ExoACP and ExoACP@Los had no apparent side-effects on mice (Figure 1).

In-vivo, ExoACP@Los treatment significantly improved the levels of kidney function in mice with ADR nephropathy. ExoACP@Los could significantly reduce renal tubular damage, interstitial fibrosis area and degree of glomerulosclerosis, suggesting that ExoACP@Los could improve the injury of renal tissue (Figure 2).

Conclusion: This study synthesized a drug-loaded exosome complex with brain targeting and good biocompatibility, and significantly improved renal function, renal tissue damage and collagen fiber deposition in the ADR model.
SGLT-2 INHIBITORS DELAY KIDNEY FAILURE PROGRESSION AND REDUCE NEED OF DIALYSIS IN CHRONIC KIDNEY DISEASE PATIENTS: A META-ANALYSIS

Aditya Indra Mahendra1, Nur Samsu2, Atma Gunawan3 and Achmad Rifai2

1Faculty of Medicine, Brawijaya University, Department of Internal Medicine, Malang, Indonesia and 2Faculty of Medicine, Brawijaya University, Nephrology Division, Department of Internal Medicine, Indonesia

Background and Aims: chronic kidney disease (CKD) is the main complication of type 2 diabetes mellitus (type 2 DM) with up to 7 million cases requiring dialysis therapy. The newest type 2 DM therapy, sodium-glucose co-transporter-2 inhibitor (SGLT-2 inhibitor), has developed into an attractive option for patients with comorbid CKD because of its effect on blood pressure and albuminuria, in addition to its effect on lowering blood sugar. Therefore, we conducted a systematic review and meta-analysis aimed at assessing the effect of SGLT-2 inhibitors in preventing the progression of renal failure and the need for dialysis in CKD patients with and without type 2 DM.

Method: We performed an analysis of randomized controlled trials of SGLT-2 inhibitors reporting renal outcomes in patients with and without type 2 DM. We searched the PUBMED, MEDLINE, and CENTRAL databases from baseline to August 2022 to identify suitable studies. The major outcome evaluated was the combination of a persistent increase in serum creatinine two times from baseline and the need for dialysis.

Results: Of the 2890 identified articles, ten studies were included in the inclusion criteria assessing the effect of using SGLT-2 inhibitors. Out of 76,312 participants, 1716 participants experienced a 2-fold increase in serum creatinine and 647 participants required dialysis. The use of SGLT-2 inhibitors significantly reduced progressive renal failure and the need for dialysis in both patients with type 2 DM (RR: 0.65, 95% CI 0.60-0.71, p = 0.000) and patients without type 2 DM (RR: 0.59, 95% CI 0.46-0.77, p = 0.000). Subgroup analysis also showed that SGLT-2 inhibitors showed a significant effect in the group with eGFR > 60 ml/min (RR: 0.53, 95% CI 0.45-0.62, p = 0.000) and the group with eGFR 30-60 ml/min (RR: 0.66, 95% CI 0.57-0.75, p = 0.000).

Conclusion: SGLT-2 inhibitors can significantly inhibit the progression of CKD and reduce the risk of needing dialysis in patients with and without type 2 DM. These effects were shown consistently across groups with varying baseline eGFR values.

REDUCING FRAILTY IN HEMODIALYSIS PATIENTS THROUGH INTRADIALYTIC VIRTUAL REALITY EXERCISE INTERVENTION: THE REVID STUDY

Vicente BenavenCaballer1, Francisco José Martínez-Olmos1, Noemí Valtuena-Gímino1, Marina Toquero1, Alicia García-Testal2, Alicia Cana-Poyatos2, Rafael García-Maset2, Pilar Royo-Maicas2, José Antonio Gil-Gómez1 and Eva Segura1

1CEU Cardinal Herrera University, Physiotherapy and Nursery, Alfar del Patriarca, Spain, 2Manises Hospital, Nephrology, Manises, Spain and 3Instituto Universitario de Automática e Informática Industrial, Instituto Universitario de Automática e Informática Industrial, Valencia, Spain

Background and Aims: People in hemodialysis experience fatigue, weakness, weight loss, exhaustion, and low physical activity - all criteria of the frail phenotype. Frailty is a critical issue in the hemodialysis population due to its link to negative health outcomes, but few studies have focused on frailty in this population, despite the knowledge that frailty can be reversed with continued exercising at their preferred time during the hemodialysis treatment. Our group has previously shown that non-immersive virtual reality exercise during hemodialysis is a safe method to mitigate and manage frailty in the hemodialysis population.

Method: A randomized trial (the REVID study) included two groups of participants, exercising at different times during the dialysis session. The present study includes participants from REVID study who, once the study finished, continued exercising at their preferred time during the hemodialysis treatment. All participants were evaluated using the five Fried frailty phenotype criteria: unintentional weight loss of more than 4.5 kg in the past year, exhaustion was assessed using two questions from the Center for Epidemiological Studies Depression (CES-D) scale, weakness was measured using a handgrip dynamometer, walking speed was assessed by timing the 4.6m distance covered at the participant's normal pace, and physical activity was measured using the short version of the Minnesota Leisure Time Physical Activity questionnaire. Each of the five criteria was scored as 0 (not frail-related) or 1 (frail-related). Participants were then stratified into three groups: a score of 0/5 for robust or not frail, a score of 1-2/5 for pre-frail, and a score of 3-5/5 for frail. After the frailty phenotype assessment, all participants performed an intradialytic exercise program consisting of a non-immersive virtual reality game (Treasure Hunting) adapted to the dialysis session. The game consists of catching treasures and avoiding bombs by moving the lower extremities, with a progressive duration of 15 to 45 minutes. Adherence to the exercise program was measured as a percentage (number of sessions attended divided by the number of sessions offered). All assessments and interventions were conducted at Hospital de Manises in Valencia, Spain from September to December 2022.

Results: The study included 12 subjects with a mean age of 71.8 (13.9) years, 9 of whom were male, median time in Hemodialysis 20 (11.3 - 56 interquartile range) months. Out of the 12 participants, 2 were classified as robust, 5 as pre-frail, and 5 as frail. A chi-square test showed a significant change in the frailty phenotype of the participants after the exercise intervention (15.400; P = 0.003). At the end of the program, 3 participants were classified as frail, 7 as pre-frail, and 2 as robust. 2 participants improved from being frail to pre-frail. Furthermore, five participants (four frail and one pre-frail) reduced the number of criteria associated with the frail phenotype. No worsening in the frailty phenotype was reported among the participants. The average adherence to the exercise program throughout the study was 54.4 (11.2) %.

Conclusion: This study suggests that an intradialytic exercise program consisting of a non-immersive virtual reality can be useful in mitigating and managing frailty in the hemodialysis population.
Table 1: Inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Age &gt; 18 years</td>
<td>➢ CKD5D/ ESA therapy</td>
</tr>
<tr>
<td>➢ eGFR (CKD-EPI equation) ≤ 60 mL/min/1.73 m²</td>
<td>➢ hsCRP levels ≥ 5 mg/L</td>
</tr>
<tr>
<td>➢ Hb levels ≤ 12 g/dL</td>
<td>➢ Presence of inflammatory, infectious disease or surgical interventions &lt; 3 months</td>
</tr>
<tr>
<td>➢ Serum Ferritin levels &lt; 500 ng/mL</td>
<td>➢ Haematological disorders</td>
</tr>
<tr>
<td>➢ TSAT &lt; 30%</td>
<td>➢ Bleeding or blood transfusions &lt; 6 months</td>
</tr>
<tr>
<td>➢ hsCRP levels &lt; 5 mg/L</td>
<td>➢ Malignancy</td>
</tr>
<tr>
<td>➢ No blood transfusion/ Iron therapy in last 6 months</td>
<td>➢ Immunosuppressive drugs</td>
</tr>
<tr>
<td></td>
<td>➢ Severe malnutrition</td>
</tr>
<tr>
<td></td>
<td>➢ Concomitant severe liver or CV disease</td>
</tr>
<tr>
<td></td>
<td>➢ Chronic alcohol or drug abuse &lt; 6 months</td>
</tr>
<tr>
<td></td>
<td>➢ HBV/HCV/HIV infection</td>
</tr>
<tr>
<td></td>
<td>➢ Pregnant or lactating women</td>
</tr>
</tbody>
</table>

Figure 1: Study model.

Figure 2: ANOVA table for clinical significance of rise in hemoglobin between different groups.

Figure 3: ANOVA table for clinical significance of rise in TSAT between different groups.
### Table 2: Demographic data.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N = 189</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean ± SD; years)</td>
<td>42.88 ± 15.79</td>
</tr>
<tr>
<td>Sex (Male:Female)</td>
<td>110:79</td>
</tr>
<tr>
<td>Height (Mean ± SD; cm)</td>
<td>167.75 ± 7.794</td>
</tr>
<tr>
<td>Weight (Mean ± SD; Kg)</td>
<td>66.86 ± 14.767</td>
</tr>
<tr>
<td>Diabetes</td>
<td>65 (34.4%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>161 (85.2%)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>10 (5.3%)</td>
</tr>
<tr>
<td>CAD</td>
<td>40 (21.16%)</td>
</tr>
<tr>
<td>CKD stage</td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>52 (27.5%)</td>
</tr>
<tr>
<td>Stage 4</td>
<td>103 (54.5%)</td>
</tr>
<tr>
<td>Stage 5ND</td>
<td>34 (18%)</td>
</tr>
<tr>
<td>Metabolic profile (Mean ± SD)</td>
<td></td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>8.7 ± 0.8</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>5.72 ± 1.49</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>154.66 ± 151.81</td>
</tr>
<tr>
<td>Baseline Hemogram (Mean ± SD)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (gm%)</td>
<td>8.63 ± 0.79</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>81.71 ± 10.6</td>
</tr>
<tr>
<td>Baseline Iron profile (Mean ± SD)</td>
<td></td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>21.66 ± 6.33</td>
</tr>
<tr>
<td>Ferritin (mcg/L)</td>
<td>217.57 ± 75.78</td>
</tr>
</tbody>
</table>

### Table 3: Correlation between baseline haemoglobin & different modifiable/non-modifiable variables.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pearson chi-square/ Pearson’s R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.043</td>
<td>0.558</td>
</tr>
<tr>
<td>Sex</td>
<td>37.302</td>
<td>0.163</td>
</tr>
<tr>
<td>Height</td>
<td>-0.053</td>
<td>0.472</td>
</tr>
<tr>
<td>Weight</td>
<td>-0.015</td>
<td>0.839</td>
</tr>
<tr>
<td>Diabetes</td>
<td>43.783</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29.546</td>
<td>0.489</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>36.123</td>
<td>0.204</td>
</tr>
<tr>
<td>CAD</td>
<td>28.898</td>
<td>0.523</td>
</tr>
<tr>
<td>CKD stage</td>
<td>66.061</td>
<td>0.276</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.069</td>
<td>0.349</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>-0.152</td>
<td>0.037</td>
</tr>
<tr>
<td>PTH</td>
<td>-0.149</td>
<td>0.041</td>
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<tr>
<td>MCV</td>
<td>0.162</td>
<td>0.026</td>
</tr>
<tr>
<td>Transferrin Saturation (%)</td>
<td>0.178</td>
<td>0.015</td>
</tr>
<tr>
<td>Ferritin</td>
<td>-0.009</td>
<td>0.898</td>
</tr>
</tbody>
</table>

### Table 4: Rise in haemoglobin & TSAT with different preparations.

<table>
<thead>
<tr>
<th>Oral iron preparation</th>
<th>Baseline Hb (mean; gm%)</th>
<th>Hb 1 month (mean; gm%)</th>
<th>Hb 3 month (mean; gm%)</th>
<th>Rise in Hb</th>
<th>Baseline TSAT (%)</th>
<th>TSAT 3 month (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous Ascorbate (n = 40)</td>
<td>8.89</td>
<td>9.295</td>
<td>9.583</td>
<td>0.695</td>
<td>22.4</td>
<td>28.7</td>
</tr>
<tr>
<td>Ferrous Bisglycinate (n = 05)</td>
<td>8.50</td>
<td>8.74</td>
<td>8.98</td>
<td>0.48</td>
<td>20.8</td>
<td>26.9</td>
</tr>
<tr>
<td>Ferrous Fumarate (n = 22)</td>
<td>8.723</td>
<td>9.127</td>
<td>9.486</td>
<td>0.763</td>
<td>22.09</td>
<td>31</td>
</tr>
<tr>
<td>Ferric Pyrophosphate (n = 52)</td>
<td>8.713</td>
<td>9.325</td>
<td>10.037</td>
<td>1.324</td>
<td>21.17</td>
<td>33.67</td>
</tr>
<tr>
<td>Ferric Saccharate (n = 18)</td>
<td>8.389</td>
<td>8.717</td>
<td>9.017</td>
<td>0.628</td>
<td>19.06</td>
<td>28.78</td>
</tr>
<tr>
<td>Ferrous Sulfate (n = 20)</td>
<td>8.315</td>
<td>8.415</td>
<td>8.695</td>
<td>0.38</td>
<td>19.5</td>
<td>26</td>
</tr>
<tr>
<td>Heme Iron Polypeptide (n = 32)</td>
<td>8.434</td>
<td>8.703</td>
<td>9.00</td>
<td>0.566</td>
<td>21.88</td>
<td>25.84</td>
</tr>
</tbody>
</table>
Method: We selected 214 variants of pharmacogenetics relevance, based on evidence and frequency criteria. We evaluated their depth of coverage on 300 patients randomly selected in our CKD cohort.

Results: Eleven of those 214 variants were not covered by ES. Three of 11 variants were in UGT1A1 and were excluded from analysis since this information is only relevant for Irinotecan treatment. The remaining 8 variants fall in CYP2C19, CYP3A5, CYP3A4, CYP2D6, HLA B (B15:02), HLA A (A31:01), IFN3, VORCR1 genes: we completed exome data by targeted sanger sequencing for these variants. One challenging region is CYP2D6 given high sequence homology with CYP2D7 and CYP2D8: to assess if we could reliably call variants in this region, we used 7 additional Coriell samples, as 8 others were also assessed with an orthogonal technique. We were able to properly detect variants in these complex regions in all cases, including hybrid genes.

Conclusion: Our preliminary data show that exome sequencing, initially ordered for CKD, could also be used to deliver pharmacogenetic meaningful information, by adding a few targeted genotyping assays. We currently evaluate the clinical utility and impact of pharmacogenetics in our CKD cohort prospectively.

#3303
SUBOPTIMAL EXTENT OF RAAS RE-INITIATION AFTER DISCONTINUATION FOLLOWING HYPERKALEMIA: AN OBSERVATIONAL STUDY OF CARDIORENAL PATIENTS IN THE US AND JAPAN

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Background and Aims: Guidelines recommend renin-angiotensin-aldosterone system inhibitor (RAASI) therapy at the maximal tolerated dose to achieve optimal treatment benefits in chronic kidney disease (CKD) and heart failure (HF). However, hyperkalemia (HK) is a barrier to achieving guideline-directed target dosing and RAASI treatment is often compromised in patients who experience HK. Current international guidelines recommend novel oral anti-HK treatments to manage HK and facilitate RAASI therapy. This study assessed the extent of both temporary and longer-term discontinuation of RAASI following an HK episode, and the magnitude of RAASI re-initiation, in cardiorenal patients in the US and Japan.

Method: This observational study used data from hospital records and claims from the US (Optum’s de-identified Market Clarity Data) and Japan (Medical Data Vision). Patients with an index HK event (ICD-10 code E87.5) during July 2019–September 2021 (US) or May 2020–February 2022 (Japan) with a prior diagnosis of CKD and/or HF and use of RAASI in the preceding 6 months were included. RAASI classes included angiotensin-converting enzyme inhibitors (ACEI), angiotensin-receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA), and angiotensin receptor neprilysin inhibitors (ARNi). In patients who discontinued RAASI treatment following their index HK episode, duration of discontinuation was described within a time frame of 6 months from the date of discontinuation (those with <6 months follow-up time were excluded). The RAASI dose prior to discontinuation versus at re-initiation was also assessed.

Results: In total, 25,963 patients from the US and 8,722 from Japan were included. The mean age was 68.3 (US) and 74.8 (Japan) years; 53% and 65% were male; and 30% and 12% of patients had a recorded history of HK prior to their index event. In the US, 85% filled a RAASI prescription in the 3 months prior to HK episode; the most common RAASI classes were ACEI (used by 46% of the overall cohort), ARB (27%), and MRA (19%). In Japan, 91% filled a RAASI prescription in the 3 months prior to HK episode; ARB was the most common (67%), followed by MRA (25%), and ACEI (16%). ARNI was used by <5% of patients in the US and <2% in Japan; it was not assessed further due to low patient numbers. Following the HK episode, ACEI/ARB were discontinued in 23–26% of patients, while MRA was discontinued in 33–46% (Table 1). In those who discontinued, re-initiation within 6 months occurred among 10–15% of patients in the US and among 6–8% of patients in Japan. In those who re-initiated, 17–37% of patients in the US and Japan had their dose reduced by >25%.

Conclusion: In clinical practice, HK leads to discontinuation of RAASI treatment despite guidelines recommending maintained treatment. Re-challenge of RAASI treatment is uncommon and, when re-introduced, the dose is commonly reduced. These findings emphasize the need for improved guideline adherence in managing HK to facilitate continued RAASI therapy.

#3015
EFFECT OF DAPAGLIFLOZIN ON ALBUMINURIA IN PATIENTS WITH TYPE 2 DIABETES AND CKD

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Background and Aims: Albuminuria in patients with diabetes presents a higher risk for adverse renal and cardiovascular (CV) outcomes. Sodium-glucose co-transporter 2 (SGLT2) inhibitors demonstrate improved albuminuria and reduces the risk of end-stage renal disease in patients with

Table 1: RAASI discontinuation and re-initiation after an HK episode in cardiorenal patients with CKD and/or HF in the US and Japan.

<table>
<thead>
<tr>
<th>RAASI</th>
<th>US</th>
<th>Japan</th>
<th>Discontinuation1 (long-term3 or temporary1), n (%)</th>
<th>Re-initiation within 6 months of discontinuation, n (%)</th>
<th>Dose reduced by &gt;25% at re-initiation, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI</td>
<td>6,717</td>
<td>893</td>
<td>1,721 (26)</td>
<td>211 (12)</td>
<td>63 (30)</td>
</tr>
<tr>
<td>ARB</td>
<td>3,876</td>
<td>4,050</td>
<td>955 (25)</td>
<td>143 (15)</td>
<td>33 (23)</td>
</tr>
<tr>
<td>MRA</td>
<td>2,395</td>
<td>1,263</td>
<td>800 (33)</td>
<td>78 (10)</td>
<td>20 (26)</td>
</tr>
</tbody>
</table>

1Includes patients with CKD or HF with the respective RAASI treatment while experiencing an HK episode who remained in follow-up at 6 months. 2Discontinuation defined as when the prescribed dose’s supply had been exhausted and no new prescription for that RAASI class had been filled in the 90 days following end of supply. 3No filled prescription within 6 months of discontinuation. 4A new fill within 91 days to 6 months of end of supply.

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blocker; CKD, chronic kidney disease; HF, heart failure; MRA, mineralocorticoid receptor antagonists; RAASI, renin-angiotensin-aldosterone system inhibitor.
chronic kidney disease. The study aim was the impact of the SGLT2 inhibitor dapagliflozin on urine albumin-to-creatinine ratio (UACR) and GFR decline.

**Method:** In the single center trial, total 132 participants with CKD and type 2 diabetes (T2D) were randomly assigned to dapagliflozin (n = 78) 10 mg once daily or placebo (n = 54). Kidney inclusion criteria were eGFR 30-60ml/min/1.73 m² and any UACR. The primary end point was a composite of sustained decline in eGFR ≥50%, end-stage renal disease, or kidney or cardiovascular death. Percentage treatment difference was estimated by geometric mean ratio for the overall cohort and by eGFR and UACR subgroups. Progression/regression of UACR were assessed. Hazard ratios, 95% confidence intervals (CI), and p-values were estimated by Cox proportional hazards model.

**Results:** Median baseline eGFR was 42.3ml/min/1.73 m², with 5% at <30ml/min/1.73 m². At baseline, median UACR was 103 mg/g, and 1/4 of patients had normal albuminuria, 2/4 had micro, and 1/4 had macroalbuminuria. Median follow up was 18 months. The UACR difference for dapagliflozin vs placebo was -25.1% (95% CI -27.5, -23.2; p < 0.001). Reductions were similar across eGFRs. In UACR 30-299mg/g and ≥300mg/g, reductions were significant in dapagliflozin (p < 0.001). Progression risk was lower and regression risk higher in dapagliflozin vs placebo (p < 0.001).

**Conclusion:** Dapagliflozin significantly slowed long-term eGFR decline in patients with CKD with T2D compared with placebo, and significantly reduced UACR and had favorable effects on UACR progression and regression.

**3204 CASE-BASED ONLINE MEDICAL EDUCATION ENHANCES PHYSICIANS' KNOWLEDGE AND COMPETENCE IN THE MANAGEMENT OF PATIENTS WITH DIABETES WITH CARDIORENOLOGICAL DISEASE**

**Joachim Trier1, Per-Henrik Groop2 and Rita Moreira Da Silva1**

1WebMD Global LLC, Medscape Education, New York, United States of America and 2Helsinki University Hospital, Department of Nephrology, Helsinki, Finland

**Background and Aims:** Patients with type 2 diabetes (T2D) and chronic kidney disease (CKD) have a substantially impaired cardio-renal health prognosis and a reduced life expectancy highlighting the urgent need for early detection and comprehensive vascular risk control. The goal of this activity for primary care physicians (PCP) and diabetologists/endocrinologists (D/E) was to improve their understanding of and competence in managing patients with diabetes with cardiorerenal disease in clinical practice.

**Method:** An interactive educational program including one detailed patient case challenges clinicians to apply most recent evidence-based guideline recommendations. Detailed scenarios prompt learners to determine the correct treatment and follow-up for the patient with expert commentaries providing in-depth advice at each stage and a conclusion at the end of the program. Educational effect was assessed using a repeated-pair design with pre-/post-assessment. 3 multiple choice questions assessed knowledge/competence, 1 question rated on a Likert-type scale assessed confidence. A paired samples t-test was conducted on overall average number of correct responses and for confidence rating, a McNemar's test was conducted at the question level (5% significance level). Cohen's d with correction for paired sample estimates the effect size of the education on number of correct responses. Data collection from 5/25/22 to 9/13/22.

**Results:** 74% of PCP (n = 74) improved their knowledge regarding the need for comprehensive vascular risk control in patients with T2D and CKD and their competence related to the practical implementation of the latest diabetes guidelines for the individualized management of these patients (p < 0.001; d = 0.56)

- 56% of D/E (n = 32) advanced their knowledge regarding the need for comprehensive vascular risk control in patients with T2D and CKD (P < 0.01, d = 0.35)
- 39% of PCP and 41% of D/E increased their confidence (p < 0.001 and p < 0.01 respectively) in proactively monitoring their patients with T2D for kidney disease

**Conclusion:** Participation of PCP and D/E in an interactive online case-based education program improved their understanding of the need for comprehensive vascular risk control and the competence of PCPs in managing patients with T2D and cardiorenal disease in clinical practice.

**REFERENCE**
THE ROLE OF RENAL DYSFUNCTION DURING ANTICOAGULANT USE IN COPD PATIENTS WITH ATRIAL FIBRILLATION
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Background and Aims: Renal dysfunction is known to be the most important predictor of outcome in patients with atrial fibrillation (AF). Purpose of the study was to evaluate the prognostic role of kidney dysfunction in terms of possible cardiovascular events and bleeding in patients with COPD and AF treated with oral anticoagulants.

Method: We examined 56 COPD patients with CHF and AF who received oral anticoagulants. Renal function (creatinine level and estimated glomerular filtration rate - eGFR) was assessed at baseline and on follow-up. The functional state of the kidneys was calculated using the CKD-EPI-2011 formula. Initially, the risk of bleeding was assessed using the HAS-BLED score. The deterioration of the functional state of the kidneys was noted with an increase in the level of creatinine or a decrease in eGFR by at least 20%.

Results: In addition to the standard treatment for COPD in the presence of AF, patients received oral anticoagulants during a six-month follow-up. The deterioration of the functional state of the kidneys was observed in 18.3% of patients. In patients with kidney dysfunction, the frequency of episodes of CHF decompensation and non-massive bleeding (MB) was significantly higher. When reduced glomerular filtration rate did not affect the frequency of bleeding and stroke. The oral anticoagulants used did not significantly affect the observed renal dysfunction and did not affect the occurrence of new cardiovascular events in patients with COPD. It turned out that the predictors of renal dysfunction in patients with COPD are age, female gender, and low hemoglobin levels. In multivariate analysis, renal dysfunction was identified as an independent predictor of non-massive bleeding (OR 2.04, 95% CI, p<0.05).

Conclusion: In patients with COPD and atrial fibrillation, the presence of kidney dysfunction was an additional aggravating factor associated with adverse cardiovascular prognosis in the medium term and the risk of bleeding. However, oral anticoagulants did not affect the degree of deterioration in renal function or the incidence of cardiovascular events.

RELATIONSHIP BETWEEN INITIAL EGFR DIP AND CHANGES IN LABORATORY PARAMETERS WITH DAPAGLIFLOZIN TREATMENT IN NON-DIABETIC CKD PATIENTS
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Nara prefecture General Medical Center, Department of Nephrology, Nara, Japan

Background and Aims: Treatment with sodium-glucose co-transporter-2 inhibitors (SGLT2i) induces an initial decline in estimated glomerular filtration rate, also termed the 'eGFR dip' and remains beneficial effects for cardiovascular and kidney outcomes, even after modified by eGFR dip in diabetic CKD. However, the difference of eGFR dip after SGLT2i between diabetic and non-diabetic CKD patients and the effects of eGFR dip on changes of laboratory parameters is not fully understood. In this study, we aimed to investigate the eGFR dip after Dapagliflozin in terms of changes of laboratory parameters and its relationship with clinical and laboratory data in non-diabetic CKD patients.

Method: We conducted a cohort study on 127 non-diabetic CKD patients receiving Dapagliflozin in whom at least two measurements of eGFR levels at three months were confirmed. eGFR dip was defined by percent eGFR change from baseline. eGFR was calculated using Japanese equation. Correlation analysis between initial eGFR dip and clinical value were conducted using the Pearson correlation coefficient.

Results: The mean age of study participants was 60±13 years and 69 (54%) were male. The underlying kidney diseases included glomerulonephritis in 59 (46%) patients and hypertensive nephrosclerosis in 57 (45%). The mean levels of baseline eGFR were 43±13 ml/min/1.73 m² and the mean proteinuria was 0.58±0.83 g/gCRE. The mean eGFR change from baseline was −0.33±4.3 ml/min/1.73 m² with eGFR dip of 0.8±9.4%. Factors including age, sex, body mass index, baseline eGFR and urinary protein were not significantly associated with the eGFR dip. Dapagliflozin increased hemoglobin levels by 0.5g/dl and decreased uric acid levels by 0.9 mg/dl. We found indirect and direct correlation of the eGFR dip with changes in proteinuria (r = 0.30, p = 0.001) and uric acid levels (r = 0.21, p = 0.015) after Dapagliflozin, respectively.

Conclusion: Our results suggest that the eGFR dip following SGLT2i initiation may be associated with the changes of proteinuria and uric acid levels in non-diabetic CKD patients.
EFFICACY OF MRNA VACCINE BNT162B2 AGAINST NOVEL SARS-COV-2 VIRUS IN END-STAGE KIDNEY DISEASE

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**Background and Aims:** Covid-19 pandemic affected more than 600 million people worldwide. Chronic kidney disease was shown to be a significant risk factor for disease severity. The introduction of the novel mRNA vaccines against SARS-CoV-2 prompted studies to evaluate their efficacy and safety. This study aims to assess the humoral response to the BNT162b2 vaccine, its durability, the booster effect, and breakthrough infections among end-stage renal disease patients (ESRD).

**Methods:** A one-year, single center, observational prospective study was conducted between 2021 and 2022. The cohort included adult dialysis patients (n = 143), kidney transplant recipients (11), and healthy controls (n = 75). Demographic and clinical data were retrieved from electronic medical records. All participants received 30 μg/dose of BNT162b2 mRNA vaccine, at 0 and 3 weeks. A third vaccine (booster) was administered at least 6 months after the first dose. SARS-CoV-2 infection was diagnosed based on PCR test of nasal and oropharyngeal swabs. Infections that occurred from January 2022 were attributed to omicron variant. Longitudinal blood samples were collected as indicated in Figure after the first vaccine dose (V1) and after the booster dose (V3). Humoral immune response was assessed by measuring serum IgG antibodies against the receptor-binding domain of the SARS-CoV-2 S1 subunit, using the ABBOTT kit. The study protocol was approved by the Institutional Review Board and was conducted in adherence to the Declaration of Helsinki.

**Results:** Twenty-eight weeks after two doses of vaccine, the median antibody levels were significantly lower in dialysis and transplant patients compared with healthy controls (122 AU/mL (2–4,557) and 6 AU/mL (1–217) vs 831 AU/mL (117–40,000), respectively). Furthermore, only 75% of dialysis patients developed positive antibody response (>50 AU/mL) as compared to 100% in controls (see Figure 1). A significant waning of immunity was seen over time in both dialysis and healthy participants (p < .0001). Four weeks after a booster...
dose, antibody levels surged and did not differ between dialysis and healthy participants $13,840 \pm 15,126$ AU/mL vs $18,080 \pm 13,354$ AU/mL, respectively ($p = .283$). Non-responder rate among dialysis patients dropped from 21% after a 2-dose vaccination to 7% after a booster dose. Lower antibody levels measured at 28-week after the first vaccination were associated with higher risk for Covid-19 infection ($p = .021$). Of note, all infection cases occurred in subjects with antibody levels below $1050$ AU/mL. However, no association was found between antibody levels and Covid-19-omicron variant infection rate among dialysis patients and healthy controls ($p = 0.650$).

**Conclusions:** Dialysis patients had a blunted humoral immune response after two doses of BNT162b2 vaccine compared with healthy controls, which improved after a booster dose. Based on the observed omicron variant breakthrough infections, further studies are needed to improve the vaccines’ efficacy against the evolving SARS-CoV-2 variants.

**#5916**

**ANALYSIS OF SARS-COV2 INFECTION AND COVID-19 VACCINATION IN TWO DIAVERUM CLINICS IN NORTH MACEDONIA**

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**Background and Aims:** Hemodialysis patients as a separate group of immunosuppressive patients are at highest risk of severe clinical complications and death caused by infection with SARS-CoV-2 virus. With the introduction of COVID-19 vaccination in hemodialysis patients, the situation has changed significantly. The aim of the study was to analyze the difference in morbidity and mortality between two groups of hemodialysis patients, vaccinated and unvaccinated for Covid-19 in two Diaverum Clinics.

**Method:** The study is based on analysis of the data of hemodialysis patients in two Diaverum clinics during the period from April 2020, when the first case of SARS-CoV-2 virus was detected in Diaverum Kochani Clinic, to August 2022, when the last case of SARS-CoV-2 virus was detected in both clinics. Analytical data are taken from IRIMS database used only by Diaverum Clinics worldwide.

**Results:** During the period of observation, a total number of 214 hemodialysis patients were treated in both Diaverum Clinics. Regarding gender distribution 63% are males and 37% are females. From the total number of patients in both clinics, 67% (143) were vaccinated with two or three doses of the COVID 19 vaccines, while the remaining 33% (71) patients were COVID-19 unvaccinated. The majority of the patients (67%) were vaccinated with Chinese vaccine Sinopharm; 19% with Sinovac; 7% with Astra Zeneca; 7% with Pfizer BioNTech (the vaccines that were available in that period in our country). In 2020 a total of 28 COVID infection occurred in both clinics, all of them were unvaccinated patients; 16 of them were hospitalized and 9 of them died. Hospitalization rate was 57% and mortality rate 32% among the positive patients. In 2021 a total of 35 COVID infections were registered, 18 were hospitalized (unvaccinated 61% vs 39% vaccinated), 26% (9) of the positive patients died, 6 were unvaccinated and 3 were vaccinated with 2 doses. Hospitalization rate was 51% and mortality rate 26%. In 2022 a total of 43 COVID infections occurred, only 4 were hospitalized and only 1 patient died; hospitalization rate 9%; mortality rate 2.3%. When the whole study period was analyzed, the infection rate between the vaccinated and unvaccinated patients in both clinics was statistically not significant, 51% vs 46.5%, $p = 0.5634$ (Fisher exact two-tailed test). But, when the hospitalization rate was compared between vaccinated and unvaccinated patients, 12.3% vs 84.8%, the difference was highly statistically significant ($p = 0.0001$). When death rate was compared between the two groups, the difference was also highly statistically significant, 5.5% vs 45.4% in the unvaccinated group ($p = 0.0001$).

**Conclusion:** The results of our study showed no difference in the infection rate between vaccinated and unvaccinated patients, but they confirmed high level of protection from hospitalization and mortality in vaccinated patients.

**#3956**

**PRIORITY OUTCOMES FOR EDUCATION AND SELF-MANAGEMENT IN NON-DIALYSIS CHRONIC KIDNEY DISEASE: A PATIENT AND PROFESSIONAL DELPHI SURVEY**

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**Background and Aims:** It is important for people living with Chronic Kidney Disease (CKD) to develop the knowledge, skills, and confidence (patient activation) to effectively self-manage their health in partnership with their healthcare team. Resources intended to educate and support self-management should be subject to robust evaluation to provide the evidence base for clinical implementation. Trials in both research and clinical practice settings should...
include outcomes which are meaningful and valued by all users, but these are not known for CKD education and self-management interventions. We carried out a Delphi survey to identify the priorities valued by both CKD patients and healthcare professionals (HCPs) in the UK.

Method: Kidney patients and multidisciplinary kidney HCPs based in the UK were invited to complete two sequential rounds of an online Delphi survey. People with CKD and their significant others (SOs) were invited via social media, and HCPs via direct email. For Round One, participants were asked to identify in their own words the 3 potential benefits (outcomes) for CKD self-management that they personally considered to be most important. These free-text responses were collated and analysed inductively using conventional content analysis to identify dominant themes and constituent items. In Round Two, participants were asked to rate each of these items on a 9-point Likert scale from 1 (least important) to 9 (most important), and overall median ratings were calculated for each theme.

Results: 135 participants contributed to Round One: 47% (64) CKD patients/SOs; 51% (69) kidney HCPs; 2 individuals identified in both groups. 58% of HCPs who were invited by email agreed to take part. Round One analysis identified 28 outcome items which fell into 5 main themes: clinical; knowledge, skills, and confidence to manage own health; behaviour and self-care; psychological and social factors; healthcare usage. 69% (44) of invited CKD patients/SOs and 77% (53) HCPs took part in Round Two. Table 1 shows the median ratings for each theme. The highest-ranked overall and for both groups was “clinical”, while “healthcare usage” was ranked the lowest.

Conclusion: Our UK Delphi survey has identified a range of potential benefits for successful self-management in non-dialysis CKD, which were categorised into 5 main themes. Clinical outcomes such as improving blood pressure management or avoiding progression to end stage kidney disease were the top priority for both CKD patient/SO and HCP participants. Aspects of patient activation (knowledge, skills, and confidence to manage health) were also rated as important by both groups. This Delphi survey identified which benefits kidney patients and HCPs value most from effective CKD education and self-management. It is important that the views of intended users of new interventions are consulted throughout the development process to ensure that the product meets their needs and expectations. The information we present here is vital for the successful design, evaluation and implementation of interventions and support tools to educate people with CKD and enable them to improve self-management behaviours.

#3439 EXERCISE, METABOLIC SYNDROME AND CHRONIC KIDNEY DISEASE (CKD): THE EX-RED STUDY
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Background and aims: Obesity and metabolic syndrome (MS) are risk factors for renal disease progression in patients with established chronic kidney disease (CKD). Although therapeutic exercise has a potential role to treat or ameliorate chronic diseases, the effect of this intervention on obesity/MS and major renal outcomes: proteinuria and/or glomerular filtration rate (GFR) in patients with CKD is scarcely known. In particular, the effect of exercise in short term changes in renal outcomes are unknown. So, the aim of the study is to evaluate the effect of therapeutic exercise on: (a) the amelioration of MS traits and (b) renal parameters, GFR and proteinuria, in patients with CKD and MS.

Method: This is a 6-month exploratory study that included clinically stable patients with CKD of different causes and MS with measured GFR of 30-90 ml/min/kg. Patients were treated with an incremental protocol of exercise which was prescribed by a physiotherapist. Baseline treatment and increments in prescription were based on physical status and individual response on follow-up, treatment involved both aerobic and strength exercise. All patients start with aerobic exercise training 30-60 minutes and 5 times per week. Strength exercise was individualized and consisted of free weight exercises. The prescription was increased every month. The following outcomes were considered: changes in GFR i.e., ≥7%, which is twice the variability of the method in our laboratory (https://lfrc.echucan.es), and weight loss ≥5%, a change associated to lower cardiovascular risk. In parallel with exercise training, we designed a plan to evaluate and promote adherence using regular telephone calls, an activity tracker, and visits to the hospital. Measured glomerular filtration rate (iohexol-DBS), urine samples (albuminuria/proteinuria), anthropometric parameters and analytics were collected at baseline, 3 and 6 months. There is no evidence in the field to evaluate the sample size of the study. Then, we designed and explorative study including 40 cases.

Results: This is a preliminary analysis of 25 cases: 3 were lost of follow-up at 3 months, and so, we show data of 22 patients that finished the study. Mean age was 58 ± 12 and 70% (N = 17) were male. All patients were obese or overweight and 17 (70%) were diabetic. The most frequent kidney diseases were glomerulonephritis (40%) and diabetic nephropathy (30%). Most patients were on ACE inhibitors/ARB (46%) and lipid-lowering agents (52%). At 6 months, 5 (22%) patients did not have major changes in weight, which was attributed to low adherence to treatment, and so, were not considered for further analyses. Of the remaining cases (N = 17, 78%), all showed a reduction in weight: from 97 ± 18 to 87 ± 18, p = 0.01. These patients were then classified in 3 groups based on GFR changes: (A) decreased GFR (N = 6, 35%), with GFR changing from 54 ml/min ± 3 ± 14 ± 14, p = 0.001; BMI decreasing from 33 kg/m2 ± 3 to 30 ± 5, p = 0.003 and TG from 211 mg/dl ± 98 to 127 ± 59, p = 0.026; (B) stable GFR (N = 7, 41%), GFR from 47 ml/min ± 22 ± 26 ± 41 p = 0.2; BMI decreasing from 35 kg/m² ± 3 ± 31 ± 3, p = 0.002 and TG from 160 mg/dl ± 57 to 105 ± 29, p = 0.02; (C) increased GFR (N = 4, 24%), GFR increasing from 39 ml/min ± 16 ± 66 ± 18, p = 0.015 and BMI decreasing from 39 kg/m² ± 3 ± 36 ± 2, p = 0.015. No significant changes were observed in albuminuria and other MS traits in the subgroups analyzed. No adverse events were found during follow-up.

Conclusion: exercise is an effective and safe intervention method to lose weight and improve dyslipidaemia in patients with MS and CKD. The effect of weight reduction on GFR is not universal. Some patients showed a reduction of GFR in line with the reduction of weight, which may reflect the correction of hyperfiltration related to obesity and MS. On the other hand, in some patients GFR remained stable or even increased after weight loss. The pathogenesis behind this aspect is clearly unexpected and unknown. The impact of GFR changes associated with weight and MS changes in CKD deserve detailed attention in ad hoc designed studies.

#6018 SODIUM-GLUCOSE CO-TRANSPORTER-2 INHIBITOR USE IN THE MANAGEMENT OF PATIENTS WITH CHRONIC KIDNEY DISEASE AND TYPE 2 DIABETES MELLITUS
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1 University of Birmingham, Medical School, United Kingdom and 2 Birmingham Heartlands Hospital, United Kingdom

Background and Aims: Sodium-glucose co-transporter-2 (SGLT-2) inhibitors were initially developed for the management of type 2 diabetes mellitus (T2DM). Results from large placebo-controlled clinical outcome trials have now highlighted efficacy of SGLT-2 inhibitors in reducing the risk of CKD progression [1,2]. NICE CKD guidelines now recommend use of SGLT-2 inhibitors alongside standard of care in those patients with T2DM [3]. This has subsequently extended SGLT-2 inhibitor licensing highlighting the importance of wider multi-disciplinary team practise awareness. The aim of this audit was to assess the level of implementation of updated NICE guidelines in patients under a specialist CKD clinic in Birmingham.
Method: A database of renal diabetics under a specialist CKD clinic in May 2022 was generated via a trust electronic patient record system. Patients with a recorded diagnosis of T2DM and estimated glomerular filtration rate (eGFR) >25 ml/min (current UK regulatory licensing for SGLT-2 inhibitor use) were included. Parameters of renal function (urine albumin: creatinine ratio (uACR) and eGFR) as well as medication histories were retrospectively collected for 158 patients and analysed using descriptive statistics.

Results: Results demonstrated 19% (n = 43) of 143 patients with an accessible drug history were prescribed an SGLT-2 inhibitor. Less than half (44%) of those prescribed standard of care (ACEI/ARB) with a uACR > 30 mg/mmol (n = 34) were prescribed an SGLT-2 inhibitor as per NICE recommendations. The prescribing of SGLT-2 inhibitors in patients at different stages of CKD was noted except in those with eGFR < 30 ml/min.

Conclusion: Results suggest a number of patients with T2DM are not prescribed an SGLT-2 inhibitor as per NICE recommendations for CKD management. Whilst considering sample size limitation as well as possible contraindications relevant to SGLT-2 inhibitor treatment, these findings may reflect the recent update to NICE guidelines and delayed dissemination of information between multi-disciplinary teams around extended SGLT-2 inhibitor licensing. Glycaemic control is less effective in later stages of CKD however, trials have demonstrated the independent role of SGLT-2 inhibitors in reducing the risk of CKD progression irrespective of their attenuated ability to lower glucose in reduced kidney function [1, 2]. It is imperative patients not currently prescribed an SGLT-2 inhibitor are reviewed for treatment eligibility and any contraindications. Results of this study were fed back to the local renal and diabetes team with the recommendation for development of clear guidelines for use of SGLT-2 inhibitors in all eligible patients in order to achieve maximum healthcare benefits. In addition, there are ongoing discussions with primary care regarding review of their use of SGLT-2 inhibitors.

REFERENCES

#5890
THE IMPACT OF CKD STATUS BEFORE KIDNEY TRANSPLANTATION ON ALPHATORQUEVIRUS DNA LEVELS
Claudia Vuste Lozano1, Celia González-García1, Paula Jara Caro Espada1, Paul Hernandez-Velasco1, Lucia Rodriguez Gayo1, Natalia Inmaculada Polanco Fernandez1, Amado Andrés Belmonte1, Enrique Morales1 and Mario Fernandez1,2
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Background and Aims: Torque teno virus (TTV) is a non-pathogenic anellovirus whose replication kinetics reflects the overall state of immuno-suppression. Although chronic kidney disease (CKD) induces a well-stabilised dysfunction of the immune system, long-term use of renal replacement therapies (RRT) itself could also modify the immune response.

Method: We analyzed TTV DNA loads at baseline (in the pre-transplant assessment), day 7 and months 1, 3, 6 and 12 after kidney transplantation (KT). Recipients were categorized according to their RRT status: pre-emptive KT (pre-KT), hemodialysis (HD) and peritoneal dialysis (PD). TTV DNA load was measured by real-time polymerase chain reaction.

Results: A total of 221 CKD patients were analyzed. The mean age was 53.9 ± 15.7 years. 72.4% were males, and hypertension (85.1%) and diabetes (30.1%) were the most common comorbidities. According to the pre-transplant TTR status, 159 (72.0%) were on HD, 35 (15.8%) on PD and 27 (12.2%) received pre-KT. There were no differences in baseline comorbidities or age between patients according to their RRT status, except for residual diuresis (P < 0.01). PD patients had higher serum albumin levels than patients receiving pre-KT or HD (4.4 ± 0.5 vs. 4.1 ± 0.6 vs. 3.9 ± 0.4 g/dL, respectively, P < 0.01). PD patients exhibited higher TTV DNA load (3.4 ± 1.2 log10 copies/mL) than HD (2.8 ± 1.6 log10 copies/mL) or pre-KT patients (2.4 ± 2.1 log10 copies/mL), although the differences were not statistically significant. PD patients had lower time on dialysis than HD patients (18.4 ± 16.2 vs. 37.5 ± 33.6 months, respectively; P = 0.038). Although PD patients had higher TTV DNA load during the post-transplant follow-up than HD and pre-KT patients, viral kinetics were comparable across these three groups by month 12 after transplantation. Time on dialysis was not associated with TTV DNA load (P = 0.18). RRT status was not associated with the incidence of post-transplant infection or a composite of opportunistic infection and/or de novo malignancy.

Conclusion: TTV DNA load could be useful identifying KT recipients at high risk of immunosuppression-related complications. Although PD patients presented a non-significant higher TTV DNA load, we did not find differences according to the modality of prior RRT or the time on dialysis.

#2808
REMDESIVIR FOR MODERATE-TO-SEVERE COVID-19 PNEUMONIA IN MAINTENANCE DIALYSIS PATIENTS: A RETROSPECTIVE COHORT STUDY
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National Kidney and Transplant Institute, Adult Nephrology, Quezon City, The Philippines

Background and Aims: Remdesivir has shown better patient outcomes and shorter time to recovery among hospitalized patients with moderate to severe COVID-19 pneumonia. However, data on its safety and efficacy in dialysis patients is lacking.

Method: Dialysis patients with moderate to severe COVID-19 pneumonia who were given remdesivir were matched 1:2 to those who received standard-of-care (SOC) based on age, sex, COVID-19 severity and CKD etiology.

Results: The final cohort comprised 201 patients and 67 were given remdesivir. Median age was 52 years, majority were male (51.7%), 94% were on hemodialysis (94%) and 48% had diabetic nephropathy. The 28-day probability of survival among moderate COVID-19 cases was 100% for both remdesivir and SOC group. In severe cases, the survival probability for remdesivir recipients was lower compared to SOC (67.63% vs 87.72%), but this was not statistically significant. Overall, median length of stay (LOS) was significantly shorter by 17 days (QR: 11-24) in the remdesivir group, compared to 21 days (QR: 16-24) in the SOC group (p = 0.0485). Median LOS in the remdesivir group was only significantly shorter in those with moderate COVID-19 pneumonia but not in severe cases. Early administration of remdesivir resulted in a significantly shorter LOS with a median of 10 days (QR: 7-15) compared to 18 days (QR: 13-25) in the SOC group (p = 0.0240). When stratified by severity, there was no significant difference whether remdesivir was given early or late.

Conclusion: Remdesivir administration within 48 hours of admission in maintenance dialysis patients with moderate COVID-19 pneumonia resulted in a significantly shorter LOS. However, there was no significant difference in 28-day mortality in early or late administration of remdesivir in both moderate and severe COVID-19 pneumonia among HD patients. Thus, survival was similar to SOC. Our study showed that it is safe to use in dialysis patients.

Figure 1a: 28-day survival: Remdesivir versus SOC.
Figure 1b: 28-day survival among moderate COVID-19 cases: Remdesivir versus SOC.

Figure 1c: 28-day survival among severe COVID-19 cases: Remdesivir versus SOC.

Figure 2: 28-day survival: (a) Early vs Late Remdesivir Administration (n = 67), (b) Early vs Late Remdesivir Administration in moderate cases (n = 10), Early vs Late Remdesivir Administration in moderate cases (n = 57).

Table 1: Clinical outcomes among moderate-to-severe COVID-19 patients (n = 64).

<table>
<thead>
<tr>
<th></th>
<th>OVERALL</th>
<th>MODERATE COVID-19</th>
<th>SEVERE COVID-19</th>
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<tbody>
<tr>
<td></td>
<td>Remdesivir (n = 30)</td>
<td>SOC (n = 34)</td>
<td>P value^a</td>
</tr>
</tbody>
</table>

^ Only survivors were included in the analysis; ^ Mann Whitney U test was used

Table 2: Clinical outcomes by timing of remdesivir administration among moderate-to-severe COVID-19 patients (n = 37).

<table>
<thead>
<tr>
<th></th>
<th>Early n(%)</th>
<th>Late n(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of hospital stay (in days), median</td>
<td>10 [IQR: 7-15]</td>
<td>18 [IQR: 13-25]</td>
<td>0.0240^a</td>
</tr>
<tr>
<td>All patients</td>
<td>14 [IQR: 5-17]</td>
<td>17 [IQR: 13-19]</td>
<td>0.2530^a</td>
</tr>
<tr>
<td>Moderate COVID-19</td>
<td>9 [IQR: 7-15]</td>
<td>21 [IQR: 11.5-26.5]</td>
<td>0.0977^a</td>
</tr>
<tr>
<td>Severe COVID-19</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

^ Mann Whitney U test was used
#4881

NEPHROPROTECTION IN BOYS WITH X-LINKED ALPORT SYNDROME: THE SOONER THE BETTER

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Background and Aims: Proteinuric (Pr) is a marker of glomerular diseases progression. The aim of study was to define the efficiency of angiotensin-converting enzyme inhibitors (ACEi) treatment in prevention of Pr development in boys with X-linked Alport’s syndrome (XLAS).

Method: Single center observation study included boys with confirmed XLAS (n = 87). Twenty-nine pts (1gr) started ACEi (enalapril 4.2–4.4 mg/m²/day) in non-proteinuric stage of disease (Pr<100 mg/m²/day); mean age 6.2±3.9 yrs. eGFR Schwartz 118±15.2 ml/min/1.73 m², Pr 67±23 mg/m²/day. Fifty eight pts (2gr) without preemptive ACEi treatment were observed from mean age 6.8±4.9 yrs, eGFR 119±17.3 ml/min/1.73 m², Pr 87±43 mg/m²/day. Follow up was 6.2±5.9 yrs, mean age at the last observation was 11.7±3.9 yrs vs 14.2±4.6 yrs (p = 0.67) in 1gr and 2gr, respectively. The occurrence of Pr (Pr>100 mg/m²/day) was defined as primary end point of the study.

Results: The pts of 1gr had lower rate (0.48 vs 0.94, p =0.001) and higher age (10.2±3.9 vs 4.9±3.4 yrs, p = 0.3) of Pr occurrence than in 2gr. ACEi treatment reduced risk of Pr onset (OR = 0.059%CI 0.013-0.23) with absolute risk reduction of Pr by 47% (RD = 0.47) and number of treated pts to prevent Pr development (NNT) 2.14. No difference was revealed between 1gr pts with and without Pr development in age of therapy start (7.1±3.3 vs 6.3±2.8 yrs). ACEi dose (2.3±0.8 vs 2.1±0.6 mg/m²/day) and COL4A5 gene mutation type (missense variants 0.72 vs 0.86). Arterial hypertension was a risk factor of Pr occurrence in 1gr (x² = 4.42, p = 0.04); children with Pr development was older at the last observation: 13.5±3.2 vs 9.9±3.8 yrs, p = 0.47. No side effects of treatment were observed.

Conclusion: The early ACEi therapy halved the risk of Pr development in boys with XLAS and may prevent the disease progression in these patients.

#6041

THE IMMUNE EFFECTS OF SARS-COV-2 INFECTION AND BNT162B2 VACCINATION IN CKD PATIENTS AND TRANSPLANT RECIPIENTS

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Background and Aims: The use of vaccination against severe acute respiratory syndrome coronavirus (SARS-CoV-2) significantly limited the spread of the coronavirus disease 2019 (COVID-19) pandemic. However, it was reported that after 6 months of vaccination (including the BNT162b2 vaccine) immunity decreases in general population. The results for chronic kidney disease (CKD) patients and solid-organ transplant (SOT) recipients appeared similar. Therefore, it was proposed to use an immune booster with the next, third immunization scheme.

Methods: We retrospectively analyzed the data of randomly selected 40 patients (37 CKD and 4 livers) who received two or three 30 μg doses of BNT162b2 vaccine. The follow up was performed in five time points (TP1-5): 4–6 weeks after the 1st dose (TP1), 4–8 weeks after 2nd dose (TP2), 9–20 weeks after 2nd dose (TP3), 21–32 weeks after 2nd dose and 1–12 weeks after 3rd dose (TP4), 33–48 weeks after 2nd dose, at the same time 4–20 weeks after 3rd dose (TP5). We assessed the anti-SARS-CoV-2 spike 1 protein IgG antibody (anti-S1 Ab) titer as well as graft function, COVID-19 history and patients’ clinical condition.

Results: We found Ab titer in IgG group higher than in SOT patients (p = 0.05). LTRs achieved higher values than KTRs. 55 patients received 3 doses of vaccination. The protective level after the 3rd dose was not observed only in 8.4% at TP4 and 5% at TP5. We demonstrated the advantage in Ab levels of a 2 doses vaccination scheme with and without COVID-19 history over a 3 doses in a group of patients with no COVID-19 history in TP 1-4 (p =<0.001 – 0.005, respectively, Table1). Subjects in 2 doses schedule had a longer time to infection from the last dose compared to the 3 doses schedule (31.5-39 vs. 9 weeks, MD). No deterioration of renal or graft function was noted and no rejection episodes were diagnosed.

Conclusion: Immunocompromised patients are non-homogeneous with respect to the vaccine response immunity. Therefore, the approach to the vaccination schedule should be individualized based on measurements of vaccination response and medical history including COVID-19 history. Combined post-infectious and post-vaccination immunization appears to be the most effective in producing anti-SARS-CoV-2 responses.

#3156

REAL WORLD CHARACTERISTICS, SYMPTOM BURDEN AND TREATMENT PATTERNS OF ANAEMIA OF CKD IN EGYPT, SAUDI ARABIA, SOUTH AFRICA, AND TURKEY

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Background and aims: Patients with chronic kidney disease (CKD) often have comorbid anaemia [1]. Real-world data on patient characteristics, disease burden, and treatment management for people with anaemia of CKD in the Middle East and Africa are limited.

Methods: SATISFY (Survey on treatment patterns in Anemia of CKD, patient Treatment satisfaction and perspectives as reported by patients with pSySc1ans) was a real-world survey conducted between 01 June to 01 September 2022 in Egypt, Saudi Arabia, South Africa, and Turkey. Physician and patient perceptions of treatment were captured via cross-sectional surveys;
patients’ clinical characteristics were recorded by physicians in electronic case report forms via retrospective review of medical records. Eligible physicians were nephrologists with ≥1 years’ experience who managed ≥12 patients with anaemia of CKD per month and with drug management experience for anaemia of CKD. Physicians collected data on the first 7–10 patients seen in routine clinical practice during the study period. Eligible patients were ≥18 years with CKD stage 3b, 4, or 5 at the time of anaemia of CKD diagnosis and with ≥2 years’ follow-up data from diagnosis to time of survey. Patients with functioning kidney transplants or acute kidney injury were excluded. Primary outcomes were to describe clinical and demographic characteristics, monitoring test results, treatment patterns of patients with anaemia of CKD, physicians’ reasons for not treating anaemia of CKD, and physicians’ and patients’ reasons for therapy choice. Data were analysed descriptively.

Results: A total of 1788 patients and 217 physicians were included; 1138 patients (64%) were non-dialysis dependent (NDD) and 611 (34%) were dialysis dependent (DD) at the time of data extraction (n = 39 [2%] data missing). Mean (standard deviation [SD]) age was 46 (14) years, mean (SD) body mass index was 24.1 (3.1) kg/m², 56% (n = 1004) were male, and median (interquartile range [IQR]) follow-up from diagnosis of anaemia of CKD was 2.6 (2.5–3.2) years. The most common comorbidities were hypertension (n = 858, 48%) and diabetes (n = 324, 18%). Symptom burden was high, with lack of energy and fatigue among the most commonly reported symptoms by physicians and patients across both NDD and DD groups (Figure 1). Differences were seen between physician and patient symptom reporting and between NDD and DD groups. Patients’ self-reported symptom burden was greater than that reported by physicians, particularly for NDD patients. The median (IQR) times per year physicians reported testing CKD patients for anaemia was 4 (4–6) for NDD patients and 12 (10–12) for DD patients. Median test levels for haemoglobin at which patients were diagnosed were lower than those reported by physicians as being used for diagnosis; similar results were seen for thresholds used to initiate treatment (Table 1). Median (IQR) days from diagnosis to first treatment was 61 (0–419). Of those who received treatment, the most common first treatment option was erythropoietin-stimulating agents + intravenous iron for both patients with NDD and DD anaemia of CKD at diagnosis (NDD n = 291/736, 40%; DD n = 170/316, 54%). A large proportion of patients never received treatment for anaemia of CKD (n = 701, 39%). The most important reasons to not initiate treatment from a physician perspective were patient refusal (n = 172, 79%) and risk of adverse reactions (n = 168, 77%); for patients, top reasons were that their symptoms were not severe (n = 168, 22%) and their physicians’ concerns about adherence (n = 116, 15%). Similar reasons were seen for both the Middle East and Africa regions.

Conclusion: Symptom burden is high in patients with anaemia of CKD in the Middle East and Africa, particularly lack of energy and fatigue. Differences were seen between physician and patient perceptions of symptom burden and between NDD and DD groups. Substantial treatment inertia exists. Physicians rated patient refusal and risk of adverse reactions as main reasons for not treating patients, while patients attributed this to a belief that their symptoms were not severe.

REFERENCE
THE IMPACT OF MOBILE HEALTH ON HOME BLOOD PRESSURE AND HEALTH LITERACY IN CHRONIC KIDNEY DISEASE

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Background and Aims: Mobile health (mHealth) management is an emerging therapeutic strategy for chronic diseases. mHealth has been considered to improve self-care management and assist in detecting a worsening health status early. However, the effect of mHealth management on the blood pressure (BP) of patients with chronic kidney disease (CKD) has not been well-studied. This study aimed to access the association between mHealth management and BP control in CKD. We also investigated the association between mHealth and health literacy (HL) in CKD.

Method: Kaohsiung Medical University Hospital designed and developed a new healthcare mobile application called iCKD. The application has several major features, including BP monitoring, alarms, and a warning system. We randomly assigned 122 CKD patients stages 1-5 to utilize iCKD or paper records (control group) for BP management. The primary outcome was the portion of reaching the target goal, defined as office BP less than 130/80 mmHg, during the 6-month study. Trained nurses interviewed CKD patients using structured questionnaires to evaluate HL.

Results: Baseline kidney function and BP were not significantly different between iCKD and control groups. During the study period, 11 participants had withdrawal. 42.3% of the iCKD group (22/52) had the BP control reaching the target goal, while only 22.4% (11/49) in the control group (p = 0.03). Regarding HL, CKD patients with BP reaching the target goal had higher total scores than those without. The score for iCKD group, ranging from 29.29 to 32.85, were higher than the control group, ranging from 28.94 to 31.03. (p = 0.01).

Conclusion: The iCKD group had a higher proportion of reaching the BP target goal and better HL score than the control group. This study demonstrates that mHealth can improve the CKD population’s health literacy and BP management.

DIALYSIS

D1 - EXTRACORPOREAL TECHNIQUES & ADEQUACY

TOWARDS SUSTAINABLE HEMODIALYSIS: FIRST STEPS TO CHANGE THE PARADIGM

Marta Arias Guillen, Marta Quintela, Miquel Gomez, Nuria Clemente and Francisco Maduell

Nephrology Department, Hospital Clinic, Barcelona, Spain

Background and Aims: In the field of nephrology, environmental awareness is booming and we claim that it is responsible for our impact. Hemodialysis treatment generates an excessive burden owing to the high consumption of water and energy, as well as the production of a large amount of waste. On the part of the European Kidney Health Alliance (EKHA), several proactive suggestions have been proposed worldwide. To this regard, we implemented different improvements in our dialysis unit, including the reverse osmosis (RO) treatment plant automation upgrade. However, to change the paradigm, it was still necessary to first know the reality from which we start to identify opportunities for improvement. The objective of our study was to determine the environmental impact of care activities in our hemodialysis center over the last 5 years.

Method: A retrospective analysis of key environmental indicators derived from hemodialysis treatments, from January 2018 to December 2022 was performed. Energy consumption (KWh/dialysis), water expenditure (L/dialysis), technical operator (TO) required time as well as the generation of sanitary waste (SW, Kg/dialysis) derived from the activity were monitored according to their classification: GI (unspecific non-hazardous waste), GII (patient care non-hazardous waste such as disposable items, used empty bloodlines and hemodialyzers) and GIII (sharp material, needles or anatomical waste). All of these data were compared with the treatment sessions carried out during the analyzed period, and the costs of the environmental impact were calculated.
Table 1:

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2022</th>
<th>Relative Increment (%)</th>
<th>Estimated difference in Kg CO₂ eq.</th>
</tr>
</thead>
<tbody>
<tr>
<td>SW (Kg/dialysis)</td>
<td>1.45</td>
<td>2.12</td>
<td>46%</td>
<td>0.014</td>
</tr>
<tr>
<td>Energy (kWh/dialysis)</td>
<td>24.21</td>
<td>26.00</td>
<td>7%</td>
<td>0.38†</td>
</tr>
<tr>
<td>Water (L/dialysis)</td>
<td>459</td>
<td>370</td>
<td>−19%</td>
<td>−0.04‡</td>
</tr>
<tr>
<td>TO total time (hours)</td>
<td>486</td>
<td>92</td>
<td>−81%</td>
<td>−111+++</td>
</tr>
</tbody>
</table>

† excluding transmission and distribution losses.
‡ assuming supply and treatment factors combined.
+++ assuming a 3Km trip in a fueled medium sized-car for every 2 activity hours.

Results: Table 1 summarizes the average generated waste, energy and water expenditure as well as TO required working time at the beginning and at the end of the study period. Additionally, an estimated Co₂ footprint of each activity is calculated. The increase in SW was associated with a change in format of presentation of certain materials by the producer, which allowed the reduction of the hazardous GIII amount of waste as was reassigned to non-hazardous GI or GII group. Regarding the upgrade in the RO plant, a slight increase in energy consumption due to the implementation of improved sensors allowed a substantial reduction of water required (with a high 75% efficiency) and a prominent reduction of TO time needed and traveled distance, which severely reduced the environmental impact. In addition, the remotely monitored RO reduced TO costs by 7101 €/year and material resources by 2892 €/year.

Conclusion: The first step in achieving 'green' dialysis should be to measure key indicators that determine the environmental impact of our activity, establishing our standards to easily analyze the possible deviation factors. Technological improvements and the remotely monitoring in our water treatment plant have made water consumption more efficient and overall reduced the environmental impact. To address the viability of hemodialysis, we need to raise awareness among professionals to minimize the carbon footprint derived from our care activities, designing action plans to reduce the environmental impact such as:

1. Use of moderated dialyzer flows (<600 mL/min).
2. Post-treatment bloodline and hemodialyzer drainage to reduce waste weight.
3. Initiate both awareness campaigns and specific training on the correct management of waste, and assess the costs of waste management before the acquisition of new materials.
4. Potentiate home based treatments whenever possible.

CHARACTERISTICS OF PROTEIN LOSS WITH MEDIUM CUT-OFF MEMBRANES COMPARED TO HIGH FLUX MEMBRANES

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Background and Aims: Medium cut-off membranes (MCO) have been introduced with the claim that larger pores enhance the removal of middle-sized uremic toxins. To date, no adequately powered randomized controlled trial has demonstrated that this membrane characteristic translates into improved mortality. A well-described consequence of larger pore sizes is a higher dialytic albumin loss [1]. In addition, other proteins could also be lost with MCO, including ones that are beneficial or even essential, e.g., to patients’ nutritional status. To better understand the spectrum of proteins cleared with MCO, we set up an ex vivo HD simulation system and compared protein loss characteristics between MCO and high-flux (HF) dialyzers.

Method: Over the course of an hour, a single reservoir of 2.5 liters EDTA human plasma was ultrafiltered using two Fresenius 2008T machines. One machine served the MCO dialyzer (Theranova 400), the other the HF dialyzer (Fresenius Optilux F180NR). Ultrafiltrate (UF) was returned to the plasma reservoir (Figure 1A). Blood flow was 400ml/min, dialysate flow was zero, ultrafiltration rate was 13ml/min. UF samples were taken at ~10 min intervals. Upon experiment completion, residual filtrate was collected from the dialysate compartment. Samples were stored at ~80°C until analysis with Bradford protein assay, silver-stained SDS-Page, and Olink Proteomics (Watertown, MA). Selected samples underwent 3K MWCO protein concentration.

Results: Figure 1B shows the UF protein concentration at several time points. Total protein loss (in mg) during the one-hour simulation was 18 (HF) and 239 (MCO) in the UF, and 10 and 359 in the residual filtrate, respectively. SDS-PAGE protein gel revealed that HF filtrate contained less amount of protein than MCO filtrate when equal filtrate volumes were loaded (Figure 1C, lane 3 vs 2, lane 6 vs 5). All 10 proteins were above the limit of detection (LOD; Table 1). The MCO-to-HF protein concentration ratio in equal filtrate volumes ranged from 1.7 to 13.1.

Conclusion: Our results show a higher amount of protein loss with MCO compared to HF. The HF filtrate protein distribution is skewed towards lower molecular weights compared to MCO filtrate. All 10 proteins identified were more abundant in MCO filtrate compared to HF filtrate. Further identification and quantification of protein loss during hemodialysis

Figure 1: Protein analysis in the filtrate. A) Ex vivo hemodialysis simulation setup to compare synchronously protein loss with MCO and HF (red, arterial line; blue, venous line; gray, UF line). Multiple UF samples were collected during the simulation. Residual filtrate was collected after the simulation from the dialysate outlet of the dialyzer. B) Trend of UF protein concentration over time. C) SDS-PAGE gel analysis of protein distribution in plasma, UF, and residual filtrate.
Background and Aims: Hospital Clínico de Barcelona, Barcelona, Spain

Jose Jesus Broseta Monzo, Diana Rodríguez, Elena Cuadrado,

CONDUCTIVITY AND PLASMA SODIUM DURING HEMODIALYSIS MONITORS SWITCHING-INDUCED VARIATIONS IN

#6844

MONITOR SWITCHING-INDUCED VARIATIONS IN CONDUCTIVITY AND PLASMA SODIUM DURING HEMODIALYSIS SESSIONS

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Hospital Clinic de Barcelona, Barcelona, Spain

Background and Aims: Until the advent of the new monitors with sodium modules, the differences between prescribed and actual sodium have been little studied. And most dialysis centers have a fixed sodium prescription. However, the sodium gradient during sessions is one of the key factors in its balance in hemodialysis patients. Predialysis plasma sodium has an important interindividual but not intraindividual variability, which supports the hypothesis of reference sodium (setpoint). This work aimed to compare the impact of switching from the 5008 Cordiax monitor to the new 6008 Cordiax monitor on the actually measured conductivity and initial and final plasma sodium.

Method: A total of 106 hemodialysis patients were included. Each patient received two dialysis sessions in which only the monitor was varied. The variables collected were: concentrate, prescribed sodium and bicarbonate, real conductivity, initial and final plasma sodium measured by ionic dialysance, and the change in plasma sodium concentration during treatment (ΔPNa), which has been related to mortality when it exceeds 4 mmol/L, was calculated. The clinical research ethics committee of Hospital Clinic de Barcelona approved the present study.

Results: The change of dialysis monitor showed small, although significant, differences in initial (138.14 mmol/L with 5008 vs. 138.81 mmol/L with 6008) and final plasma sodium (139.58 mmol/L vs. 140.97 mmol/L), as well as in the actual conductivity obtained (13.97 vs. 14.1 mS/cm). The ΔPNa also increased significantly, with the percentage of patients with a ΔPNa greater than 4 mmol/L going from 6 to 22% with the monitor change. All these differences were statistically significant regardless of the concentrate used. All sessions were performed without notable clinical incidents, hypotension, cramps or thirst episodes.

Conclusion: The ultimate goal of hemodialysis should be to achieve isonatremia that allows complete elimination of interdialytic sodium gain and avoid intradialytic sodium loading. The change from 5008 to 6008 monitor is associated with an increase in conductivity, higher plasma sodium, and an increase in ΔPNa. Knowing and confirming this change will allow us to individualize the sodium prescription to find adequate isonatremic dialysis and, thus, avoid possible adverse effects.

#3989

INTERACTIVE-HD 2.0 PROJECT – PRELIMINARY RESULTS OF LUGANO DATABASE

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1 Politecnico di Milano, Department of Chemistry, Materials and Chemical Engineering “Giulio Natta”, Milan, Italy and 2 Ente Ospedaliero Cantonale, Ospedale Regionale di Lugano, Nephrology Unit, Lugano, Switzerland

Background and Aims: Computational models can be used in nephrology and dialysis divisions in order to predict the intradialytic trends of the main electrolytes, breakdown products, and body fluids volumes. However, predictive models need to be trained with consistent clinical data for a certain amount of HD sessions: if successfully trained, these models can be a useful support tool for a therapy customization, mainly needed for ESRD patients characterized by multiple comorbidities. Strength and limits of similar approaches have to be evaluated before their daily clinical use.

Methods: The multi-compartmental, multi-solute model optimized during the INTERACTIVE-HD 2.0 study needs to be trained with one week’s HD sessions, during which data machine and hourly blood compositions are given in input to the model itself. After the training, this model allows an accurate prediction of the patient’s response using only the clinical data recorded at the beginning of the therapy, not only in the same sessions used for the model training (ID mode) but also in independent sessions (PRED mode). The preliminary results refer only to the center of Lugano, in which 25 patients were enrolled and whose sessions were monitored in consecutive phases over a 7-month span (for a total of n = 292 sessions); model performance (stratified by age, presence of diabetes and heart disease or hypertension) has been evaluated in terms of normalized Root Mean Squared Error defined as follow:

\[
\text{nRMSE} = \sqrt{\frac{1}{N} \sum_{i=1}^{N} \left( \frac{y_{\text{cl},i} - y_{\text{mod},i}}{y_{\text{ref},i}} \right)^2}
\]

where the subscript \(i\) stands for the \(i\)th of \(N\) intradialytic acquisition time-points, while \(y_{\text{cl},i}\) and \(y_{\text{mod},i}\) refer to the clinically measured data of interest and to the model simulated ones, respectively; \(y_{\text{ref},i}\) is the variable of interest, i.e., electrolytes’ hematic concentrations. Inter-stratification variability in terms of model performance has been analysed via a Kruskal-Wallis test.

Results: From the results’ stratification, it can be observed a good ability of the model to describe all variables, with bias with respect to pathologies in the short term. From 2 months onwards, the presence of hypertension, alone (n = 23), or the presence of cardiovascular diseases, alone (n = 38), leads to an increase in the error. Error that is instead very limited in the main group of patients (n = 229). Regarding age groups’ stratification, all variables are well simulated in the short term; however, already at 2 months, it is highlighted an increase in the error only for patients under 70 years of age (n = 87). On the other hand, for patients older than 70 years (n = 203), the stratification shows more stability. Finally, regarding the stratification based on the presence of diabetes, it can be observed that glycaemia is no longer simulated well only in insulin-dependent patients (n = 75) compared to non-insulin-dependent patients (n = 89) around 5 months; in the case of insulin-dependent patients, for K+ and urea the model is not able to avoid some other phenomenon to be modelled as they are tracked with lower precision already in the short term.

Conclusions: The stratification highlighted that hypertensive patients should be reevaluated more often, preferably two months after the first training of the model. Moreover, it was observed that the most sensitive group is the
one with patients under 70 years of age, thus requiring re-evaluation, already at 2 months; on the other hand, for patients older than 70 years, in the absence of other pathologies, this re-evaluation can be postponed at least 7 months. Finally, the ability to simulate blood glucose is always acceptable in the 7 months, except for insulin-dependent patients in whom a re-evaluation between 2 and 5 months is necessary. Either way, given the general results and what the stratifications have evidenced, we claim the clinical effort is worth it and the model can represent an important support for clinical decisions.

#4298

**DOES STARTING RENAL REPLACEMENT THERAPY WITH INCREMENTAL HAEMODIALYSIS WORSEN OUTCOMES?**

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**Background and Aims:** Most patients start maintenance haemodialysis (HD) with a fixed dose of 3 HD sessions per week (3HD/Wk), regardless of their residual kidney function (RKF). This intense schedule is considered the “standard” or “conventional” modality (cHD). It is widely accepted, and no randomised controlled trial (RCT) has examined whether other less frequent schedules are inappropriate or harmful. Thus, the optimal modality for incident patients is currently unknown. Incremental HD (iHD), on the other hand, adjusts the frequency of sessions to the RKF, increasing their number to compensate for any subsequent reduction in RKF. While iHD approaches precision medicine by customising the number of sessions, it raises concerns about long intersession periods and the risk of under-dialysis. Pending ongoing RCTs [1], our aim is to analyse the efficacy and safety of iHD in our incident patients.

**Method:** The policy of our Centre is to try to start with iHD in incident patients who are clinically stable and with RKF. We start with 1 session (1HD/Wk) if the RKF is above 4 ml/min/1.73 m2 and with 2 sessions (2HD/Wk) if the RKF is between 2.5 and 4 ml/min/1.73 m2. We progress from 1HD/Wk to 2HD/Wk and from 2 to 3HD/Wk depending on the RKF and ultrafiltration rates required, which are assessed at least monthly. Since 2012, we have treated 186 incident patients with iHD, of whom 168 had a follow up ≥ 90 days. 72% (128 patients) started with 1HD/Wk and the remaining 28% (40 patients) with 2HD/Wk. We compared the results with 410 incident patients who from baseline receive 3 sessions/Wk (cHD) and with 80 incident patients on Peritoneal Dialysis (PD). We also analysed 27 iHD patients who after 60 days were already dialysed with 3 sessions (3HD/Wk/60d group). We calculated the mortality rate (deaths/365 days in %) in each group and survival in the iHD technique (sessions not performed).

**Results:** The mean age in the iHD group was higher than in cHD or PD (Table 1). Mortality in iHD patients was similar to cHD patients, although the latter were younger. Patients who stayed less time in iHD (3HD/Wk/60d group) had the highest mortality rate (Table 1). Survival in technique (time in which 50% of patients remain on iHD) was 12 months, avoiding 86 sessions/patient. The cost reduction was €17,200/patient (session + transport = €200).

**Conclusion:** iHD is efficient, as it considerably reduces the number of sessions performed and thus costs, thereby improving quality of life. It is safe, as it has a similar mortality rate to cHD. Being on iHD for more than 60 days does not worsen the results. On the contrary, requiring 3 weekly sessions at the beginning of HD treatment may be associated with a poor prognosis.

**REFERENCE**


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**Table 1: Data of the patients included according to their treatment modality.**

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Patients in treatment</th>
<th>Age M±SD</th>
<th>Years of treatment</th>
<th>Deaths</th>
<th>Annual Mortality Rate (in %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>iHD</td>
<td>168</td>
<td>71±12.4</td>
<td>492</td>
<td>63</td>
<td>12.80</td>
</tr>
<tr>
<td>1HD/Wk</td>
<td>128</td>
<td>71±10.3</td>
<td>362</td>
<td>47</td>
<td>12.98</td>
</tr>
<tr>
<td>2HD/Wk</td>
<td>40</td>
<td>71±12.9</td>
<td>130</td>
<td>16</td>
<td>12.31</td>
</tr>
<tr>
<td>3HD/Wk/60d</td>
<td>27</td>
<td>73±13.4</td>
<td>79.4</td>
<td>13</td>
<td>16.4</td>
</tr>
<tr>
<td>cHD</td>
<td>410</td>
<td>63.4±12.7</td>
<td>743.6</td>
<td>83</td>
<td>11.16</td>
</tr>
<tr>
<td>DP</td>
<td>80</td>
<td>59.2±13.5</td>
<td>178.71</td>
<td>14</td>
<td>7.83</td>
</tr>
</tbody>
</table>
NOVEL REAL-TIME PREDICTION SYSTEM FOR HYPOTENSION IN DIALYSIS COMBINING RISK INCIDENCE AND NUMERICAL PREDICTION MODEL

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Abstract: Although there have been many studies on the machine learning prediction model of intradialytic hypotension, the high prediction accuracy in the academic field needs to be transferred to the clinical environment to aid in medical professionals’ decision-making process. Before this clinical trial, our team built a data storage, edge computing, and decision support system. However, to achieve real-time decision support, real-time data transmission is also needed along with the system to achieve clinical decision needs. Therefore, this study aims to integrate the AI predictive model with edge computing to build an overall decision support system for intradialytic hypotension in the real-world clinical environment; we have developed a system architecture to deploy the system.

Method: Development of the IDH decision support system: We developed a complete IDH prediction system to be implemented in dialysis centers and hospitals, which incorporates patient data retrieval to AI prediction models to the web application and monitoring dashboard for medical professionals. The system architecture includes a bridge service used to retrieve the HIS database (patient history), DIS database (dialysis information), and NIS database (nursing care). The data is stored in a data warehouse and then converted into a structured format for AI model training and prediction. Furthermore, an API Server, a communication service for the database and front-end web, is used to present the warning signals in real-time. Lastly, there is a multi-bed monitoring dashboard presenting personalized patient information, the incidence rate of hypotension, and numerical prediction of the actual blood pressure value.

Design and validation of the online AI prediction model: The real-time AI prediction model is built through automatic machine-learning training, which retrains the model every week, utilizing the data of the past 180 days. The features of the input data include biochemistry lab data, nursing records, demographical characteristics, hemodialysis machine parameters and vital signs; it then uses the SMOTE method to fill in missing values and via RFECV to do feature extraction and selection. Lastly, the model is trained through improved RNN models of LSTM (Long short-term memory) and GRU (Gated Recurrent Unit) integrated with machine learning models of XGboost and LightGBM algorithms to generate a combination of binary classification and numerical prediction. Hypotension’s output label is defined when systolic blood pressure drops below 90 mmHg. Finally, the validation of the AI machine learning models for binary classification used accuracy score, specificity, and sensitivity, whereas the numerical prediction model used RMSE and MAE.

Results: With the implementation of the edge computing and decision support system, clinical and dialysis data of the patients upload directly to the data warehouse in real-time, and it presents the hypotension prediction information to the medical professional’s computer. As a result, the online real-time AI prediction system for the binary classification model yielded an accuracy score, specificity and sensitivity of 0.95, 0.99 and 0.86, respectively, and the RMSE and MAE yielded 17.5 and 11.6, respectively. Furthermore, the model predicted within 15 seconds to ensure a real-time and automatic parameters update.

Conclusion: Introducing and implementing this integrated intelligence AI prediction system reduces the occurrence of hypotension in dialysis, improves patient safety and satisfaction of patients, and enhances the work environment of medical professionals. Furthermore, this framework and validation can also be provided to home dialysis patients to improve their quality of care. In addition, this system architecture can also be extended to other medical conditions in developing intelligent decision support systems for practical clinical applications.

#3472 PRELIMINARY DATA FROM MOTHER HDx STUDY: A MULTICENTRE OPEN-LABEL RCT STUDY TO EXPLORE THE MORBIMORTALITY WITH THE THERANOVA HDx VS OL-HDF

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Background and Aims: Dialysis patients have a high rate of cardiovascular morbidity and mortality. For this reason, new technical advances are necessary to be introduced in clinical practice. Medium cut-off (MCO) membranes are a new generation of membranes that allow the removal of a greater number of medium-sized molecules compared to high-flux hemodialysis (HF-HD) but retaining albumin. Theranova, a MCO membrane has an increased permeability and also produces high convective volume in the form of internal filtration. For these special properties, MCO generated a new concept of therapy called expanded HD (HDx). Until now, online hemodiafiltration (OL-HDF) has demonstrated its superiority, in terms of survival, compared to HF-HD. But the comparison between OL-HDF and HDx is a question not solved.

Method: The MOTHéR HDx study trial (NCTO3714386) is an open-label, multicentric, prospective, 1:1 randomized, parallel-group trial designed to evaluate the efficacy and safety of HDx compared to OL-HDF in incident HD patients in Spain for up to 36 months. The main endpoint is to determine if HDx is non inferior to OL-HDF at reducing the combined outcome of all-cause death and stroke (ischemic or hemorrhagic), acute coronary syndrome (angina and myocardial infarction), peripheral arterial disease (amputation or revascularization) and ischemic colitis (mesenteric thrombosis).

Results: Now we have enrolled 513 patients, 44 excluded and 469 were randomized. 229 were allocated to HDx and 240 to OL-HDF. No differences were found in neither baseline characteristics, hemodialysis or pharmacological treatment, nor laboratory parameters. Follow up time was similar in both groups: 15.06 (12.8) vs 13.73 (11.51) months [HR 0.84 (0.50-1.40)] without differences in mortality: 29 (12.7%) vs 31 (12.9%) [HR 0.89 (0.54-1.48)] in HDx and HDF respectively (Figure 1).

Conclusion: These preliminary results from Mother study support that HDx is not inferior to OL-HDF in reducing the all-cause mortality outcome.

Figure 1: Data architecture of IDH decision support system.
### #5660

**ULTRAFILTRATION RATES IN INCIDENT PATIENTS ON INCREMENTAL HAEMODIALYSIS WITH 1 SESSION PER WEEK: ARE THESE RATES DANGEROUS?**

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**Background and Aims:** Most patients start haemodialysis (HD) with a fixed dose of three sessions per week, regardless of their residual renal function (RKF). This schedule is considered “standard HD or conventional HD” and is widely accepted without any randomised controlled trial (RCT) having examined whether other schedules with fewer sessions per week are inadequate or harmful. Incremental HD (iHD), by contrast, adjusts the number of sessions to the RKF, increasing the frequency to compensate for the drop in RKF. While iHD approaches precision medicine by customising the number of sessions, it raises concerns about the risk of under-dialysis and long intersession periods. In the absence of RKF, these long periods are associated with high weight gain (WGI), which leads to high ultrafiltration rates (UF rates). UF rates greater than 10 ml/kg/h are known to be associated with poor prognosis [1]. Pending ongoing RCT [2], our aim is to quantify WGI and UF rates in incident patients on iHD with a single weekly session (1HD/Wk).

**Method:** The policy of our Centre is to start with iHD in those patients with RKF and clinically stable. We start with 1HD/Wk if residual urea clearance (KrU) > 4 ml/min/1.73 m². We moved from 1 to 2, and from 2 to 3 sessions/week, depending on KrU and ultrafiltration rates. We analysed 2777 HD sessions of 66 incident iHD patients, with intersession period ≥ 6 days. Mean age was 73±12.5 years and 73% were male. WGI, rate UF and Blood Pressure (BP) pre- and post-HD were analysed for each session. We calculated the monthly dialysis dose using Solute Solver (www.ureakinetiQ.org). We considered an adequate dose if weekly stdKrU ≥ 2.1 or if EKRU + KrU ≥ 12 [3]. Pending ongoing RCT [2], our aim is to quantify WGI and UF rates in incident patients on iHD with a single weekly session (1HD/Wk).

**Results:** WGI was 1.47±1.3 kg (median 1.4), equivalent to ±1.5% of patient weight. According to BIS, pre-HD overhydration status was 1.9±1.6 (median 1.6L), similar to WGI. The UF rate, for each session, was 5.03±3.84 ml/kg/h (median 5). 9.1% of the sessions exceeded 10 ml/min/h and 2.6% exceeded 13 ml/kg/h. Pre-dialysis BP was 158±23/78±19 mmHg (median 157/76) and post-dialysis BP was 152±27/76±16 mmHg (median 150/75). RKF measured by urinary volume was 1931±491 ml (median 1900) and KrU was 5.1±1.8 ml/min/1.73m² (median 4.8). Dialysis dose was adequate, with a weekly stdKrU of 2.31±0.7 volumes (median 2.23) and EKR+KrU was 14.22±3.7 ml/min (median 13.8). Nutritional status as measured by PCR was 1.04±0.3 g/kg/day (median 1). LTI index at BIS was 12.1±4.8 kg/m² (median 12), desirable >10.5, and FTI index was 12.8±8 kg/m² (median 14), desirable >7.

**Conclusion:** Patients on iHD do not present large weight gains, nor are they subjected to high UF rates, avoiding significant changes in their BP during HD sessions. On the contrary, RKF allows them to maintain a low number of weekly sessions without presenting volume overload, underdialysis or malnutrition.

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### #6768

**TIO2/TI3C2 NANOCOMPOSITES FOR BILIRUBIN CLEARANCE FROM BLOOD**

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**Background and Aims:** The artificial liver treatment based on blood purification is an important and commonly used treatment for liver failure. Aggressive management of hyperbilirubinemia is one of the key steps to reduce mortality in patients with liver failure. Herein, targeting bilirubin in nanosized, we synthesized a TiO2/Ti3C2 nanocomposite from Ti3C2 MXenes via hydrothermal oxidation for bilirubin clearance from whole blood.

**Method:** Firstly, Ti3C2 MXene was prepared by hydrofluoric acid etching method reported in our previous work [1]. Then, it was transferred into Teflon-lined stainless-steel autoclaves (2 mg/ml, 30 ml) and was undergone the hydrothermal process at 180 °C for 6 h and 12 h. TiO2/Ti3C2 nanocomposites were obtained after lyophilization. Hemocompatibility evaluation assays include hemolysis ratio test, complement activation (human complement fragment 5a (C5a)), contact activation (Thrombin–anti-thrombin (TAT) complex) and platelet activation (platelet factor 4 (PF 4)) were systemically conducted in vitro to evaluate the feasibility of the novel nanocomposites (0.5 mg/ml) in contact with blood. We evaluated the bilirubin adsorption capacity of original Ti3C2 (0 h) and TiO2/Ti3C2 (6 h and 12 h) at the concentration of 0.5 mg/ml, respectively, in bilirubin solution (250 mg/L 10 ml) for 2 h at 37 °C in an air bath away from light. The sphere-forming properties of TiO2/Ti3C2 with polyethersulfone (PES), a commonly used blood purification material, were first verified using a liquid-liquid inversion method.
Figure 1: The hemocompatibility evaluation assays of the original Ti3C2 (0 h) and TiO2/Ti3C2 (6 h and 12 h) in vitro. (a), Haemolysis ratio and digital photos. (b), CSa levels after incubation of Ti3C2 (0 h) and TiO2/Ti3C2 (6 h and 12 h) in whole blood. (c), TAT levels after incubation of Ti3C2 (0 h) and TiO2/Ti3C2 (6 h and 12 h) in whole blood. (d), PF4 levels after incubation of Ti3C2 (0 h) and TiO2/Ti3C2 (6 h and 12 h) in whole blood.

Results: TiO2/Ti3C2 (6 h and 12 h) showed better hemocompatibility than the original Ti3C2 (0 h) (Figure 1). The bilirubin adsorption capacities by the original Ti3C2 (0 h) and TiO2/Ti3C2 (6 h and 12 h) were 354.11 mg/g, 492.83 mg/g and 492.52 mg/g, respectively. From the original Ti3C2 (0 h) to TiO2/Ti3C2 (6 h), the clearance rate of bilirubin improved from 70.82% to 98.57%. Therefore, we chose TiO2/Ti3C2 (6 h) to verify the sphere-forming properties of TiO2/Ti3C2 with PES. TiO2/Ti3C2-PES spheres were constructed successfully by a liquid-liquid inversion method. More 3D porous structure was observed via a scanning electron microscope (SEM) images and energy dispersive spectroscopy (EDS) mapping images (Figure 2).

Conclusion: The TiO2/Ti3C2 nanocomposite showed excellent bilirubin clearance capability, superior hemocompatibility, and the great application potential in the form of spheres for hemoperfusion, which may provide a promising choice in the performance enhancement of artificial liver.

REFERENCE
**Table 1**: Concentrations of biocompatibility markers prior to and after 15 minutes of expanded hemodialysis with regional citrate anticoagulation and unfractionated heparin.

<table>
<thead>
<tr>
<th></th>
<th>Prior to HDx with RCA</th>
<th>After 15 min of HDx with RCA</th>
<th>Prior to HDx with UFH</th>
<th>After 15 min of HDx with UFH</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3a (µg/L)</td>
<td>276.2 (IQR 218.4-333.7)</td>
<td>253.7 (IQR 211.6-293.8)</td>
<td>256.2 (IQR 226.3-313.1)</td>
<td>345.9 (IQR 288.0-415.7)</td>
</tr>
<tr>
<td>MPO (µg/L)</td>
<td>28.6 (IQR 13.9-45.3)</td>
<td>21.9 (IQR 8.7-34.8)</td>
<td>39.4 (IQR 18.4-57.8)</td>
<td>80.7 (IQR 40.2-161.4)</td>
</tr>
<tr>
<td>PF4 (IU/mL)</td>
<td>46.5 (IQR 17.3-96.8)</td>
<td>19.4 (IQR 8.7-41.4)</td>
<td>16.5 (IQR 9.3-44.0)</td>
<td>123.4 (IQR 55.9-161.3)</td>
</tr>
</tbody>
</table>


deposition on the membrane with comparable clotting score: 2 (IQR 1-3) for RCA vs. 2 (IQR 1-2.25) for UFH (p = 0.40).

**Conclusion**: Given the higher activation of complement, leukocytes and platelets during HDx with UFH, we conclude that RCA offers superior biocompatibility compared to UFH during HDx. Whether improved biocompatibility has clinical relevance remains to be explored.

**REFERENCE**


**#2704**

**MANAGEMENT OF HAEMODIALYSIS PATIENTS UNDERGOING RADIOACTIVE IODINE THERAPY FOR THYROID CANCER**

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**Background and Aims**: Radioactive iodine (RAI) 131I is used in the adjuvant treatment of thyroid carcinoma following thyroideectomy. 131I is renally excreted, with reduced clearance in patients with end-stage kidney disease (ESKD). There are no established protocols for RAI dosing, timing of dialysis and safety in this population [1]. We describe a single-centre experience with a modified protocol and setup for RAI in haemodialysis (HD) patients including serum 131I measurements to monitor for red marrow toxicity. We present the outcomes in two HD patients.

**Method**: A protocol was developed for performing HD post-RAI administration. HD sessions were performed at 24, 72 and 144 hours post-treatment. Custom HD plumbing was installed within existing lead-lined infrastructure. Specific considerations were made for radiation safety including emergency protocols, handling of blood samples, nursing education, patient self-cannulation and dose-reduction of thyrogen pre-treatment. In addition to standard dose-rate meter measurements of radiation, serum 131I measurements were taken pre- and post-HD as a more accurate measurement of red marrow toxicity.

**Results**: The two patients included in the study were aged 41 and 60 years. Special considerations for these patients included anuric state in one patient (bilateral nephrectomy) and morbid obesity in the other. Both had early-stage papillary thyroid cancer treated with thyroideectomy. Retained radioactivity measured by dose-rate meter is shown in Figure 1. The largest reduction in radioactivity occurred after the first HD session (approximately 60%). The highest risk of radiation exposure was in the 24 hours prior to the first HD session. Pre-and post-HD serum 131I measurements estimated the radiation dose to red marrow to be below 0.2Gy (maximum tolerated radiation dose for red marrow is 2.0Gy2). Radiation received by HD nurses is shown in Figure 2. Overall exposure was well within national regulatory dose limit of 0.5mSv for members of the public.

**Conclusion**: HD at 24, 72 and 144 hours produced a radiation clearance profile similar to controls with normal renal function. The effect of residual renal function on 131I clearance was minimal and HD was the main determinant of 131I clearance in ESKD. Non-routine serum measurements of 131I can be used to assess toxicity to red marrow and guide HD session timing during RAI therapy. Performing HD at 24 and 72hrs post- 131I resulted in a radiation burden to the red marrow well below the accepted radiotoxicity threshold of 2Gy [2]. RAI can be given safely to HD patients with thyroid cancer in centres with the appropriate protocol and setup.

**REFERENCES**


Figure 1: Retained radioactivity (%) over time (hours) in patients 1 and 2 (red and blue plots) compared with controls with normal renal function (grey plots).

Figure 2: Nursing staff radiation exposure by HD session (session 1, 2 and 3 corresponds to HD at 24, 72 and 144 hours respectively). Safety threshold indicated by red dotted line (0.5mSv).
LESS MICROBUBBLES ENTERED THE PATIENTS USING THE VENOUS CHAMBER EMBOLESS DURING HEMODIALYSIS
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**Background and Aims:** The extracorporeal circuit (ECC) enables haemodialysis (HD) of patients. Air contamination of the blood appears when it passes the ECC and consequently microemboli (MBs) enter to the patient [1]. MBs were verified at autopsy of HD patients and covered by clots as microemboli deposited within tissue from lungs, heart and brain [2]. A venous chamber is inserted in the ECC to reduce contamination of MBs. However, chambers in clinical use have limited capacity to eliminate MBs from entering the return bloodline. In an in vitro preclinical study the Emboless chamber showed best results compared to common models in clinical use; the best of those was for Fresenius 5008 [3]. We compared if the venous chamber Emboless differs in capacity to limit MB exposure from the original venous chamber of Fresenius 5008 (F5008).

**Method:** Thirty-eight HDs were performed as 19 paired HD sessions. Eleven patients were included. Venous chambers used were either F5008 or Emboless, in a randomised order. Dialyzers, blood-pump speed, HD or HDF and ultrafiltration was kept similar between the pairs. Microembobles were measured at the ‘Inlet’ and ‘Outlet’ of the venous chamber with an ultrasound device adjusted for HD (hil mode, BCC200, GAMP3PT). Measurements were made for MBs between all sizes 20μm-500μm diameter. If HDF was performed the first 30min measured were by HD and the subsequent 30min by HDF (extended time if less than 1000 detected inlet MBs). The percentage of change in ‘Outlet’ versus ‘Inlet’ counts were compared (paired Wilcoxon test). Total reduction was 100% while increase of MBs (worsened) caused unlimited (+) percentage. If a diameter was without counts it was not included in the analysis.

**Results:** The median overall change of MBs were for F5008 −33% (mean −20 ±76%, N = 8544) and for Emboless −69% (mean −56 ±54%, N = 8402; and pairwise N = 8093; p<0.001). The Table 1 shows more results.

**Conclusion:** Less MBs and subsequently less microemboli entered to the patient using the EmbolessTM compared to using the Fresenius 5008 venous chamber during haemodialysis. Considering our previous autopsy studies this supports less tissue damage of the patients using EmbolessTM.

**REFERENCES**

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**#5831**

LIGHT CHAIN REMOVAL IN MULTIPLE MYELOMA PATIENTS WITH HFR-SUPRA HEMODIALYSIS: OUR EXPERIENCE
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Hospital Universitario Virgen Macarena, Sevilla, Spain

**Background and Aims:** Kidney injury is a common complication in multiple myeloma (MM) and it has a negative prognostic implication. Most common cause of Acute Kidney Injury (AKI) in these patients is Light chain Cast Nephropathy, where free light chains precipitate in the tubules and bind with uromodulin, turning into intratubular casts that obstruct the tubules and also promote local giant cell reaction and interstitial inflammation and fibrosis. Free light chains (FLCs) can also damage the kidneys due to direct tubular toxicity when excessive amounts are reabsorbed by the proximal tubules. Targeted therapy to reduce FLC load can help recover renal function. Both total reduction and reduction speed are relevant for prognosis. FLC removal through extracorporeal techniques can be used as an adjuvant therapy, having an important part on the evolution of the disease. We gathered data from our experience treating MM patients with AKI with HFR-supra hemodialysis (HD) and analyzed the evolution and possible influence of this technique on renal recovery.

**Method:** This is an observational retrospective study. We included all patients with a diagnosis of multiple myeloma and acute kidney injury who received HFR-Supra hemodialysis in between years 2016-2022 in Hospital Virgen Macarena (Seville). We initially performed 6-10 daily HFR-Supra HD sessions and then modulated the frequency based on renal response (if renal replacement therapy had to be continued they underwent a usual hemodialysis regime 3 days a week). We continued these sessions until renal recovery was achieved or free light chain levels were reduced in agreement with the Hematology team. Measurement of pre and post dialysis FLCs was made always at first and last session and at least once in between, depending on the total number of sessions.

**Results:** 12 patients, with mean age at diagnosis 63.6 (43-86) years, presented with AKI stage KDIGO 3. 1 of them was oliguric. Median serum creatinine at diagnosis was 4.4 mg/dL [2.2-17], mean proteinuria was 4.1g/24h [0.7-8.7] and 66.7% had positive Bence Jones proteinuria (mean 2.3g/24h). 2 of the patients had previous chronic kidney disease stage 3a. All of them were diagnosed with Light Chain Multiple Myeloma (75% kappa, mean 10346 mg/L; 25% lambda, mean 5990 mg/L). Mean clonal bone marrow plasma cell was 20.7% [2-55]. According to the Revised International Staging System (R-ISS), 25% were stage 2 and 75% were stage 3. Renal biopsy was performed in 4 patients, all showed evidence of Cast Nephropathy. The indication for starting HFR-Supra HD was FLC removal in 9 patients, need of renal replacement therapy in 1 and both in 2 patients. We have experience in our center with using this therapy as an adjuvant treatment and often we start the technique in patients who present with AKI but would not necessarily have immediate need for renal replacement therapy. The goal is to remove FLCs and avoid further damage to the kidney tissue. Out of the 12 patients, 9 were able so stop dialysis (75%). They received an average number of 12,4 [3-41] sessions in 3,7 [0,2-25] months). Free light chain removal per session was 24% on average [5-43%]. All of them were started on bortezomib-dexamethason regime as initial chemotherapy for...

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Table 1:

<table>
<thead>
<tr>
<th>Size group</th>
<th>Chamber</th>
<th>N=</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Min.-Max.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small (20-199μm)</td>
<td>Emboless</td>
<td>3417</td>
<td>−42</td>
<td>43</td>
<td>−50</td>
<td>−100 + 350</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>F5008</td>
<td>3410</td>
<td>−2</td>
<td>65</td>
<td>−14</td>
<td>−100 + 650</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medium (200-299μm)</td>
<td>Emboless</td>
<td>1837</td>
<td>−57</td>
<td>51</td>
<td>−73</td>
<td>−100 + 400</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>F5008</td>
<td>1831</td>
<td>−19</td>
<td>74</td>
<td>−36</td>
<td>−100 + 900</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Large (300-500μm)</td>
<td>Emboless</td>
<td>3100</td>
<td>−71</td>
<td>63</td>
<td>−100</td>
<td>−100 + 900</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>F5008</td>
<td>3255</td>
<td>−40</td>
<td>83</td>
<td>−67</td>
<td>−100 + 900</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The Table shows values when divided into MB diameter size groups. P-value represent paired test. N represents the numbers of measurements.
MM. As per renal recovery, at 3 months 33.3% achieved complete response, 11.1% partial response and 55.6% minimal response. At 1 year, 42.9% achieved complete response, 14.3% partial response and 42.9% minimal response. One-year survival rate was 91.7% (1 patient died from respiratory sepsis less than 1 month after diagnosis).

**Conclusion:** HFR-Supra hemodialysis achieved a 24% free light chain removal per session on average. After presenting severe AKI (KDIGO 3), almost 43% of patients who received this adjuvant therapy obtained full renal recovery at 1 year and in 75% of patients withdrawal from hemodialysis was possible. 1 year survival was 91.7%.

**#3205**

**A 2-YEAR STUDY FOR CHANGE OF PLASMA BIOMARKERS INCLUDING LARGER MIDDLE MOLECULES IN DIALYTIC PATIENTS USING DIALYZERS WITH MEDIUM CUT-OFF MEMBRANES**

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**Background and Aims:** Uremic toxins with middle molecular weight usually develop uremic symptoms. The larger middle molecules are regarded as causative molecules of uremic symptoms. Medium cut-off (MCO) membrane newly developed can remove larger middle molecules which can be not removed through high flux membrane and hemodiafiltration. Larger middle molecules are mainly related to cardiovascular complications. Therefore, long-term use of MCO membrane may have beneficial effects in dialytic patients, in terms of lowering concentrations of larger middle molecules associated with cardiovascular complications. Now, we report interesting 2-year results of long-term use of MCO membrane in dialytic patients.

**Method:** Thirty-four patients undergoing hemodialysis were prospectively analyzed during 24 months. We randomly divided enrolled patients into two groups: control and MCO group. Patients in the control group used dialyzer with high flux membrane and patients in MCO group used MCO membrane.

We measured plasma levels of biomarkers with 3 or 6-month to investigate efficacy of the MCO membrane for small (3-month interval) to larger middle molecules (6-month interval). Particularly, we performed comparative analysis with larger middle molecules in both groups. We calculated reduction ratio of biomarkers per one session at 24-month.

**Results:** The levels of larger middle molecules at baseline did not show significant difference between two groups. However, compared with the control group, plasma sclerostin levels at 6-month and 12-month in MCO group did not increased significantly compared to baseline levels. Plasma sclerostin were lower in MCO group throughout 2 year, but the significant difference of plasma sclerostin levels between two groups unfortunately disappeared after 12 months. The levels of other biomarkers including FGF23, leptin and GDF15, also did not show significant difference between two groups. However, β2MG levels in MCO group compared to control group decreased significantly throughout 2 years (MCO group: 18-month, p = 0.001 and 24-month, p < 0.001, respectively; control group: 18-month, p = 0.003 and 24-month, p < 0.001, respectively). Interestingly, even in MCO group, there was no statically significant decrease in total protein and albumin levels after 24 months (p = 0.429 and p = 0.101, respectively) (Figure 1). The reduction ratio of larger middle molecules compared to small molecules per one session prominently increased in MCO group (sclerostin, p < 0.001; GDF15, p < 0.001; FGF23, p < 0.01; RBP4, p < 0.01; phosphate, p = 0.821; calcium, p = 0.827; CRP, p = 0.729 and β2MG, p = 0.286, respectively) (Figure 2).

**Conclusion:** Conclusively, in MCO group, the significant change of plasma sclerostin associated with cardiovascular complications after 12 months disappeared. However, in MCO group compared to control group, there was a continuous decrease of β2MG and RBP4 throughout study period. In addition, the clearance of larger middle molecules is also prominently high in MCO group. Interestingly, there were also no significant differences of albumin between 24-month and baseline in MCO group. Therefore, the MCO membrane can be a good tool for controlling uremic symptoms or sings without protein loss even when used for a relatively long time in dialytic patients.

Figure 1: The change of serological markers during 2-year treatment.
DIALYSATE SODIUM: IS IT STILL MYTH OR NOT?
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Background and Aims: Pre-hemodialysis serum sodium levels can vary among patients, therefore, a single dialysate sodium prescription may not be appropriate for all patients. The aim of the study was to investigate whether dialysis patients will have some beneficial effects of prescription of different models of dialysate sodium.

Method: 77 nondiabetic subjects performed 12 months hemodialysis (HD) sessions with dialysate sodium concentration set up at 138 mmol/L, followed by additional 4 models of dialysate sodium (each one 4 months sessions lasted) wherein dialysate sodium was set up: model 1: according to pre-hemodialysis serum sodium concentration, model 2: sodium concentration in UF fluid, model 3: sodium profiling (144-136 mmol/L, every hour decreasing of dialysate sodium during dialysis), model 4: stepwise dialysate sodium (starting dialysis with a dialysate sodium of 138 mmol/L and reducing it every week by 1 mmol/L sodium for the next 4 weeks). Blood pressure (BP), interdialytic weight gain (IDWG), thirst score, sodium gradient were analysed. After the standard dialysate sodium hemodialyses, the subjects were divided into normotensive, hypertensive and hypotensive based on the average pre-hemodialysis systolic BP during the standard dialysate sodium hemodialyses.

Results: Model 1: resulted in significantly lower BP (153.60±14.26 versus 133.61±11.88 mmHg; p = 0.000) and IDWG (2.21±0.93 versus 1.87±0.92 kg; p = 0.018) in hypertensive patients, whereas normotensive patients showed only significant decrease in IDWG (p = 0.004). Hypertensive patients had significant highest sodium gradient compared to other patients (p<0.05), followed by significant increase of 0.6% IDWG confirmed with univariate regression analysis. Thirst score was significantly lower in all patients with individualized-sodium HD and no relationship between the sodium gradient and the subjective feeling of thirst was confirmed (p = 0.368). Model 2: resulted in significantly lower BP in normotensive and hypertensive patients, with no influence on IDWG and thirst score compared to standard dialysate sodium (p = 0.474 and p = 0.212, retrospectively). Patients who were hypertensive, due to frequent collapses and unmeasurable blood pressure values, as well as for ethical reasons, were excluded from analysis with this dialysate sodium model. Model 3: confirmed significantly higher BP and IDWG in all 3 groups (p = 0.006) and significantly higher thirst score in normo and hipotensive patients (p = 0.000), with no influence in hypertensive patients. Model 4: significant decrease in SBP and DBP in hypertensive patients and insignificant increase in IDWG, but with no effects in normotensive and hypotensive patients on BP, IDWG and thirst score.

Conclusion: Model 1 resulted in better clinical outcome in hypertensive and normotensive patients compared to standard dialysate sodium, whereas other 3 models didn’t show any clinical benefits.

THE APPLICATION OF MODERN MEDICAL INFORMATION SYSTEMS WITH ARTIFICIAL INTELLIGENCE ELEMENTS FOR PERSONALIZED TREATMENT OF PATIENTS ON HEMODIALYSIS
Evgeny Shutov1,2, Stepan Bolshakov3 and Galina Kotlyarova3

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Background and Aims: The quality of life and survival of patients on hemodialysis significantly depend on modern technology. Treatment requires control of dynamically changing large volume of data, which must be analyzed and interpreted in real time. Achieving the ideal balance between adequate fluid removal, effective dialysis dose, and low risk of adverse events on the hemodialysis procedure is a complex multifactorial problem. The heterogeneity of the dialysis population, comorbid burden, the use of concomitant medications, nutritional status and adherence to diet, patient compliance are a noncomplete list of factors that must be considered when setting the dialysis regimen. Thus, despite significant progress in the technical aspects of the “artificial kidney devices”, personalization of the treatment regimen remains an important and difficult task. Introduction of modern automated medical information systems (MIS) for management of treatment and diagnostic process can provide invaluable assistance in treatment process and improve treatment outcomes. The aim of our study was to improve the prevention and treatment of hemodynamic disorders in hemodialysis patients using a special own program “Maximus”, which collects and analyzes indicators from dialysis machines in real time.

Method: The study was conducted from May to November 2022. The study included 120 patients on hemodialysis. The average age of the participants was 62.3±23.4 years. All participants underwent bioimpedance testing with a hydration score (InBody S10) compared to the prescribed dry weight at inclusion. A total of 9360 hemodialysis procedures (all HDF) were analyzed. The data of all procedures were collected directly from dialysis machines and analyzed in MIS in real time, identifying deviations from the target values. Episodes of both hypertension (140/90 mm Hg) and hypotension (100/60 mm Hg) were considered. MIS analyzed the actual duration of the procedure, blood flow rate, volume of fluid removal, rate of ultrafiltration and level of Na. In case of deviations from the established normal values, the system actively notified the doctor (via SMS/messengers) about detected deviations and proposed solutions. The medical staff timely corrected dry weight, duration of procedures, UF rate, volume of fluid removal, sodium content and blood pressure.

Results: In patients with arterial hypertension (63% of patients), mean systolic BP decreased by 12±6 mmHg and diastolic BP by 10±8 mmHg before dialysis procedure. In this group mean systolic BP decreased by 11±10 mmHg and diastolic BP by 9±8 mmHg during the procedure of hemodialysis. In patients with hypotension, due to “dry weight” increase, correction of Na level,
stabilization of BP level was achieved, and mean systolic BP increased by 14±5 mmHg, and diastolic BP by 9±5 mmHg before dialysis procedure. Correction of hemodynamically significant parameters led to a decrease in the incidence of both intradialytic hypotension and hypertension during the hemodialysis procedure.

Conclusion: Correction of treatment, carried out using MIS with SMS notification of medical staff, improved hemodynamic parameters. Modern medical information systems with a Decision Support System can improve the quality and efficiency of treatment, reduce the risk of cardiovascular complications in patients on hemodialysis.

#5115
8-ZONE LUNG ULTRASOUND AND BIOIMPEDANCE ANALYSIS FOR ASSESSMENT OF HYDRATION STATUS IN HEMODIALYSIS: A PROSPECTIVE SINGLE CENTRE EXPERIENCE

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Background and Aims: Chronic volume overload is a major contributor to cardiovascular mortality in patients receiving maintenance hemodialysis (HD). Hence, accurately assessing volume status in this population is crucial. Bioelectrical impedance analysis (BIA) is a validated, non-invasive, and straightforward bedside technique that estimates total body water (TBW), extracellular water (ECW), intracellular water (ICW), and over hydration (OH). However, it is not suitable for use in patients with limb amputation or metallic medical devices. On the other hand, lung ultrasound (LUS) is used to evaluate extravascular lung water (EVLW) and has been shown to predict all-cause mortality and cardiac events in HD patients. Although a 28-zone LUS is the reference standard for LUS studies, recent studies have shown that an 8-zone LUS protocol can be as accurate. The aim of this study was to compare the performance of an 8-zone LUS protocol with bioelectrical impedance analysis to evaluate hydration status in an outpatient haemodialysis unit.

Method: Adult patients under thrice-weekly 4h HD sessions using high-flux membrane dialyzers for at least 1 month were prospectively enrolled between June and August 2022. We excluded patients with systemic infections, advanced neoplasia, metallic medical devices, decompensated cirrhosis, and limb amputations. The dry weight (DW) was established by the attending nephrologist, blind to the results. All measurements were performed in the first session of the week. BIA was assessed before HD using a portable whole body BIA device (BCM—Fresenius Medical Care D GmbH) and the OH was normalized to ECW. LUS using 8-zone protocol was performed before and after HD, with patients in the near-to-supine or supine position using a 2–5 MHz convex probe (Acuson X150®), Siemens, Germany), and the total number of B lines was recorded.

Results: A total of 37 patients with median age of 60 (IQR 15) years, 75% males, 65% with residual diuresis >300 mL/24 h were included. The median HD vintage was 9 (IQR 10) months, and median body mass index (BMI) of 22.7 (IQR 9) Kg/m². At the beginning of HD, the median systolic blood pressure (BP) was 140 (IQR 24) mmHg and the median diastolic BP was 79 (IQR 16) mmHg. The median interdialytic weight gain was 4.2% (IQR 2.8%) and median ultrafiltration (UF) was 2600 (IQR 1300) ml. The BIA showed median TBW of 38.2 (IQR 11) L, ECW 18.2 (IQR 7.73) L, ICW 20.8 (IQR 6.55) L, and normalized OH 0.138 (IQR 0.147). There was a positive correlation between BMI, TBW (r = 0.375, p = 0.045), and ECW (r = 0.486, p = 0.006), but not with ICW (r = 0.061, p = 0.755), nor normalized OH (r = 0.14, p = 0.468). Systolic BP, but not diastolic, was correlated with the water volume measured in both compartments (ECW: r = 0.498, p = 0.005; ICW: r = 0.421, p = 0.023, TBW: r = 0.423, p = 0.022). The 8-zone LUS showed a statistically significant (p<0.001) reduction in the number of B lines between pre and post HD evaluation (16.5 (IQR 17.25) lines to 8.5 (IQR 10.25) lines). Total evaluation time was under 8 minutes. When comparing LUS before HD with BIA assessment we found that the number of B lines correlated with the normalized OH (r = 0.454, p = 0.018), ECW (r = 0.501, p = 0.007), TBW (r = 0.418, p = 0.030), but not ICW (r = 0.239, p = 0.23). The total number of B lines post HD was also correlated with the ECW (r = 0.568, p = 0.002), TBW (r = 0.465, p = 0.017), and normalized OH (r = 0.408, p = 0.039).

Conclusion: The 8-zone LUS protocol provides a quick and efficient way to evaluate patients prior to HD sessions. Our study reveals a strong correlation between the total number of B lines determined by the 8-zone protocol and BIA parameters such as TBW, ECW, and normalized OH. This demonstrates that the 8-zone protocol can effectively be used in routine evaluations of HD patients. Although these techniques reflect different over-fluid compartments, they have a complementary role for fluid overload determination and dry weight guidance.

#4107
THE ROLE OF CYTOKINE ADSORBER IN REDUCTION INTERLEUKIN-6 LEVELS: A MATCHED CASE-CONTROL SINGLE CENTER ANALYSIS

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Background and Aims: Extracorporeal cytokine adsorption is used with the aim to reduce pathogenic levels of cytokines in critically ill patients. Although technically and theoretically plausible, little convincing data exist to support wide use of cytokine adsorber in clinical practice. We aimed to retrospectively compare the time course of interleukin-6 (IL-6) in patients treated with or without the adsorber (CytoSorb®).

Method: In this retrospective, case-control study all patients treated between Jan 2017 and Dec 2021 in a medical ICU were screened and included, if at least two IL-6 measurements were available. Patients were divided to adsorber group and standard of care group based on the treatment received. Unmatched and matched groups were compared regarding IL-6, lactate, CRP, procalcitonin, and vaspessor demand at predefined time points. Mortality rates were also compared.

Results: We screened 3865 patients and included 52 patients in the adsorber group and 94 patients in the standard of care group. After matching, there were 21 patients in each group. Patients had similar age (53 (41, 68) vs. 61 (56, 67) years), ECMO was used in 24% (both groups) and renal replacement therapy in 100% of patients (both groups), baseline noradrenaline requirement (0.04 vs. 0.03 mg/kg/h), serum lactate (6.8 vs. 5.4 mmol/l), pH (7.27 vs. 7.21), CRP (182 vs 167 mg/l), and IL-6 (2441 vs. 2552 ng/l) were comparable between adsorber group and SOC group. There were no significant differences in the time course of IL-6, lactate, CRP, procalcitonin, and noradrenaline requirement between the groups. Two-day (33% vs. 28%) and ICU (57% vs. 62%) mortality and Kaplan-Meier survival curves (log-rank p = 0.9) were comparable.

Conclusion: In our matched case-control study, no difference in IL-6 or inflammatory parameters reduction, noradrenaline demand, or mortality was observed between patients, treated with adsorber (CytoSorb) or standard of care.
VALIDITY AND ADEQUACY OF ANIMAL MODELS IN HAEMODIALYSIS RESEARCH: A SYSTEMATIC REVIEW
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Background and Aims: with the worldwide dialysis population growing rapidly, improving haemodialysis (HD) outcomes is crucial and HD innovations are urgently needed. Prior to clinical application, novel HD technologies must undergo extensive preclinical testing. However, to date there is no consensus on the induction method of kidney failure in animal models nor which animal species is most suitable for research on HD innovations. Moreover, there is no consensus on which parameters should be used to validate adequate induction of kidney failure and functioning of novel HD devices. Using a systematic review approach, we summarized available literature of HD in kidney failure animal models.

Method: we performed a systematic search on PubMed and Embase for relevant studies up to February 4th 2022. After removal of duplicates, 5723 abstracts were screened for eligibility by three independent reviewers (JdV, KW and MK). Inclusion was based on publication of a HD intervention in an animal model with adequate (acute or chronic) kidney failure (independent of induction method). Detailed inclusion and exclusion criteria were registered in PROSPERO 2022 CRD42022307144. Data from individual reports, including animal species and sex, kidney injury parameters and HD details, were extracted in a pre-set data extraction form. Future efforts will focus on risk of bias and key quality indicators.

Results: of the 5723 abstracts screened, 195 records were included as full text and 41 full text articles were included for data-extraction (Figure 1). Current data extraction is completed for 31 articles (75%). Publication years range from 1973 to 2021 with over half (16/31) published after 2000. HD experiments were most frequently performed on dogs (45%), followed by rats (29%), goats (13%), pigs (10%), and sheep (3%) respectively. Parameters such as weight (81% reported), sex (58%) and age (29%) were not systematically reported. Most studies (67% of records reporting sex) used male animals only. Dog models were found in older studies, with no records after 2009. Other large animal studies were almost exclusively (88%) performed from the year 2007 onwards. Independent of animal species, studies mainly used acute kidney injury (AKI) models (84%), induced by bilateral nephrectomy (48%) or bilateral ureteral ligation (29%). The majority confirmed kidney failure by an increase in BUN and/or plasma creatinine. In AKI models, dialysis was on average initiated on AKI day 2 ± 0.8, and generally either HD (61%) or veno-venous hemofiltration...
LONG TERM EFFECT OF MEDIUM CUT-OFF DIALYZER ON MIDDLE UREMIC TOXINS
Irena Rambabova-Bushljetik1, Zhaklina Shterjova-Markovska1, Aleksandra Canevska-Tanaska1, Zoran Janevski1, Stefan Filipovski1, Igor Nikolov1, Galina Severova-Andreevska1, Oliver Bushljetikj2, Nikola Gjorgjievski1, Vladimir Pushevski1, Goce Spasovski1 and Lada Trajcheska1

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2University Clinic of Cardiology, Skopje, Republic of North Macedonia

Background and Aims: Better removal capacities for middle and large middle molecules in hemodialysis was achieved in (HD) treatment with the new medium cut-off (MCO) membranes. The aim of this study was to evaluate the long term removal efficacy of Theranova® in standard HD in comparison with standard high-flux HD.

Method: 11 patients were assigned to high flux and 11 to MCO membranes in 12-months observational study. Each patient was assessed every three months from T0 with high-flux dialyzers, T1 to T5 with MCO at first, third, sixth, ninth and twelfth month by measuring pre- and post-HD samples of β2-microglobulin (β2M), myoglobin, albumin, free light chains kappa (FLC-k), and free light chains lambda (FLC-λ). The cumulative change from as RR from T0 to T5 was defined as long term outcome.

Results: The data showed a higher average removal rate (RR) for all the uremic toxins with Theranova® dialyzers for β2M, myoglobin, FLC-k, and FLC-λ (66.1, 53.2, 59.2, 59.0%, respectively) compared to high flux (57.1, 10.8, 29.9 and 27.4%, respectively). The analyses on the cumulative RR from T0 to T5 found significant decrement of β2M, myoglobin, FLC-λ in MCO vs high flux group where those values significantly raised (14.9 ± 6.1, p = 0.043; 27.7 vs –7.8, p = 0.001; 21.9 vs –4.2, p = 0.017, respectively). The FLC-λ showed borderline significantly better removal with MCO (17.8 vs 8.4, p = 0.067). The distribution of patients with 12 month middle molecules reduction was much better in the MCO group. Albumin retention was better in MCO group and did not change between T0 and T5 (p = 0.824).

Conclusion: Compared to high-flux membranes, MCO membranes show greater permeability for middle molecules and albumin stability in long-term report. Their use in HD standard setting is effective and safe.

REFERENCES

#6648

THERAPEUTIC PLASMA EXCHANGE AS A TOOL IN THE TREATMENT OF NEUROLOGICAL DISEASES: A SINGLE CENTER EXPERIENCE
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1Hospital Central do Funchal, Department of Nephrology, Funchal, Portugal and 2Department of Nephrology, Porto, Portugal

Background and Aims: Plasmapheresis is an extracorporeal technique that removes immunological active substances, such as antibodies or immune complexes, from plasma. Simultaneously, it can provide essential factors in deficit, when supplementing with plasma. Therapeutic plasma exchange (TPE) can be used in numerous diseases with systemic involvement and, more recently, it has assumed an increasingly relevant role in the treatment of neurological diseases. Our aim was to review neurological indications, technique prescription, clinical outcomes and complications of these procedures.

Methods: We conducted an observational retrospective single-center study of the neurological diseases treated with TPE in our unit. We analyzed all procedures performed between January 2010 and December 2012 and collected indications, technical factors, complications and clinical outcomes of all treatments conducted. TPE was performed removing 1 to 1.5 of plasma volume per session. All procedures used Human Albumin 5% as replacement fluid and two units of fresh frozen plasma (FFP) were given in the end of each session. Hypocoagulation of the extracorporeal circuit was maintained with unfractionated heparin.

Results: Seventy-seven cycles of TPE (a total of 421 procedures) were performed on 45 patients [55.6% female; median age of 51 years (SD±16.8)]. The main indications of TPE in neurological diseases included myasthenia gravis (n = 35), Anti-N-methyl-d-aspartate (NMDA) encephalitis (n = 7), Guillain-Barré syndrome (n = 7), neuromyelitis optica spectrum disorders (n = 6), acute disseminated encephalomyelitis (n = 5), paraneoplastic syndromes (n = 4) and multiple sclerosis (n = 2). Intravenous immunoglobulin was given before TPE in 25 cases, 34 patients were on steroid and 6 patients had received pyridostigmine. Eighteen patients had coadjuvant immunosuppression [Myophenolate mofetil or Azathioprine (n = 13), Rituximab (n = 3), tacrolimus (n = 1), Tocilizumab (n = 1) or Eculizumab (n = 1)]. The median number of TPE sessions per patient was 5 (range 1-20) and most cycles (63.6%) were performed every day for 3 sessions and 2 sessions every other day. Most of TPE (59.7%) was performed in ward, 27.3% in Intensive Care Unit (ICU) and 10 treatments were conducted in ambulatory. Near 84% of treatments were done through central venous catheters (CVC) and one patient had an arteriovenous (AV) fistula. Twenty-four (5.7%) complications were seen in 421 procedures. These complications were infection (18.2%), catheter-related (7.8%) and allergic reactions (1.3%). TPE procedure was terminated in 7.8% of sessions depending on these complications. Overall response to TPE were noted in 81.8% of patients and 6 patients had at least one relapse during follow-up.

Conclusion: TPE is an effective and safe treatment option in several neurologic diseases. In our center, principal indications for TPE were myasthenia gravis, NMDA encephalitis and Guillain-Barré syndrome. In this study, clinical outcomes were favorable in the majority of the cases, with a minimum rate of complications per procedure. Therefore TPE should be considered in an early phase of the presentation of disease. In relapsing diseases like myasthenia gravis, refractory to immunosuppression therapy, an AV fistula could be an alternative access to minimize the CVC-related complications.
HFR USING A HIGH-FLUX DIALYZER (SUPRA-H) AS NEW EFFECTIVE ALTERNATIVE TO ON-LINE HEMODIAFILTRATION: A SINGLE SESSION ANALYSIS

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Background and Aims: Hemodiafiltration with regeneration of the ultrafiltrate (HFR) is a highly biocompatible dialysis technique that combines convection, diffusion, and adsorption. SUPRA-H is a new HFR system which uses a high-flux dialyzer in the diffusive stage to improve large uremic toxin removal. The aim of our study was to compare the toxin removal of the SUPRA-H system with high-volume online-hemodiafiltration (OL-HDF).

Method: In an open, randomized, cross-over, single-center, controlled study, 16 adult chronic hemodialysis patients were treated with SUPRA-H or OL-HDF. Hemodialysis sessions were delivered with Flexya dialysis monitor (Medtronic) in the middle-week session, lasting four hours. OL-HDF session was performed in post-dilution mode with the same high-flux dialyzer (Phylter HF17G, Medtronic) as that used in the diffusive stage of the SUPRA-H system. All other dialysis parameters were kept constant in both study arms. The reduction rate (RR) of urea, creatinine, phosphate, β2-microglobulin (β2mglob), kappa (κFLC) and lambda (λFLC) free light chains, interleukin-6 (IL-6) p-Cresyl sulfate, indoxyl sulfate and albumin, was intrindividually compared for the two dialysis types with linear mixed models.

Results: Whereas urea RR was significantly lower, SUPRA-H had significantly higher RR for κFLC (Median: 58.63%, IQR: 49.91-70.24) than those obtained with OL-HDF (Median: 51.97%, IQR: 37.12-62.71; p = 0.03). The RRs for the other large and protein-bound uremic toxins tended to be higher with the SUPRA-H system (Figure 1). There were no significant differences in the RRs for creatinine, phosphate, IL-6, and albumin.

Conclusion: The new HFR system SUPRA-H, appears to be a potential technologic step ahead in terms of improved large molecule removal for dialysis patients, and might contribute to a more adequate dialysis therapy.

Figure 1: Comparison of uremic toxin reduction ratios (in percentages).
FACTORS ASSOCIATED WITH THE CIRCUIT LIFESPAN OF CONTINUOUS KIDNEY REPLACEMENT THERAPY (CKRT)
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Background and Aims: Approximately half of patients in intensive care unit (ICU) experienced acute kidney injury (AKI). ICU patients with severe AKI and hemodynamic instability sometimes require continuous kidney replacement therapy (CKRT). Termination of CKRT circuits leads to blood loss, attenuation of therapeutic effects of CKRT, and a heavy workload and resource burden for medical staff. Identification of the factors which can prolong the lifespan of CKRT circuits is clinically essential. We aimed to elucidate the factors affecting the lifespan of CKRT circuits in ICU patients.

Method: We evaluated the lifespans of 559 CKRT circuits used for 63 ICU patients at the Okinawa Prefectural Nanbu Medical Center and Children’s Medical Center from April 1st, 2021 to March 31st, 2022. We enrolled all ICU patients who required CKRT. Our research team prospectively collected information on the patients’ basal characteristics, CKRT prescription, activated clotting time (ACT) after the hemofilter, CKRT circuit lifespan, and causes of termination of circuits prospectively. Effects of ACT were examined by grouping patients into three with their ACT values: <140, 140 ≤ and <180, and ≥180 seconds. The primary outcome of this study was a termination of the CKRT circuit within 24 hours after the initiation of the CKRT circuit. The secondary outcome was the cause of terminating CKRT circuits. Primarily, we examined the impacts of factors associated with CKRT circuit lifespan using multivariable Cox-proportional hazards regression.

Results: Our cohort’s median follow-up period of CKRT hemofilter was 18.5 hours. The total number of participants was 63, and 63.5% were male. In the multivariate Cox regression analysis, targeting ACT between 140 to 180 seconds was associated with a longer circuit lifespan (HR = 2.11(1.43-3.11), p < 0.0001) than the group of CKRT circuits with ACT < 140 seconds.

Based on our results, targeting ACT between 140 to 180 seconds extended the median survival time of the circuit lifespan to 1.4 times longer than the group of circuits with ACT less than 140 (Fig. 1). There were no differences in the causes of hemofilter occlusion among the three ACT groups. Notably, COVID-19 was not significantly associated with a reduction in circuit lifespans (HR = 0.63(0.35-1.11), p = 0.110).

Conclusion: Appropriate monitoring of ACT during CKRT may help prolong circuit lifespan, and the optimal ACT range was 140 to 180 seconds. In contrast, COVID-19 was not a risk factor for an early occlusion of CKRT circuits.

Figure 1: Difference in lifespan of CKRT circuits among three ACT groups.
#6780

EFFECTS OF ISONATREMIC DIALYSIS ON INTERDIALYTIC WEIGHT GAIN RELYING ON AN AUTOMATED SODIUM CONTROL ALGORITHM: INTERIM ANALYSIS OF DISON-IRC STUDY

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Background and Aims: Sodium (Na) is a major determinant of extracellular fluid volume and osmolality homeostasis. Chronic fluid overload (FO) is present in 30 to 50% of hemodialysis patients (HD). HD patients are mostly treated with fixed dialysate Na concentration irrespective of plasma Na concentration. This fixed approach tends to displace patient’s osmolar set point and stimulates thirst and weight gain. An automated personalized dialysate Na alignment to patient’s natremia to avoid unwanted diffusive Na gain and toxicity change induced by HD seems preferable. Several studies exploring individualized dialysate Na prescription have reported inconsistent results. In this prospective interventional multicenter study, we aimed to explore the impact of dialysate Na individualization through isonatremic HD on interdialytic weight gain (IDWG) (primary outcome) and dialytic HD-related symptoms (secondary outcome). For this purpose, we have used the automated “Na Control” option for adjusting dialysate Na to minimize dialysate-plasma sodium gradient and deliver an isonatremic dialysis.

Method: This is a longitudinal study comparing 2 periods: Period-1 = observational phase (2 months) → Period-2 = isonatremic phase by activation of “Na Control” in isonatremic mode (2 months) → comparison of IDWG between both periods. The embedded “sodium control” option in HD machine was used in all cases of Period-2 to actively align dialysate sodium concentration to natremia and quantify net sodium mass transfer. Results are expressed as mean±SD or median [25th-75th].

Results: We present preliminary results obtained through 6 dialysis facilities including 51 patients, 33 (64.7%) females, 75 [65-81] years old, dry weight 71.9 [60.5-78.0] kg. Main findings are as follows: Firstly, an excellent agreement was observed between plasma Na concentrations, measured (laboratory) and estimated (machine) from HD monitor (mean difference before dialysis: 0.05, after dialysis: 0.62). Secondly, plasma Na estimated was as follows: before dialysis plasma Na (137.6 [136.2-139.0] vs 137.2 [136.0-139.3] and after dialysis plasma Na (139.0 [137.6-139.7] vs 137.1 [135.7-138.9]) in Period-1 and Period-2 respectively; Thirdly, the primary outcome (IDWG) as well as the diffusive Na balance were significantly reduced by isonatremic condition (IDWG: 1.27±0.92 versus 1.95±0.86 kg, p<0.0001; diffusive Na balance 13.9 [1.9-5.1] versus 0.7 [0.0-2.7] g of Na, p<0.0001).

Conclusion: Isonatremic dialysis condition automatically driven by “Na control” embedded in HD monitor was confirmed safe and easily implemented in clinical workflow. In addition, these preliminary results show that isonatremic dialysis improved dialysis patient perception and significantly reduced IDWG.

#3379

DESIGN OF A NEW DIAPHRAGM PRESSURE TRANSDUCER FOR DIALYSIS MACHINE

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Background and Aims: Diaphragm pressure transducers can cause the dialysis process to be performed at higher quality. Pressure transduction is committed to concave, disc-shaped, impervious membranes that divide the respective chambers into two hermetically separate compartments: one contains liquid (blood/dialysate) while in the other there is trapped air. One of the sensitive parts in the design of a dialysis machine is the transducer to guide the flow toward the diaphragm and distributed the pressure over an area of its surface. The pressure is then measured by a transducer which is used as a pressure gauge. The proper design of the diaphragm makes it sensitive to pressure changes and as a result, the pressure can be measured with high accuracy. Simulation of the flow inside the transducer can be used as a tool for designing the transducer and its housing.

Method: The behavior of whole blood is non-Newtonian. Under high shear forces, viscosity approaches an asymptotic value that corresponds to blood viscosity when considered as a Newtonian fluid. The Carreau-Yasuda model is used to express the relationship between shear stress and shear strain. Three modified and three novel geometries are suggested for pressure transducers. Each geometry is discretized with meshing software. Pyramidal cells are used to mesh the computing domain. Ansys Fluent software is an analyzer program that is used to simulate the field of fluid flow, heat transfer, etc. The solution is selected based on pressure. Due to the complexity of the geometry and the convergence of the problem, only implicit formulation has been used for the model. The flow is assumed to be steady. The governing equation in this problem is continuity and momentum conservation and the k-ε model has been selected as for turbulent flow. Simple algorithm is considered for solving.

Results: The main output data is pressure distribution. Pressure and velocity distribution are related to each other. Figure 1 shows the velocity vector distribution in three modified schemes. The flow does not affect the pressure distribution inside the transducer housing for the straight port and is partially impressed in the shows-center port. The results of Figure 1 show that port location modification cannot affect the flow inside of the housing in such a way as to increase the sensitivity of the diaphragm. So, it was decided to redesign the geometry of the transducer’s housing so as to apply the pressure variation on the diaphragm more sensibly. A curved part is added to the lower face of the transducer to guide the flow toward the diaphragm and distributed the pressure to the entire surface of the diaphragm to reach a uniform pressure. To find the best port location three configuration is used; i.e. straight, 90-degree, and 120-degree. Figure 2 is the velocity vector distribution for the other three novel geometries. In these schemes, flow circulates in the housing and has an effect directly on the diaphragm. The 90-degree port of the newly designed transducer has not had proper performance and pressure is concentrated on one side of the diaphragm which is between the ports. The uniformity of pressure becomes higher in the 120-degree. But in the straight scheme, the concentration is located exactly in the middle of the diaphragm and it is a desirable and optimal condition that the designer is seeking.

Conclusion: A series of simulations are carried out in the Ansys Fluent software to investigate a diaphragm pressure transducer flow after port locations and housing geometry modifications. The results show that if the fluid is directed to the diaphragm tangentially, the concentration of pressure is located on the diaphragm while the uniformity is preserved. The results show that this consideration leads to an optimal design using a new housing geometry with a curved shape wall to deflect the flow and distributed the pressure uniformly.

Abstracts
Figure 1: Velocity vector distribution of port-modified transducer.

Figure 2: Velocity vector distribution of housing-modified transducer.
ASSESSMENT OF FLUID STATUS BY COMBINATION OF LUNG ULTRASOUND, BIOIMPEDANCE, AND INFERIOR VENA CAVA MEASUREMENT IN HEMODIALYSIS PATIENTS

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Background and Aims: Assessment of fluid status in hemodialysis patients (HD) remains a major challenge for nephrologists. Fluid overload is one of the most common modifiable risk factors directly associated with hypertension. The purpose of our study was to investigate whether the combination of three bedside methods-lung ultrasound comets (LUC), multifrequency bioimpedance (MBIS), and inferior vena cava diameter (IVCD) measurement—could provide complementary information to guide the management of HD patients.

Method: We assessed MBIS, LUC at 28 typical sites, and IVCD in 18 HD patients enrolled in the HD maintenance program. LUC and IVCD measurements were performed three times-before, during, and after HD. For MBIS measurement, we used the Body Composition Monitor (Fresenius Medical Care, Bad Homburg, Germany), and for LUC and IVCD, we used an ultrasound machine (Esaote MyLabOmega, Genoa, Italy). Ultrafiltration during HD was not adjusted for LUC, IVCD, and MBIS only before and after HD. Overhydration (OH) was defined as > 2L with MBIS, > 15 LUC, and < 40% collapsibility index (CI) on IVCD.

Results: The mean age of participants was 61 (IQR, 47-74) years, and thirteen (72.2%) were male. The average dialysis vintage of our patients was 105 months (IQR, 30-155). According to the OH criteria before, during, and after HD, 13 (72%), 2 (11%) patients were overhydrated according to MBIS, 10 (56%), 7 (39%), 3 (17%) patients according to LUC, and 13 (72%), 12 (67%), and 11 (61%) patients according to CI. We found no correlation between systolic blood pressure (BP), diastolic BP, MBIS, LUC, and CI before, during, and after HD, except that systolic BP after HD correlated with MBIS (OH) after HD (r = 0.491; p = 0.039). Using the paired-samples T-test, we found a statistically significant difference between OH before and after HD (p < 0.001), between LUC before and during HD (p = 0.006), between LUC during and after HD (p = 0.002), and between LUC before and after HD (p < 0.001). Using the paired-samples T-test, no statistically significant difference was found between systolic, diastolic BP and CI before, during, and after HD.

Conclusion: Optimal assessment of fluid status in HD patients remains challenging and, according to our results, may require a combination of LUC and MBIS parameters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.1±3.5</td>
</tr>
<tr>
<td>Average systolic BP before HD (mmHg)</td>
<td>145±25</td>
</tr>
<tr>
<td>Average diastolic BP before HD (mmHg)</td>
<td>79±11</td>
</tr>
<tr>
<td>Average systolic BP between HD (mmHg)</td>
<td>140±24</td>
</tr>
<tr>
<td>Average diastolic BP between HD (mmHg)</td>
<td>79±10</td>
</tr>
<tr>
<td>Average systolic BP after HD (mmHg)</td>
<td>139±21</td>
</tr>
<tr>
<td>Average diastolic BP after HD (mmHg)</td>
<td>78±11</td>
</tr>
<tr>
<td>Ultrafiltration during HD (ml)</td>
<td>3128±553</td>
</tr>
<tr>
<td>Lung comets before HD (number)</td>
<td>22±16</td>
</tr>
<tr>
<td>Lung comets between HD (number)</td>
<td>15±11</td>
</tr>
<tr>
<td>Lung comets after HD (number)</td>
<td>9±7</td>
</tr>
<tr>
<td>CI before HD (%)</td>
<td>34±15</td>
</tr>
<tr>
<td>CI between HD (%)</td>
<td>34±15</td>
</tr>
<tr>
<td>CI after HD (%)</td>
<td>33±10</td>
</tr>
<tr>
<td>OH with MBIS before HD (L)</td>
<td>3.02±1.9</td>
</tr>
<tr>
<td>OH with MBIS after HD (L)</td>
<td>0.25±1.9</td>
</tr>
</tbody>
</table>

BP = blood pressure; HD = hemodialysis; CI = collapsibility index; MBIS = multifrequency body bioimpedance; OH = overhydration; *N = 15
Background and Aims: To observe the clinical efficacy and safety of fractionated plasma separation and adsorption integrated with continuous veno-venous hemofiltration (FPSA-CVVH) treatment in patients with acute liver failure (ALF).

Method: In this retrospective study, we enrolled patients with ALF (serum total bilirubin >10mg/dl or Model for End-Stage Liver Disease (MELD) Score >25) from 2017 to 2022. All patients received the treatment of FPSA-CVVH. The primary measure of treatment efficacy was the reduction ratios (RRs) of bilirubin after each session of FPSA-CVVH.

Results: 8 sessions per patient were performed using the Fresenius equipment. The median number of sessions per patient was 6. The mean exchange volume was 2.9 l/patient/session. The replacement fluid used was albumin on 100% of patients and 4 patients required albumin plus fresh frozen plasma. 75 percent of the patients had a positive response with partial remission or stability of the disease and 88 percent had no recurrences. Patients' neurological response to the therapy was the expected, and similar to the one reported in the medical literature.

Conclusion: In our experience, plasmapheresis is a safe and effective therapy in patients with neurological diseases that should be required as a therapeutic option. We, as nephrologists must be aware of this and promote the management of this technique by publishing the joint experience in neurology and nephrology to broaden the level of evidence in clinical practice. The importance of coordination in early referral by other different medical specialties may obtain better results.
## Table 1: Prevalence according to Category and Grade Recommendations for Therapeutic Apheresis.

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Disease</th>
<th>Grade</th>
<th>Frequency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myasthenia Gravis I</td>
<td>1B 2</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Guillain Barré II</td>
<td>1A 4</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Multiple Sclerosis II</td>
<td>1A 5</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Voltage-Gated Potassium Channel Antibody Related antiLGi-1 II</td>
<td>1B 2</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Neuromyelitis optica (NMO or Devic’s disease) II</td>
<td>2B 1</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Chronic inflammatory demyelinating polyneuropathy I</td>
<td>1C 1</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Areflexic paraplegia uncertain etiology IV</td>
<td>2C 1</td>
<td>6%</td>
<td></td>
</tr>
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</table>

## Table 2: Results.

<table>
<thead>
<tr>
<th>Results</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>16</td>
</tr>
<tr>
<td>Age, y</td>
<td>47</td>
</tr>
<tr>
<td>% Male</td>
<td>31%</td>
</tr>
<tr>
<td>% Female</td>
<td>69%</td>
</tr>
<tr>
<td>Previous steroids treatment</td>
<td>75%</td>
</tr>
<tr>
<td>Previous Immunoglobulins treatment</td>
<td>56%</td>
</tr>
<tr>
<td>Previous immunosuppressive treatment</td>
<td>13%</td>
</tr>
<tr>
<td>Apheresis sessions</td>
<td>92</td>
</tr>
<tr>
<td>Median of apheresis sessions</td>
<td>6</td>
</tr>
<tr>
<td>Frequency</td>
<td>48h</td>
</tr>
<tr>
<td>Average column treated (cc)</td>
<td>2977</td>
</tr>
<tr>
<td>Replacement fluid: Albumin</td>
<td>94%</td>
</tr>
<tr>
<td>Replacement fluid: PFC</td>
<td>25%</td>
</tr>
<tr>
<td>Anticoagulant (heparin)</td>
<td>100%</td>
</tr>
<tr>
<td>Replacement of Fibrinogen (sessions)</td>
<td>33%</td>
</tr>
<tr>
<td>Allergic event</td>
<td>31%</td>
</tr>
<tr>
<td>Infection</td>
<td>13%</td>
</tr>
<tr>
<td>System coagulation</td>
<td>19%</td>
</tr>
<tr>
<td>Total recovery</td>
<td>13%</td>
</tr>
<tr>
<td>Partial recovery</td>
<td>75%</td>
</tr>
<tr>
<td>No recovery</td>
<td>13%</td>
</tr>
<tr>
<td>No recurrence</td>
<td>88%</td>
</tr>
</tbody>
</table>

#4858

THE CHANGES OF THE C REACTIVE PROTEIN LEVEL DURING THE CRRT PROCEDURE

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**Background and Aims:** Continuous renal replacement therapy (CRRT) is recommended for critically ill patients (pts). Various infections and sepsis often occur in these pts. In addition to being frequently used as an inflammation parameter, C reactive protein (CRP) is considered an important regulator of inflammatory processes and may have an active role in atherosclerosis. Changes in its level can have indirect effects on these processes. The aim of this study was to monitor change of CRP level during the CRRT procedure and to evaluate the potential correlation between this change and other monitored parameters.

**Method:** The study was done as the observational, retrospectively prospective study on 154 pts, on whom 343 CRRT procedures (proc) were performed. All pts were treated at the Clinics of the University Clinical Centre of Vojvodina, by the Dialysis Department, during 2021 and 2022. Procedures that lasted longer than 3 hours were included. CRRT modalities were CVVHD and CVVHDF, with the use of different filters (EMiC2, K88/CiCa1000, oXiris, ST150), according to the device (MultiFiltrate, PrismaFlex) and anticoagulation used. Demographic, clinical and CRRT proc data were collected from the medical documentation. Blood for laboratory testing was sampled at the beginning and the end of the proc. An increase or decrease of CRP level by more than 5% compared to the initial value was considered significant. The collected data were statistically processed.

**Results:** From 154 pts, 86.83% were men, 13.17% women, with average (avg.) age of 56.52 years. From 343 proc, 41.69% were CVVHD, 58.31% CVVHDF, with avg. duration of 1033 min. Average ultrafiltration (UF) was 2670mL, with avg. UF/hour of 161.54mL/h. Average initial CRP level was 176.25mg/l, with avg. level of 174.6mg/l at the end of the proc. In 44.9% proc an increase and in 43.44% proc a decrease in the CRP level was verified. The CRP level did not change significantly during 11.66% proc (40/343). Patients’ age (p = 0.868) and gender (p = 0.752) did not affect the change in CRP level during CRRT proc. Procedures in which CRP level decreased lasted longer (1084min) than those with CRP level increase (1023min), but the difference is not statistically significant (p = 0.199). Prescribed CRRT dose (p = 0.485), nor total UF (p = 0.164) did not affect change in CRP level during proc. Hourly UF was significantly lower for CRRT proc during which CRP level decreased (148.18mL/h) compared to those with the CRP level increase (172.23mL/h) (p = 0.000). CRRT modality had a significant impact on changes of CRP level during the proc. In a higher percentage of CVVHD proc (48.32%) a decrease in CRP level was seen compared to CVVHDF proc (36.36%) (p = 0.035). A significant difference was found in the changes of CRP levels in relation to the filters used (p = 0.011). The use of the EMiC2 filter most often resulted in a decrease in CRP level (56.25%), compared to the use of other filters.
Septic condition was present in 85.91% of proc that ended with a decrease of CRP level and in 66.23% of proc with the CRP level increase (p = 0.000). In proc with the CRP level decrease, basal levels of PCT and fibrinogen were significantly higher than in those with the CRP level increase (p = 0.037, p = 0.000 retrospectively). Initial number of WBC did not differ between two groups (p = 0.424). Comorbidities such as diabetes (p = 0.489), malignancy (p = 5) or autoimmune disease (p = 25) did not affect change in CRP level during CRRT proc, nor did surgery precede the proc (p = 782). No association between the changes of CRP level during the CRRT proc and the subsequent pts mortality (p = 289) or recovery of renal function (p = 808) was found.

Conclusion: During the CRRT procedure, the level of CRP in significantly influenced by the average hourly ultrafiltration, the CRRT modality, the filter used, and the presence of septic condition, with high levels of PCT and fibrinogen.

#4865

OBSERVATIONAL PILOT STUDY TO EVALUATE THE RELATIONSHIP BETWEEN LUNG ULTRASOUND AND BIOIMPEDANCE IN HEMODIALYSIS

Gabriel Ledesma Sánchez, Veronica Ruth Mercado Valdivia, Yesika María Amezquita Orjuela, Raquel Díaz Mancebo, Ángel Gallegos Villalobos, Yolanda Hernández Hernández, Rocío Echarri Carrillo, Silvia Caldés Ruisánchez, María Covadonga Hevia Ojanguren and Antonio Cirugeda García

Infanta Sofía University Hospital, Nephrology, San Sebastián de los Reyes, Spain

Background and Aims: There is a clear relationship between volume overload and morbidity and mortality in hemodialysis patients, which makes it essential to accurately adjust the normohydration weight. For this, bioimpedance has become an indispensable tool in dialysis units. In recent years there has been a rapid development of lung ultrasound for the evaluation of pulmonary congestion through the quantification of B lines. Several studies have shown a correlation between the number of B lines and the volume overload estimated by bioimpedance in patients on dialysis. However, all these studies perform a 28-zone lung ultrasound protocol, which may be a limitation in clinical practice. Several studies have recently been published showing a correlation between 28-zone lung ultrasound protocol and simplified 4, 6, and 8-zone ultrasound protocols, which have been widely studied in patients treated in intensive care or emergency units. We set out to evaluate the relationship between bioimpedance and simplified 8-zone lung ultrasound protocol in hemodialysis patients.

Method: Pilot cross-sectional observation study that included 29 patients on hemodialysis at Infanta Sofía University Hospital during March 2022. Bioimpedance predialysis and postdialysis, 8-zone lung ultrasound protocol (delimited by the parasternal, anterior axillary, posterior axillary, and 4th intercostal space) and inferior vena cava ultrasound. Predialysis proBNP and Ca-125 were measured.

Results: There is a significant reduction in overhydration estimated by bioimpedance and in the number of B lines after the hemodialysis session (p < 0.05). No correlation has been established between the two parameters, neither pre-dialysis nor post-dialysis. Neither with the pre-dialysis levels of proBNP or Ca125. There is a correlation of r = 0.45 (p < 0.05) in the subgroup of patients of the afternoon shift (n = 9) between the number of B lines and extracellular water.

Conclusion: Lung ultrasound allows the evaluation of the degree of lung congestion, and therefore of extracellular water, becoming a useful tool for adjusting the dry weight of hemodialysis patients. In our study we found no association between the number of B lines in the simplified 8-zone lung ultrasound protocol. It is possible that this type of lung ultrasound is not sensitive enough in outpatients on hemodialysis, but it is sensitive enough in critically ill patients in whom lung overload is greater. Further studies with a larger number of patients are needed for evaluation.

#6419

PYTHON LANGUAGE TO APPLY DATA SCIENCE METHOD TO DAILY DIALYSIS PATIENT CARE

Ugo Donini¹ and Sara Donini²

¹Ospedale Privato Donus Nova (Gruppo GHC), Ravenna, Italy and ²Dialysis and Renal Transplant Unit, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

Background and Aims: Python is a high-level programming language. It was created by Guido van Rossum in 1991 and it is known for being user-friendly thanks to a readable code and a clear syntax. Python is widely used in scientific computing and big data analysis. Dialysis monitors can collect and record a wealth of data concerning the patient during dialysis. The purpose of this study is: 1) writing a Python code that automatically processes dialysis data from a selected period and a) provides printouts with the most significant values acquired; b) prepares graphs to visualize the trend in the progression of the selected parameters over time. The printouts and graphs should help set up each dialysis session. 2) Stimulating the formation of a Python community within the nephrologists for the development of the data science style in daily practice.

Method: Hemodialysis sessions were carried out using monitors of Fresenius Medical Care (FMC) mod. 5008. FMC's Therapy Support Suite (TSS) application allows data obtained from the monitor and data entered by the nurse during the dialysis session to be saved on a dedicated server. TSS selected data are then exported to excel file. Using the open-source Python 3.9 program, with the support of Pandas, Numpy and Seaborn libraries, a code was written in order to: 1) load the excel file with the selected data, 2) isolate the data of interest, on a selected period of time, concerning patients currently on dialysis. 3) create the tables and graphs for individual patients to set up the current dialysis session.

Results: Running the Python script produces three main sheets to check body weight (W), hemoglobin (HB) values, and blood pressure (BP) values. Other parameters are also examined graphically, drawing the linear regression line of the main parameter and the superimposed plot of other parameters.

Conclusion: Data collected during individual dialysis sessions can provide valuable information about a patient’s condition and help healthcare professionals make informed decisions about their treatment. Python and its libraries provide the nephrology community with an open source and easy-to-use tool to automatically process each patient's data scientifically. In daily practice this method helps better understand and evaluate the dialysis treatment.

Table 1: List of elaborations of the analyzed parameters with their abbreviations for legend purposes.

<table>
<thead>
<tr>
<th>Parameter observed</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry W</td>
<td>DW</td>
</tr>
<tr>
<td>Pre-dialysis W</td>
<td>PRE_W</td>
</tr>
<tr>
<td>Delta W between pre-dialysis W and dry W</td>
<td>DELTA_W</td>
</tr>
<tr>
<td>Delta W between pre-dialysis W and dry W in percent</td>
<td>DELTA_W_PERC</td>
</tr>
<tr>
<td>Interdialytic W gain</td>
<td>IDWG_ABS</td>
</tr>
<tr>
<td>Interdialytic W gain in percent</td>
<td>IDWG_PERC</td>
</tr>
<tr>
<td>W at end of dialysis</td>
<td>POST_W</td>
</tr>
<tr>
<td>Total ultrafiltration</td>
<td>TOTAL_UF</td>
</tr>
<tr>
<td>Initial HB at the beginning of dialysis</td>
<td>INI_HB</td>
</tr>
<tr>
<td>HB at the end of dialysis</td>
<td>FIN_HB</td>
</tr>
<tr>
<td>Delta HB from the beginning of dialysis to the end</td>
<td>DELTA_HB</td>
</tr>
<tr>
<td>Ratio of Delta HB to total Ultrafiltration</td>
<td>DELTA_HB/TOTAL_UF</td>
</tr>
<tr>
<td>Minimum achieved value of RBV during dialysis</td>
<td>RBV_min</td>
</tr>
<tr>
<td>Recirculation percentage</td>
<td>RECIRCULATION%</td>
</tr>
<tr>
<td>Systolic BP at the beginning of dialysis</td>
<td>INI_SYS_BP</td>
</tr>
<tr>
<td>Systolic BP at the end of dialysis</td>
<td>FIN_SYS_BP</td>
</tr>
<tr>
<td>Kt/V</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Values of body weight and total ultrafiltration statistics during the selected observation period.

<table>
<thead>
<tr>
<th>Name</th>
<th>IDWG</th>
<th>ABS</th>
<th>DW</th>
<th>DELTA W</th>
<th>DELTA W MEDIAN</th>
<th>DELTA W minus</th>
<th>TOTAL UF MEDIAN</th>
<th>TOTAL UF STD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CATHERINE FREDERICK</td>
<td>2.3</td>
<td>79</td>
<td>2.1</td>
<td>2.6</td>
<td>-0.5</td>
<td>2.9</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>CHRISTOPHER SANCHEZ</td>
<td>1.2</td>
<td>63.5</td>
<td>1.7</td>
<td>1.1</td>
<td>0.6</td>
<td>1.6</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>JAMES KELLER</td>
<td>3.8</td>
<td>55</td>
<td>5.1</td>
<td>4.7</td>
<td>0.4</td>
<td>3.8</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>JESSICA WRIGHT</td>
<td>1.9</td>
<td>61.7</td>
<td>1.8</td>
<td>2.8</td>
<td>-1</td>
<td>3.2</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>JOHN PEREZ</td>
<td>1.9</td>
<td>62.5</td>
<td>1.8</td>
<td>2</td>
<td>-0.2</td>
<td>2.1</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>JOHN RAY</td>
<td>3</td>
<td>92.5</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>3.8</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>RAYMOND LEONARD</td>
<td>1.6</td>
<td>77</td>
<td>1.4</td>
<td>1.3</td>
<td>0.1</td>
<td>1.6</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>RITA SIMS</td>
<td>1.4</td>
<td>104</td>
<td>1.2</td>
<td>1.6</td>
<td>-0.4</td>
<td>2.4</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>SAMANTHA FITZGERAL</td>
<td>2.9</td>
<td>83.5</td>
<td>2.9</td>
<td>2.5</td>
<td>0.4</td>
<td>2.3</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>SUSAN PADILLA</td>
<td>1.9</td>
<td>72</td>
<td>1.9</td>
<td>2.5</td>
<td>-0.6</td>
<td>3</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>TERRY SMITH</td>
<td>0.4</td>
<td>72</td>
<td>0.4</td>
<td>1.8</td>
<td>-1.4</td>
<td>2.2</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

Example of the graphs produced in Fig. 1.
The other two tables are not shown here but are always intended to direct the dialysis program of the day based on the processing of data from the previous selected period. Patients were anonymized using fictitious names.

Figure 1: Graphical representation produced automatically by Python code.

#3062
ROLE OF ONLINE HEMODIAFILTRATION (OL-HDF) IN THE
CONTINUOUS MEASUREMENT OF THE DIALYSIS DOSE
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Avericum Haemodialysis Centre, Las Palmas de Gran Canaria, Spain

Background and Aims: OL-HDF provides multiple advantages and benefits to patients compared to conventional high-flow hemodialysis (HFHD). Current monitors have a wide variety of biosensors and devices that provide continuous information on the patient's biological parameter and the efficiency of the dialysis session. Monofrequency bioimpedance (BIVA) provides information regarding the state of hydration (HE) and nutrition (EN) of our patients.

Method: Observational study in 493 patients, distributed in 8 dialysis centers and with a three different model of dialysis monitor. Demographic data, dialysis techniques and regimens, mean values for one month of ultrafiltration rate readings and KT are analyzed. The continuous measurement of DD is estimated by the ion dialysance biosensor. The OL-HDF technique is post-dilutional. The BIVA measurement is performed between 10 and 30 minutes after the end of the session. The Kt/V is estimated from the total TBW (V) by BIVA, using the Watson and Hume-Wiers formulas. Statistical analysis: descriptive, t-Student for statistics of groups and independent samples, Chi square for the association in cross tables.

Results: See Table 1.

Conclusion: Obtaining lower dialysis dose values in OL-HDF than in HFHD in some monitor models, despite longer dialysis times and greater dialyzer surface area, is probably due to dilution due to post- re-infusion and/or to the positioning of the dialysance sensors within the hydraulic circuit. This makes us think about the advisability of maintaining urea Kt/V measurements, by laboratory, to ensure adequate dialysis quality.
Abstracts i719

TRIAL OF ISOLATED HAEMODIALYSIS WITH PATIENT-ENTRY HFHD: 1 vs 1 b p = 0.24; 3a vs 3 b p < 0.001; 6a vs 6 b p = 0.02; 13a vs 13 b p = 0.047; 13a vs 13 c p = 0.03; 14a vs 14c p = 0.04.
OL-HDF: 1d vs 1f p = 0.027; 1e vs 1f p = 0.04; 3d vs 3 e p = 0.02; 4d vs 4 f p < 0.001; 9d vs 9 f p < 0.001; 9e vs 9 f p < 0.001; 11e vs 11 f p < 0.001; 11d vs 11f p < 0.001; 12d vs 12 e p = 0.02; 12d vs 12 f p < 0.001; 13 d vs 13 e p = 0.012; 13 d vs 13 f p < 0.001; 14d vs 14 e p < 0.001; 14d vs 14 f p < 0.001; 14e vs 14 f p = 0.047.

Monitor A, HFHD vs OL-HDF: 1a vs 1d, p < 0.001; 4a vs 4d, p = 0.03; 5a vs 5d, p < 0.001; 8a vs 8d, p = 0.009; 9a vs 9d, p = 0.038; 10a vs 10d, p = 0.006; 11a vs 11 d, p < 0.001; 12a vs 12 d, p < 0.001; 13a vs 13 d, p < 0.001; 14a vs 14 d, p < 0.001.

Monitor B, HFHD vs OL-HDF: 1b vs 1 e, p < 0.001; 2b vs 2 e, p < 0.01; 3b vs 3 e, p = 0.042; 5b vs 5 e, p = 0.004; 10b vs 10 e, p = 0.025.

Monitor C, HFHD vs OL-HDF: 4c vs 4d, p = 0.038; 7c vs 7 f, p = 0.009; 9c vs 9 f, p < 0.001; 11 c vs 11 f, p = 0.001; 12 c vs 12 f, p = 0.011; 14 a vs 14 f, p < 0.001

#3351
TRIAL OF ISOLATED HAEMODIALYSIS WITH PATIENT-ENTRY TENT AND HYPOCHLORITE MIST
Kazuhiko Shibata¹, Kiyotaka Imoto¹ and Masato Osawa²
¹Toshin Clinic, Yokohama City, Kanagawa Prefecture, Japan and ²Yokodai Central Clinic, Yokohama City, Kanagawa Prefecture, Japan

Background and Aims: The global spread of COVID-19 has posed a serious threat to patients receiving renal replacement therapy and to the staff who treat them. Every time they treat a patient or operate a machine, they have to wear personal protective equipment (PPE). In order to reduce the burden on our staff, we have introduced two pieces of equipment. One is a hypochlorous acid mist for room and surface disinfection using CLFine®. The other is an AIR ZIPPER® patient isolation tent in the existing isolation room. Both products were manufactured by Nipro Corporation of Osaka, Japan. However, there was no evidence to support the use of hypochlorous acid in an ultrasonic humidifier. Therefore, Nipro Corporation conducted a “28-day repeated inhalation toxicity study” on rats with a third party organisation and confirmed the results as toxicologically safe. According to the Occupational Safety and Health Act, also in the school environmental health, the concentration of chlorine in the air is 0.5 ppm or less (8 hours/day, 5 days/week or less). CL Fine® has shown an antiviral effect within these regulations. The size of the AIR ZIPPER® is about a fifth of the standard 10m³ size, down to about

Table 1: Measured and estimated parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Monitor A (a)</th>
<th>Monitor B (b)</th>
<th>Monitor C (c)</th>
<th>Monitor A (d)</th>
<th>Monitor B (e)</th>
<th>Monitor C (f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Number</td>
<td>141</td>
<td>153</td>
<td>18</td>
<td>87</td>
<td>79</td>
<td>33</td>
</tr>
<tr>
<td>Age (years) (1)</td>
<td>68.95 ±13.35</td>
<td>71.10 ±13.13</td>
<td>72.78 ±11.21</td>
<td>62.20 ±12.36</td>
<td>60.44 ±11.55</td>
<td>68.88 ±12.39</td>
</tr>
<tr>
<td>Time (month) in HD (2)</td>
<td>61.23 ±82.55</td>
<td>38.22 ±53</td>
<td>63.50 ±64.81</td>
<td>64.05 ±87.23</td>
<td>73.85 ±113.70</td>
<td>58.58 ±63.57</td>
</tr>
<tr>
<td>Height (cm) (3)</td>
<td>167.21 ±8.62</td>
<td>162.43 ±9.99</td>
<td>164.89 ±6.95</td>
<td>168.84 ±8.57</td>
<td>164.86 ±9.61</td>
<td>166.24 ±9.11</td>
</tr>
<tr>
<td>Weight (kg) (4)</td>
<td>72.72 ±17.10</td>
<td>72.79 ±14.77</td>
<td>72.75 ±15.91</td>
<td>79.45 ±21.32</td>
<td>76.25 ±15.42</td>
<td>83.20 ±21.56</td>
</tr>
<tr>
<td>TBW (BIVA) (5)</td>
<td>37.40 ±7.25</td>
<td>39.15 ±6.89</td>
<td>40.39 ±7.71</td>
<td>41.32 ±8.20</td>
<td>39.52 ±6.25</td>
<td>41.97 ±8.56</td>
</tr>
<tr>
<td>Hidration % (6)</td>
<td>75.05 ±3.52</td>
<td>77.10 ±5.95</td>
<td>76.67 ±4.26</td>
<td>75.36 ±4.00</td>
<td>75.02 ±4.27</td>
<td>76.12 ±3.75</td>
</tr>
<tr>
<td>Dializer Surface (m²) (7)</td>
<td>1.94 ±0.15</td>
<td>1.98 ±0.19</td>
<td>1.97 ±0.14</td>
<td>1.99 ±0.13</td>
<td>2.02 ±0.17</td>
<td>2.05 ±0.09</td>
</tr>
<tr>
<td>Body Surface (m²) (8)</td>
<td>1.82 ±0.21</td>
<td>1.78 ±0.21</td>
<td>1.80 ±0.21</td>
<td>1.86 ±0.24</td>
<td>1.84 ±0.19</td>
<td>1.91 ±0.26</td>
</tr>
<tr>
<td>KT (9)</td>
<td>56.21 ±8.33</td>
<td>55.23 ±10.51</td>
<td>55.67 ±6.39</td>
<td>54.34 ±6.58</td>
<td>56.86 ±9.53</td>
<td>64.99 ±9.77</td>
</tr>
<tr>
<td>KT target (10)</td>
<td>49.96 ±3.82</td>
<td>49.33 ±3.77</td>
<td>49.68 ±3.95</td>
<td>51.35 ±4.22</td>
<td>50.35 ±3.50</td>
<td>51.64 ±4.99</td>
</tr>
<tr>
<td>Difference KT (11)</td>
<td>6.25 ±7.82</td>
<td>5.90 ±10.48</td>
<td>5.98 ±5.62</td>
<td>2.99 ±5.99</td>
<td>6.51 ±10.31</td>
<td>13.35 ±8.68</td>
</tr>
<tr>
<td>KTV (TBW BIVA) (12)</td>
<td>1.52 ±0.29</td>
<td>1.44 ±0.33</td>
<td>1.40 ±0.19</td>
<td>1.35 ±0.22</td>
<td>1.47 ±0.33</td>
<td>1.59 ±0.30</td>
</tr>
<tr>
<td>Session hours (13)</td>
<td>3.52 ±0.38</td>
<td>3.61 ±0.40</td>
<td>3.85 ±0.29</td>
<td>3.84 ±0.31</td>
<td>3.69 ±0.38</td>
<td>3.95 ±0.20</td>
</tr>
<tr>
<td>Dializer Clearance (14)</td>
<td>266.40 ±31.35</td>
<td>255.89 ±47.85</td>
<td>241.15 ±24.52</td>
<td>235.68 ±22.42</td>
<td>257.22 ±37.24</td>
<td>273.38 ±35.58</td>
</tr>
</tbody>
</table>

AIR ZIPPER® mist for room and surface disinfection using CLFine®. The other is an AIR ZIPPER® patient isolation tent in the existing isolation room. Both products were manufactured by Nipro Corporation of Osaka, Japan. However, there was no evidence to support the use of hypochlorous acid in an ultrasonic humidifier. Therefore, Nipro Corporation conducted a “28-day repeated inhalation toxicity study” on rats with a third party organisation and confirmed the results as toxicologically safe. According to the Occupational Safety and Health Act, also in the school environmental health, the concentration of chlorine in the air is 0.5 ppm or less (8 hours/day, 5 days/week or less). CL Fine® has shown an antiviral effect within these regulations. The size of the AIR ZIPPER® is about a fifth of the standard 10m³ size, down to about
Powerful, high-efficiency particulate air filter pumps have been fitted to replace the air in the tent in less than 5 minutes at low flow rates (0.4 m3/min airflow), enabling it to operate below the negative pressure standard of 2.5 Pascal. In addition, the AIR ZIPPERR® is equipped with air intake valves that open and close in a single direction towards the inside of the tent. Prior to the introduction of the AIR ZIPPERR®, staff had to wear PPE with an N95 mask when operating the machine, puncturing and returning blood to the patient.

**Method:** Patients with a fever or who have been in contact with COVID-19 patients and infected patients were asked to enter the AIRZIPPERR®. Both exceedingly male/female:19/3, age:69.8 years, HD duration:5.38 years) with SARS-CoV-2 infection in our clinic. Fortunately, there was no transmission to staff or other patients, and no patients died.

**Conclusion:** These infection control measures helped to reduce staff workload and prevent infections. In conclusion, the present method should be equipped by all haemodialysis providers to deal with Covid 19 infections as well as with new infections in the future.

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**Table 1: Dialysances estimated by the model for each session of weeks W1, W2, W4 of the clinical study (in mL/min). Averages and standard deviations of all 20 patients.**

<table>
<thead>
<tr>
<th></th>
<th>W1 HD2</th>
<th>W1 HD3</th>
<th>W2 HD2</th>
<th>W2 HD3</th>
<th>W4 HD2</th>
<th>W4 HD3</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_{HCO_3}$</td>
<td>$191 \pm 52$</td>
<td>$237 \pm 250$</td>
<td>$198 \pm 164$</td>
<td>$144 \pm 72$</td>
<td>$189 \pm 74$</td>
<td>$184 \pm 51$</td>
</tr>
<tr>
<td>$K_{CO_2}$</td>
<td>$74 \pm 41$</td>
<td>$73 \pm 85$</td>
<td>$45 \pm 37$</td>
<td>$42 \pm 26$</td>
<td>$54 \pm 32$</td>
<td>$55 \pm 44$</td>
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**Figure 1:** Plasma bicarbonate concentration profiles for treatments A, B and C: simulation (continuous lines) vs. data (A – circles, B – squares, C – triangles). Averages of weekly sessions for all patients (N = 20). *p < 0.05 vs. treatment A.
COMPARISON OF CLINICAL PERFORMANCE AND HEMOCOMPATIBILITY OF DIALYZERS APPLIED DURING POST-DILUTION ONLINE HEMODIAFILTRATION (HDF) – EMPORA III STUDY

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Background and Aims: Performance and hemocompatibility are the two main functions of a hemodialyzer. Synthetic dialysis membranes made from polysulfone (PSU) or polyethersulfone (PES) are mainly used for dialysis treatments and are blended with the hydrophilic agent polyvinylpyrrolidone (PVP), to improve hemocompatibility during dialysis treatments. A novel PSU-based dialyzer (FX CorAL) with an increased and stabilized PVP content has been developed and has shown strong performance and a favourable hemocompatibility profile within previous short term clinical studies. In the present clinical study, we now investigated the performance and hemocompatibility of the FX CorAL vs. two comparators over a longer follow-up time and applied an extended panel of hemocompatibility biomarkers. This allowed us to analyse treatment-specific performance as well as an extensive intra- and interdialytic hemocompatibility profile.

Method: EMPORA III was a prospective, open, controlled, multicentre crossover trial with randomized treatment sequences conducted in DE, CZ and HU. It randomized stable patients receiving regular post-dilution online HDF to FX CorAL 600, FX CorDiax 600 (both Fresenius Medical Care) and xevonta Hi15 (B. Braun), each for 4 weeks. The primary outcome was β2-m removal rate (RR) during 4 hrs HDF. Non-inferiority (margin: 5%) and superiority of FX CorAL 600 versus comparators were tested at α = 0.25 (one-sided), with adjustment for multiple tests. Secondary endpoints were RR and/or clearance of β2-m and other molecules, as well as intra- and interdialytic changes of markers of complement activation (C3a, sC5b-9), cell activation / inflammation (white blood cells (WBC), PMN elastase, IL-6, IL-8, LTB-4, sICAM-1, hsCRP), platelet activation (platelet count, β-TG, TXB-2), and oxidative stress (MDA, GSH-Px). Intraindividual hemocompatibility markers were analysed descriptively as differences vs. the values determined at the start of the HDF session (LS means).

Results: Eighty-two patients were included and analysed in the safety population, with n = 76 presenting data for the primary outcome (ITT population). FX CorAL 600 showed the highest β2-m RR (LS mean: 76.31%), followed by FX CorDiax 600 (75.71%) and xevonta Hi15 (74.49%). Non-inferiority to its comparators was statistically significant (p<0.0001 each). Superiority was shown vs. xevonta Hi15 (p<0.0001), but not vs. FX CorDiax 600 (p = 0.0606). The secondary endpoints β2-m clearance as well as myoglobin clearance and RR affirmed these results; small molecule clearances and/or RR were similar between dialyzers. Analyses of hemocompatibility markers within one HDF session, found the following significant differences:

- C3a 15 min: FX CorAL: 31%; FX CorDiax: 59% (p = 0.003 vs. FX CorAL); xevonta: 41% (p = 0.029 vs. FX CorAL)
- sC5b-9 60 min: FX CorAL: 24%; FX CorDiax: 25% (p = 0.337); xevonta: 41% (p<0.0001)
- Cell activation / Inflammation
  - WBC 15 min: FX CorAL: -7.7%; FX CorDiax: -11.1% (p = 0.015); xevonta: -10.1% (p = 0.246)
  - Monocytes 15 min: FX CorAL: -30.9%; FX CorDiax: -30.3% (p = 0.533); xevonta: -38.2% (p = 0.012)
  - Neutrophils 15 min: FX CorAL: -3.0%; FX CorDiax: -7.5% (p = 0.019); xevonta: -6.1% (p = 0.258)
- PMN elastase 60 min: FX CorAL: 18%; FX CorDiax: 42% (p = 0.003); xevonta: 52% (p = 0.0003)
- LTB-4 15 min: FX CorAL: 170%; FX CorDiax: 217% (p = 0.047); xevonta: 186% (p = 0.539)
- Platelet activation
  - β-TG 60 min: FX CorAL: -15%; FX CorDiax: 4% (p<0.0001); xevonta: 18% (p<0.0001)

Hemocompatibility markers showed no interdialytic changes, i.e., no significant changes within treatment periods. Nine serious adverse events occurred in this study, none of which was dialyser related.

Conclusion: FX CorAL 600 efficiently removed middle and small molecules and was non-inferior to both comparators and significantly superior to xevonta Hi 15 in β2-m RR. The typical drop in WBC, monocyte, and neutrophil count during dialysis as well as the rise of complement (C3a, sC5b-9) and cell / platelet activation markers (PMN elastase, LTB-4 and β-TG) were lower or comparable during treatment with FX CorAL vs. both comparators, indicating superior hemocompatibility properties.
THE EFFECT OF HEMOPERFUSION ON SURVIVAL AMONG COVID-19 CRITICALLY ILL PATIENTS IN A TERTIARY HOSPITAL IN DAVAO CITY, PHILIPPINES

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Background and Aims: Cytokine storm in COVID-19 is an excessive immune response through the overproduction of inflammatory cytokines which significantly increases mortality. Hemoperfusion has been granted Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) in an effort to eliminate circulating inflammatory mediators among COVID-19 critical patients to improve clinical outcomes and survival. This study aims to determine the 8 – day survival of critical COVID-19 patients who received hemoperfusion.

Method: This is a descriptive study conducted among critically ill COVID-19 patients who completed hemoperfusion treatment admitted from October 2020 to October 2021 in a tertiary hospital in Davao City, Philippines. The inclusion criteria were adult patients greater than 18 years of age with RT-PCR confirmed SARS-CoV-2 infection who underwent and completed hemoperfusion during hospitalization for COVID-19. While those patients who did not complete the hemoperfusion treatment because of hemodynamic instability or death were excluded. All of the patients classified as COVID-19 critical received the standard treatment for COVID-19 such as steroids (dexamethasone) and antiviral (Remdesivir). Among the 1,037 COVID-19 adult patients admitted from October 2020 to October 2021, 28 of them were classified as critical and received hemoperfusion, but only 19 patients completed the treatment.

Results: Majority of patients in the study were males (14/19, 73.68%) with a mean age of 59 years (SD 12.90). Hypertension (n = 15, 78.95%) and Diabetes Mellitus (n = 14, 73.68%) were the most common comorbid illnesses. Cough (n = 15, 78.95%), fever (n = 11, 57.90%), and dyspnea (n = 7, 36.84%) were the frequent symptoms. The laboratory parameters (median hemoglobin, leukocytes, thrombocytes, creatinine, and ALT were within normal range except for an elevated median AST (54 U/L). Forty-two percent (8/19) of patients survived at day 8 (Figure 1). Survivors had higher baseline oxygen saturation compared to non-survivors (89% vs 78%), but in both groups, the oxygen saturation increased after hemoperfusion (Figure 2). All inflammatory markers (CRP, ferritin, LDH, and procalcitonin) decreased among survivors.
Figure 2: Oxygen Saturation of Critical COVID-19 Patients Before and After Hemoperfusion.

Figure 3: A. CRP of Critical COVID-19 Patients Before and After Hemoperfusion. D. Procalcitonin of Critical COVID-19 Patients Before and After Hemoperfusion.

Figure 3: B. Ferritin of Critical COVID-19 Patients Before and After Hemoperfusion.
Figure 3: C. LDH of Critical COVID-19 Patients Before and After Hemoperfusion.

Figure 3: D. Procalcitonin of Critical COVID-19 Patients Before and After Hemoperfusion.

Figure 4: Median Time Between the Onset of Symptoms to Hospital Admission and Hemoperfusion.
post-hemoperfusion. However, the ferritin, LDH, and procalcitonin remained elevated among non-survivors (Figure 3A, B, C, D). The median time from symptoms onset to hemoperfusion initiation was longer in non-survivors compared to survivors (10 days vs 8 days) (Figure 4).

Conclusion: Close to half (42.11%) of the critical COVID-19 patients who underwent hemoperfusion survived at day 8. Therefore, hemoperfusion remains to be a beneficial adjunct treatment for critical COVID-19 patients especially if initiated early.

#4657

COMPARISON OF TWO BIOIMPEDANCE SPECTROSCOPY DEVICES: A PRACTICAL STEP FORWARD ON THE WAY TO DAILY BIOIMPEDANCE MEASUREMENTS FOR DIALYSIS PATIENTS

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Background and Aims: Bioimpedance spectroscopy (BIS) is a non-invasive diagnostic tool to assess volume status and body composition through the measurement of voltage drops in alternating currents and subsequent extrapolation of extracellular (R0), intracellular (Ri), and total body (RInf) resistances. Currently available devices mostly rely on disposable electrodes and require supine body position. Here we tested whether a new, more versatile BIS device with reusable electrodes matches an established system in various setups, aiming to enable daily BIS-measurements in the near future.

Method: Two BIS devices ("Cella" and the "Body Composition Monitor" [BCM]) were compared both with four resistance testboxes (circuit boards with resistors and capacitors simulating different body conditions) and in 40 healthy volunteers. In-vivo comparisons included supine hand-to-foot (HF) reference measurements with adhesive disposable electrodes and hand-to-hand (HH) measurements with adhesive disposable and prototype reusable electrode sets (Figure 1).

Results: Analyses of testboxes were reproducible in both devices (intra-device coefficients of variation <1%). Mean differences from testbox components were similar and small for R0 (2-3 Ohm) but not for Ri, where Cella was off by 101 Ohm compared to the BCM’s 29 Ohm in a testbox designed with a deliberately low R0/Ri ratio. In-vivo, HF measurements with disposable electrodes differed significantly between both devices (p < 0.001). Prototype reusable HH electrodes exhibited a bias towards larger resistances than HF measurements (R0: 738.36 Ohm vs. 643.09 Ohm; Ri: 1508.18 Ohm vs. 1257.17 Ohm; RInf: 500.03 vs. 423.81 Ohm, respectively) and the HH/HF ratio varied between 1.0-1.4 (R0 and RInf) and 0.9-1.6 (Ri).

Conclusion: While the Cella BIS device was shown to produce results with comparable consistency to the BCM in-vivo, the latter measured more accurately under testbox conditions. Accuracy of in-vivo measurements could not be determined for lack of gold-standard measurements. Implementation of HH reusable electrodes will require per-patient calibration against HF measurements due to the large inter-patient fluctuations in the HH/HF ratio. We recommend further longitudinal analyses of intra-patient HH/HF ratios to investigate long-term variabilities.
Figure 1: Setups, Absolute and Normalized Resistances of BIS Measurements. Panels A-E illustrate all in-vivo BIS measurements conducted within this study (Cella: Setups 1, 3 and 5-10; BCM: Setups 2 and 4). Setups 1 and 2 were carried out after participants lay flat on their backs for 10 minutes to achieve fluid equilibrium and were followed by Setups 7 and 8, 5 and 6 and finally 3 and 4. Setups 9 and 10 took place prior to the 10-minute-long supine body positioning right after the participants’ arrival at the study facility. The sequence of setups was rearranged to reflect the increase in normalized error to Setup 1. Panels F-J depict $R_{\infty}$, $R_0$ and $R_i$ in absolute numbers while Panels K-O present normalized $R_{\infty}$, $R_0$ and $R_i$ values, computed by dividing measurements of Setups 2-10 by Setup 1 on an intra-patient basis. Colored points depict mean relative values and error bars delimit mean ±1.96 standard deviations of the mean. BIS, bioimpedance spectroscopy; BCM, Body Composition Monitor; $R_{\infty}$, resistance at infinite frequency; $R_0$, extracellular resistance; $R_i$, intracellular resistance.
Background and Aims: Symptoms associated with the accumulation of large uremic toxins (the development of chronic inflammation, accelerated progression of cardiovascular diseases and an increase in the incidence of protein-energy malnutrition) are common for patients who get chronic hemodialysis (HD) for a long time. HD effectively removes small and medium molecules (up to 15 kDa), while convection techniques, which are not always available, are used to remove substances of higher molecular weight. An alternative strategy for removing uremic toxins, especially large medium molecules, is the use of sorption techniques. The aim of the study was to compare the removal efficiency of substances with a molecular weight from 11.8 to 45 kDa using HD on a high-flux membrane and a combination of a high-flux membrane with hemo sorption.

Method: The study included patients with a duration of hemodialysis therapy for more than 5 years. Blood sampling was carried out before and after the procedures, in the average RRT session per week. The following indicators were determined: β-2-microglobulin, leptin, free light chains (FLC) κ and λ, IL-6. The first HD session was performed on a Fresenius Px 80 high-flux membrane. The second procedure (one week after) was carried out using the same filter, but with the connection of a Jafon HA130 sorption column (HD+HP). The duration of the both procedures was 4 hours. Blood flow did not exceed 300 ml/min.

Results: Total 10 patients were included in the study. Mean duration of renal replacement therapy was 12±5 years. The ratio of men and women was equal. Mean age 54±12 years. All patients used AV fistulas as vascular access. When determining and comparing the concentrations of β-2-microglobulin, leptin, IL-6, a comparable significant decrease in concentrations was noted after both procedures without significant statistical differences between the methods. At the same time, the efficiency of FLC removal on HD and HD+GP was convincingly different:

- average kappa-FLC concentration change after HD was +1.8±9.1 mcg/ml, after HD+GP: -9.4±7.5 mcg/ml, p = 0.04.
- average lambda -FLC concentration change after HD/HD+GP was +3.2±16.3 and -12.9±4.4 mcg/ml respectively, p = 0.02.

Conclusion: The use of sorption techniques as an adjunct to standard HD therapy can increase the excretion of medium-large molecular substances, such as FLC kappa/lambda, which may help reduce the severity of symptoms associated with the accumulation of these uremic toxins. Additional studies are required to evaluate the clinical effectiveness of the new sorption method in chronic HD.

Figure 1: Change in free light chain concentrations both fractions (kappa/lambda) after HD and HD+HP.
function was not related in this review to increased patient survival. Analytical parameters such as peak creatinine, hypoalbuminemia and type and amount of circulating LC could be studied as prognostic factors in this entity.

#6866
FRENCH EXPERIENCE OF HOME HEMODIALYSIS PATIENTS TREATED WITH NXTAGE HAEMODIALYSIS CYCLER WITH THE PURE FLOW SL SYSTEM

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Background and Aims: NxStage haemodialysis cycler with the Pure Flow SL system was introduced for the first time in France in June 2022. This system is designed to produce an ultrapure dialysis fluid and mixing a concentrate to the source water to prepare 60 L batch of dialysate. It can be used for a maximum of 3 home treatments. No major plumbing modifications are required to install this system at home. Here, we report to our knowledge the first French clinical evaluation of the use of the Pure Flow system in haemodialysis patients using this device and trained in NephroCare Villejuif haemodialysis center and Rouen Hospital.

Method: This retrospective study was performed in a cohort of 8 haemodialysis patients From June 2022 to January 2023. We describe the clinical benefits of Pure Flow including dialysis demographics, dialysis vintage, and short-term biological parameters. Patient related outcomes based on a specific questionnaire, at 3 and 6 months are also analyzed

Results: 8 patients were included with 5 women. The mean age was 48 years. The dialysis vintage was 24 months. The median follow-up was 4 months. 2 Patients were treated by pre-mixed 5L dialysate bags 6 months prior the implementation of Pure Flow, and 6 patients started the haemodialysis program directly with Pure Flow after a period of 10 days of training. We show that PF provide adequate dialysis dose. The mean stdk/V was 2.3. The mean of weekly dialysate volume was 146L. We note optimal ultrafiltration rate, improvement of biological markers of adequacy. Moreover, good results technique survival was recorded. We also show Reduced handling, and setup

Conclusion: The NxStage with Pure Flow system is a major advantage against the premixed bags with a simple installation and a low water consumption. Its use is associated with great clinical outcomes in patients. The Pure Flow should reduce shipments and storage of dialysis treatments and facilitate the development of home haemodialysis in France. Prolonged follow-up on a cohort with a larger number of patients is necessary and will allow an appropriate evaluation of the clinical benefit of the use of the Pure Flow.

#3798
A MULTICENTER CLINICAL STUDY OF CELLULOSE TRICATECT MEMBRANES AND POLYSULFONE MEMBRANE DIALYZERS IN MAINTENANCE HEMODIALYSIS PATIENTS

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Background and Aims: With the continuous improvement of dialysis membrane materials, polysulfone (PS) has replaced traditional cellulose membranes with excellent biocompatibility and dominates the market applications. In our clinical work, we found that the allergic reaction disappeared after the application of cellulose triacetate (CTA) in patients who were allergic to PS. In this study, we compared the differences in biocompatibility and solute clearance of CTA and PS dialyzers during long-term dialysis treatment.

Method: In this study, a multicenter clinical study was conducted, and patients attending Fuja dialysis Bureau Hospital, Northeast Hospital and Shengying Medical College Affiliated Central Hospital receiving maintenance haemodialysis from April 2019 to April 2020 were selected as the study population. The patients were divided into a polysulfone membrane group (n = 10) and a cellulose triacetate membrane group (n = 13) based on whether they tolerated the polysulfone membrane dialyzer, and all patients in the CTA group had an allergic reaction to the polysulfone membrane dialyzer.

Results: There were no statistically significant differences between the two groups in the comparison of basic information such as age, gender, dialysis age and primary disease. Before the application of CTA and PS dialyzer treatment, there was no statistically significant comparison between groups for all observed indicators. After application of CTA and PS single dialysis: (i) The difference between the 2 groups of β2-MG (Z = -2.039, P = 0.041) and TNF-α (Z = -2.491, 0.013) was statistically different. (ii) There were no statistically significant differences between two groups in the comparison of hematological system, such as WBC, PLT, Hb; complement, such as C3, C4; inflammatory factors, such as IL-1, IL-6, hs CRP, IgE; uremic toxins, such as P, CR, BUN, PTH (P > 0.05). After the 12th month of regular hemodialysis treatment with PS and CTA: (i) The differences between the 2 groups for P (Z = -2.096, P = 0.036), BUN (Z = -2.038, P = 0.042), and spKt/V (Z = -2.147, P = 0.049) were statistically significant. (ii) The difference between the 2 groups after 12 months of regular hemodialysis treatment (P = 0.114, P = 0.041) and before dialysis was not statistically different between groups, and the other indexes mentioned above were not statistically different.

Conclusion: After a single dialysis session, TNF-α in the PS group was elevated and the biocompatibility of CTA was better than PS. The CTA group had better clearance of β2-MG than PS, and spKt/V reached the standard. After long-term dialysis, the effect of CTA on inflammation and complement system was not different compared with PS, and there was no difference in biocompatibility between the two membranes. spKt/V in the CTA group reached the standard, and the clearance of BUN and P was better than that of PS.

D 2 - VASCULAR ACCESS & COMPLICATIONS

#4524
TRIBOELECTRIC EVALUATION OF ARTERIOVENOUS FISTULA FOR HAEMODIALYSIS: A PILOT STUDY

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Background and Aims: Determination of stenosis in an arteriovenous fistula (AVF) for hemodialysis is an essential step in the management of patients with end-stage kidney disease. Stenosis, or narrowing of the blood vessels, can significantly reduce blood flow and ultimately lead to thrombosis and dysfunction of the AVF. Therefore, accurate and frequent surveillance is crucial for detection of stenosis and for the proper management of AVF. Surveillance of AVF is based on direct methods including ultrasound imaging and magnetic resonance angiography both dependent from examiner availability and not ever regularly repeatable.

The triboelectric effect refers to the phenomenon where certain materials become charged after coming into contact with another material. In blood vessels the rubbing of erythrocytes against each other and arterial and vein wall generates a negative triboelectric charge and an electric potential range directly related to flow rate. The aim of our study was firstly to investigate the potential reliability of a wearable device able (Figure 1A) to record this constant potential and consequently evaluating the aptitude of waveforms generated to detect AVF stenosis in comparison to standard doppler evaluation.

Method: Between September 2022 and January 2023, we screened forty-eight patients from two hemodialysis centers in Catanzaro (Italy) Patients were divided in two groups basing on the assessment from two blinded experienced examiners for recognized criteria for stenosis: 2 major criteria (reduction of vessel size greater than 50% and a ratio between systolic peak velocity (SPV) in the stenotic region and SPV in pre-stenotic region major of 2 (>2)) and a supplementary finding like drop of the access flow (QA) below 500ml/min or drop of QA ≥25% as compared to the previous measurements in FAV with QA <1000ml/min or residual diameter <2mm). Patients were then evaluated using the PVDF/Kapton triboelectric sensor placed in contact with the skin on the lower surface, and with the thumb in contact with the upper surface to close the circuit and graphically recording typical pattern waveform generated. AVFs were analyzed considering the following acquisition sites: the chamber which corresponds to the site where surgery anastomosis was performed, a site located 5 cm from the chamber, and finally at the level of the humeral artery.

Results: There was an almost perfect (R = 0.97) correlation between the blood flow measured at the humeral artery level and the maximum-time derivative
equation computed for each patient (Figure 1B). Based on doppler evaluation, 14/48 patients (29%) were classified as stenotic. Of these, 13 patients (93%) presented a typical wave pattern (B-point) with a 'Notch' shape (Figure 1D) which, conversely, was found in only 1 patient out of 34 without evidence of stenosis. The presence of Notch reflected the presence of stenosis with a Sensitivity of 92.8% (95%CI 66.1 to 99.8%), a specificity of 97% (95%CI 84.7 to 99.9%), holding an overall accuracy of 95.8% (95%CI 85.7% to 99.5%). Patients without stenosis assumed a different waveform (Figure 1C).

Conclusions: In chronic hemodialysis patients, the evaluation of AVF by a biosensor based on triboelectric potential measurement might represent an accurate and easy-to-perform surrogate of standard eco-doppler method for a quick and reliable evaluation of AVF functioning and, particularly, for a rapid risk stratification of patients with high suspect of AVF stenosis.

#5411
CARDIO-FISTULA RECIRCULATION REDUCTION IN OLDER ADULTS: IT'S NOT THAT EASY

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Background and Aims: Older adults are approximately 40% of all prevalent HD patients [ERA Annual report]. Cardiovascular disease is the leading cause of death in this cohort. It is well-known that the cardiotoxic effect of arteriovenous fistula (AVF) is fully realized when cardio-fistula recirculation (CFR) is above 20-30%. We believe that the reduction of AVF blood flow (Qa) in the elderly is often less effective than in the younger patients. Aim: to evaluate the outcomes of Qa reduction in the elder and the younger HD patients.

Method: The prospective cohort study included 21 patients over 60 years old and 36 patients under 60 years old: the median age was 74 years [IQR 69; 78, min-max 64-81] and 41 years [IQR 35; 45, min-max 31; 55], respectively. Qa before reduction was more than 25%: 32.8% [IQR 29.2; 35.1, min-max 27.3; 38.9] and 33% [IQR 31; 35.125, min-max 27.1; 39.3], respectively. Qa reduction was performed by banding of the paraanastomotic AVF segment with intraoperative control (Doppler ultrasonography) until reaching Qao of 1.5 l/min or less.

Results: In all patients, we noted a significant (p<0.0001 in all cases) decrease in Qa as a result of the banding: in older adults from 2.1 l/min [IQR 1.9; 2.4, min-max 1.8; 2.8] to 1.2 l/min [IQR 1.1; 1.4, min-max 0.8; 1.5], delta Qa was -1 l/min [IQR -1.2; -0.9, min-max -1.5; -0.7], in younger patients from 2.8 l/min [IQR 2.5; 3.1, min-max 1.9; 3.5] to 1.3 l/min [IQR 1.1; 1.4, min-max 0.9; 1.5], -1.5 l/min [IQR -1.7; -1.3, min-max -2.3; -0.9], respectively. In both older and younger patients, we noted a significant decrease in CFR - Fig. 1. However, after Qa reduction, only 5 of 21 elderly patients had CFR value less than 20%. Thus, 17 of 21 patients had CFR in the «gray zone» - 20-30%: 22.8% [IQR 21.85; 27.3, min-max 21; 29.2]. In younger patients, 25 of 36 had CFR less than 20% after Qa reduction, while 11 stayed in the «gray zone» - 21.15% [IQR 20.575; 22.3, min-max 20.3; 23.4]. The probability of reducing CFR to a safe level (less than 20%) after surgery was significantly less in the elder patients: RR = 0.3429 [95% CI 0.1495; 0.6852], p = 0.0011. We consider the lower baseline cardiac output in the elderly to be the main reason of the lower efficacy of Qa reduction: the difference between medians (older adults-younger patients before Qa reduction, Hodges-Lehmann method) was 1.9 l/min [95% CI 1.5; 2.4], p <0.0001. At the same time, Qa before reduction did
Changes in ejection fraction as a result of Qa reduction in HD patients > 60 and < 60 years old.

not differ much between the older and the younger: 0.61/ min [95% CI 0.4; 0.8], p < 0.0001. Moreover, the reduction of Qa in elderly patients led to a decrease in the ejection fraction (EF), which was not noticed in young patients - Fig. 2. Notably, in all patients of both groups the initial value of the EF was more than 55%. We believe that this can be explained by an abrupt increase in afterload against the background of a decreased compensatory heart capability in the elderly. At the same time, decrease in the EF after Qa reduction in the elderly may indirectly indicate that conventional EF in the elderly is maintained by a presence of a high-flow AVF. Evaluation of EF against this background creates a putative picture of well-being and can mask the development of heart failure with reduced EF for a long time.

Conclusion: We noted a lower efficacy of Qa reduction as a method of reducing both cardio-fistula recirculation and cardiovascular risk in the elderly patients compared to the younger patients on maintenance HD. Elder patients seem to require a different approach to reduce cardiovascular risk than younger patients.

#4588
EFFECT OF TRISODIUM CITRATE 30% VERSUS HEPARIN AS A CATHETER LOCK SOLUTION ON INFLAMMATORY RESPONSE AND DIALYSIS ADEQUACY IN HEMODIALYSIS PATIENTS
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Background and Aims: In hemodialysis (HD) patients, the majority of bloodstream infections are caused by infection of vascular access catheters. Commonly, Central venous catheters (CVCs) are the only option when HD is needed for patients without definitive vascular access. However, in addition to infection, CVCs are associated with other complications, such as thrombosis, and dysfunction, leading to higher mortality and expenditures. In Egypt, recent data show that 6.6% of HD patients use catheters as a vascular access, of which short term catheters represent 59.6% and 40.4% with long-term catheters. Many data show that the use of HD catheter-locking solutions could contribute to reduction of catheter-related complications, especially infections.

Aim: to assess the possible effect of using Trisodium citrate 30% (TSC 30%) in comparison to unfractionated heparin, as a lock solution for HD catheters, on inflammatory status, incidence of catheter related Bacteremia (CRB) and dialysis adequacy in HD patients.

Method: This was a randomized controlled clinical trial, conducted on 70 prevalent HD patients on regular dialysis using HD catheters as a vascular access, recruited from hemodialysis unit in Nasser Institute Hospital in Cairo government at the time of catheter insertion. Patients were divided into two groups: Citrate Group; 35 patients received trisodium citrate 30% as a catheter lock after HD session, Heparin Group; 35 patients received unfractionated heparin (5000i.u) as a catheter lock solution after HD session. Both groups were followed up for 3 months period and monitored for signs of CRB. Also, Urea reduction ratio (URR) were measured monthly. Highly sensitive CRP were measured at baseline and 3 months after start using the lock solutions. Blood cultures were withdrawn in patients who developed signs of CRB.

Results: In our study, the catheter-related bacteremia (CRB) episodes were significantly lower in the Citrate group when compared to Heparin group. Only 2 patients (5.7%) in Citrate group had CRB, whereas in Heparin group, 8 patients (22.9%) had CRB (P = 0.04) (Fig. 1). Also, Bacteremia-free time was longer in the Citrate group. The mean bacteremia free time in Citrate group was 10.97 ± 2.36 weeks, while in Heparin group it was 9.43 ± 3.91 weeks.

Figure 1: Comparison between the two studied groups according to CRB.
CRB: Catheter Related Bacteremia.
Figure 2: Kaplan-Meier curve for Bacteremia Free Time.  
Group 1 = citrate group.  
Group 2 = heparin group.

Figure 3: Comparison between the two studied groups according to CRP.  
CRP: C-reactive protein.

Figure 4: Comparison between the two studied groups according to URR.  
URR: Urea Reduction Ratio.
(P = 0.032) (Fig. 2). At base line, there was no significant difference between both groups regarding hsCRP (P = 0.596) and WBCs (P = 0.528). While after 3 months of using TSC 30% as a lock solution, there was a significant difference as regards levels of hsCRP (P = 0.030) (Fig. 3) and WBCs (P = 0.036), with the higher levels of inflammatory markers showed in Heparin group. There was no difference between the two studied groups regarding thrombosis events. However, dialysis adequacy and catheter performance, assessed by URR, were higher in citrate group compared to heparin group after 3 months (P = 0.005) compared to baseline (P = 0.108) (Fig. 4).

Conclusion: we may conclude that, using Trisodium citrate 30% as lock solution for HD catheters was associated with reduction in the inflammatory markers and CRB incidence compared to the standard heparin lock. Also, its use was associated with better catheter performance and dialysis adequacy. We therefore believe that TSC 30% may be a potential alternative to standard heparin as a catheter lock solution for HD patients.

Figure 2: Correlation between change in flow during 28 days of AVF maturation and end-diastolic volume at the first day post-AVF creation (EDV1).

Conclusion: Hemodynamic parameters of the brachial artery, precisely peak systolic volume and end-diastolic volume at the first day post-AVF creation, play a significant role in AVF maturation. CDU measurements of those hemodynamic parameters at day 1 may be useful for an early identification of AVF maturation outcomes.

Figure 1: Correlation between change in flow during 28 days of AVF maturation and peak systolic volume at the first day post-AVF creation (PSV1).
presence of complications was statistically related to age (p = 0.046), with more events in older patients at the time of AVF construction. There was no statistical difference between complications’ occurrence and AVF type, sex, gender, PLR, and NLR.

**Conclusion:** The utilization of AVF for HD has been growingly recognized as a safe and efficient alternative for the performance of KRT in pediatric patients. Although larger studies are needed, we demonstrate positive results in its usage in younger patients, as complications were associated with older age. PLR in a pediatric population, with high primary and secondary patency rates. Although larger studies are needed, we demonstrate positive results in its usage as a safe and efficient alternative for the performance of KRT in pediatric patients.

**Table 1.** Showed the characteristics of the patients according to AVF outcome.

<table>
<thead>
<tr>
<th></th>
<th>Total (N = 159)</th>
<th>Mature AVF (n = 148)</th>
<th>Non-mature AVF (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>60.99±14.93</td>
<td>60.74±15.03</td>
<td>64.30±13.84</td>
</tr>
<tr>
<td>Female: Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetess</td>
<td>94 (59.1%)</td>
<td>87 (58.8%)</td>
<td>7 (63.6%)</td>
</tr>
<tr>
<td>Smoking history</td>
<td>29 (18.2%)</td>
<td>26 (17.6%)</td>
<td>2 (37.3%)</td>
</tr>
</tbody>
</table>

**Table 2.** Showed the patient characteristics and AVF outcome according to the angle of anastomosis.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (≤45°) (n = 102)</th>
<th>Group 2 (&gt;45°) (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>61.72±14.86</td>
<td>59.75±15.12</td>
</tr>
<tr>
<td>Female: Male</td>
<td>28(74)</td>
<td>19(38)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>59 (57.8%)</td>
<td>35 (61.4%)</td>
</tr>
<tr>
<td>Smoking history</td>
<td>17 (16.7%)</td>
<td>12 (21.1%)</td>
</tr>
<tr>
<td>AVF outcome:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor maturity</td>
<td>7 (6.9%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>Good maturity</td>
<td>95 (93.1%)</td>
<td>53 (93%)</td>
</tr>
</tbody>
</table>

**Conclusion:** This study has not established nor confirmed to any meaningful degree any relationship between the anastomotic angle using 45° as a cut-off and the maturation rate of AVF in Chinese patients at 3 months. Our overall AVF maturation rate was very high and none of the traditional risk factors for failed AVF nor the degree of anastomotic angle have any demonstrable effect on AVF maturation. The success might have been in part due to the skill and dedication of the nephrologists as operators. A prospective study involving a bigger patient group is necessary to further explore the effect of anastomotic angle on AVF maturation if any.
Conclusion: In our study sample, most patients started HD through a CVC, despite the majority having at least 3 months of pre-HD nephrology care. When adjusting for other covariates in a multivariate model, the first VA did not present a strong association with survival outcomes. The appropriate VA in the very elderly patient is an ongoing debate, and doubts remain regarding the applicability of the “Fistula First, Catheter Last” policy in octogenarian and nonagenarian patients. Our results are in line with recent reports which suggest that initial CVC use with later placement of an AVF, shortly after HD initiation, does not confer worse prognosis than initial AVF use in very elderly patients [2]. One of the limitations of our study was not having collected data regarding timings of AVF construction and use, which might have been informative regarding the impact of catheter-dependence time in survival.

REFERENCES

Table 1: Multivariate Cox proportional hazard model of survival in incident HD patients (multivariate).

<table>
<thead>
<tr>
<th></th>
<th>HR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at HD initiation</td>
<td>1.03 (1.02-1.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female vs male</td>
<td>0.93 (0.80-1.09)</td>
<td>0.4</td>
</tr>
<tr>
<td>PKD vs DKD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glomerular nephropathies</td>
<td>0.55 (0.40-0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular nephropathy</td>
<td>0.59 (0.31-1.41)</td>
<td>0.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.44 (0.30-0.64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tubulointerstitial disease</td>
<td>0.55 (0.39-0.78)</td>
<td>0.001</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>0.26 (0.13-0.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>0.47 (0.35-0.64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.59 (0.48-0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular access at HD initiation vs AVF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporary CVC</td>
<td>1.51 (1.20-1.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TUNneled CVC</td>
<td>1.83 (1.42-2.36)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

A national strategy should be implemented to improve CKD care, aiming to increase both the rate of AVF usage at HD, and the conversion from CVC to AVF in the six months.

Figure 1: mNTRC, gentle movement in and out though a venotomy of proximal to cuff part of a CTC with flashing.
published with modification including mandatory CTC lines flushing and locking lines with antithrombotic agent after the dialysis session.

**Results:** A number of 205 mNTCR were performed in 110 patients with CTC. Effective blood flow CTC was obtained after 115 procedures (56%), partial failure followed 73 procedures (35.6%), and 17 attempts (8%) failed. Over 90% interventions improved a CTC patency allowing start of effective haemodialysis. The procedure could be successfully repeated with similar effect after the first, and the second attempt (28 vs 22 hemodialyses performed respectively). In the group of 50 elderly patients (median age 74 years) with CTC as the only vascular access, mNTCR was successful in 31 patients allowing dialysis continuation for median period 54 months. The mNTCR is safe as minor complications were observed after 5.1% of all procedures.

**Conclusion:** The novel mNTCR manoeuvre was safe and effective in a majority cases of CTC dysfunction. It permitted immediate dialysis without time-consuming fibrinolytic agents usage protocols before the dialysis session, saving costs and nursing staff time.

#6037

**VALUE OF ARTERIAL CALCIFICATION DETECTED BY UPPER LIMB DOPPLER ULTRASOUND IN ADVANCED CHRONIC KIDNEY DISEASE**

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**Background and Aims:** Vascular calcification is a common complication of chronic kidney disease (CKD), particularly in end-stage renal disease (ESRD) and is predictive of subsequent cardiovascular disease and mortality. The aim of the present study was to evaluate the relationship between arterial calcification assessed by doppler ultrasound (DUS) performed by the same team of-care therapy for CKD-MBD.

**Calcifications can be a surrogate of CKD-MBD and cardiovascular burden.**

Vascular calcification on DUS was associated to mortality. In patients with vascular calcifications, moderate/severe calcification was associated with diabetes mellitus (OR 2.85, p < 0.000), male gender (OR 1.69, p < 0.012), PAD (OR 2.43, p < 0.001) and hemodialysis therapy for more than 5 years (OR 3.00, p < 0.010). Cinacalcet, phosphate binders, serum calcium, phosphorous, PTH and mortality did not correlate with calcification severity. In the multivariate logistic regression analysis adjusted to age, gender, PAD and serum calcium, only phosphate binders and cinacalcet use were predictive of absence of vascular calcifications, however no causality could be advanced with these data. Serious calcification, in our multivariable model, only PTH had statistical significance. It is widely recognized the importance of monitoring serum PTH, calcium and Pi to reduce the adverse clinical events associated with CKB-MBD. Widespread implementation of DUS in pre-surgical mapping for VA construction is also an opportunity for vascular study and features as calcifications can be a surrogate of CKB-MBD and cardiovascular burden.

**Results:** The demographics and biochemistry of the study population are summarized in Table 1. Arterial calcification was observed in 91.6% (n = 416) of the patients, 62.3% (n = 229) had mild calcification and 37.7% (n = 157) presented moderate/severe calcification. In univariate analysis, male gender (OR 2.2, p < 0.023), age (OR 1.03, p < 0.003), phosphate binders (OR 0.55, p value < 0.03) and cinacalcet use (OR 0.28, p < 0.019) were independently associated with the presence of arterial vascular calcification. Presence of vascular calcification on DUS was associated to mortality. In patients with vascular calcifications, moderate/severe calcification was associated with diabetes mellitus (OR 2.85, p < 0.000), male gender (OR 1.69, p < 0.012), PAD (OR 2.43, p < 0.001) and hemodialysis therapy for more than 5 years (OR 3.00, p < 0.010). Cinacalcet, phosphate binders, serum calcium, phosphorous, PTH and mortality did not correlate with calcification severity. In the multivariate logistic regression analysis adjusted to age, gender, PAD and serum calcium, only phosphate binders and cinacalcet use were predictive of absence of vascular calcifications, however no causality could be advanced with these data. Serious calcification, in our multivariable model, only PTH had statistical significance. It is widely recognized the importance of monitoring serum PTH, calcium and Pi to reduce the adverse clinical events associated with CKB-MBD. Widespread implementation of DUS in pre-surgical mapping for VA construction is also an opportunity for vascular study and features as calcifications can be a surrogate of CKB-MBD and cardiovascular burden.

**Conclusion:** Concerning CKB-MBD related markers our study showed that only phosphate binders and cinacalcet use were predictive of absence of vascular calcifications, however no causality could be advanced with these data. Serious calcification, in our multivariable model, only PTH had statistical significance. It is widely recognized the importance of monitoring serum PTH, calcium and Pi to reduce the adverse clinical events associated with CKB-MBD. Widespread implementation of DUS in pre-surgical mapping for VA construction is also an opportunity for vascular study and features as calcifications can be a surrogate of CKB-MBD and cardiovascular burden.

**Table 1: Demographics and biochemistry of study population.**

| Age (y) | 65.52 ± 15.28 |
| Male (%) | 57.05 (n = 259) |
| Pre-dialysis (%) | 57.96 (n = 262) |
| HD < 1 year (%) | 28.98 (n = 131) |
| HD > 1 and < 5 years (%) | 6.19 (n = 28) |
| HD > 5 years (%) | 6.86 (n = 31) |
| CKB etiology (%) | |
| ADPKD | 4.42 (n = 20) |
| Diabetic nephropathy | 21.46 (n = 97) |
| Multifactorial | 21.68 (n = 98) |
| Glomerular/tubulointerstitial disease | 16.15 (n = 73) |
| Urologic disorders | 8.19 (n = 37) |
| Unknown | 12.61 (n = 57) |
| Miscellaneous | 5.09 (n = 23) |
| Diabetes mellitus (%) | 44.37 (n = 201) |
| Hypertension (%) | 92.49 (n = 419) |
| Heart Failure (%) | 33.11 (n = 150) |
| Periperal artery disease (PAD) (%) | 17.48 (n = 79) |
| Coronary or cerebrovascular disease (%) | 27.81 (n = 126) |
| Obesity (%) | 29.74 (n = 135) |
| Current or previous Smoking (%) | 35.46 (n = 161) |
| Calcium (mg/dL) | 8.6 ± 0.94 |
| Phosphorous (mg/dL) | 4.61 ± 1.32 |
| Magnesium (mg/dL) | 2.02 ± 0.65 |
| PTH (pg/dL) | 439.76 ± 693.91 |

**#3197**

**A NOVEL INVESTIGATION OF AVF WITH A SECOND HARMONIC GENERATION MICROSCOPY IN PATIENTS WITH END STAGE RENAL DISEASE**

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**Background and Aims:** The population of patients with end-stage renal disease is rapidly growing and hemodialysis (HD) remains the most common treatment option. In clinical practice, the formation of arteriovenous fistulas (AVFs) is considered a priority in order to ensure optimal vascular access for HD patients. One of the complications in the formation of AVF is the hyperplasia of the neonotal layer of the vein, which leads to the failure of the fistula. The impact of the arrangement of collagen fibers in the veins of AVFs is little studied and opens wide opportunities for investigations. The structural tissue can be imaged with polarimetric nonlinear microscopy. Collagen fibers have a non-centrosymmetric structure, so they can be effectively imaged by second harmonic generation (SHG) microscopy [1]. The polarimetric nonlinear microscopy, exploiting the multidimensional tensor nature of light-matter interactions, is emerging as a valuable research tool in biomedical investigations and applications to digital pathology, and is only now becoming technically feasible for potential clinical translation [2,3]. This proposal represents a novel application of multidimensional polarimetric nonlinear microscopy in histopathology, and biomedical imaging. The aim of this study is to determine the influence of the arrangement of collagen fibers in veins on the formation efficiency of AVFs by using the innovative method of nonlinear SHG microscopy.

**Method:** In this prospective study, we first used a novel SHG microscopy method to investigate AVFs venous intima hyperplasia. V. Cephalica segment is being obtained during arteriovenous fistula formation surgery from patients with end stage renal disease and after the removal of aneurysmatic or fibrotic AVF. Cross-sections of venous specimens are being fixed in 10% buffered

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formalin and stained with hematoxylin and eosin (H&E). Further, sample investigation is being performed in Laser Research Centre, Vilnius University using a home-built multiphoton laser-scanning microscope. The investigation is being performed with the permission of Lithuanian Biomedical Research Ethics Committee.

**Results:** We determined the arrangement of collagen fibers in veins before AVF formation and after the removal of aneurysmatic AVFs. It was observed that tunica intima of V. Cephalica is dominated both by endothelial cells and connective tissue made up of high-density collagen fibers. Whereas tunica adventitia consists mainly of collagen fibers. Collagen in tunica intima and adventitia are found to be highly noncentrosymmetric. Thus a strong SHG signal, resulting in high-contrast structural visualization of the V. Cephalica segment is generated.

**Conclusion:** Our initial investigations of AVF show clearly visible collagen fibers. The future work will focus on the structural changes of collagen fibers in the vein intimal hyperplasia. Further investigations need to be done to create artificial intelligence-based identification of new predictive collagen markers.

**REFERENCES**


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**#5863**

**A NOVEL SELF-SEALING DIALYSIS PORT EVALUATION**

Jacob Wright1, Alan Benvenisty2, Kenneth Nakazawa2, Marina de Cos Gomez2, Philip Nasser3, Hynton Gordon4, Jonathan Cohen4, Kirk Campbell1, Eric Lima5 and Evren Azeloglu1

1Icahn School of Medicine at Mount Sinai, Surgery, New York, United States of America, 2Icahn School of Medicine at Mount Sinai, Comparative Medicine and Surgery, New York, United States of America, 3Icahn School of Medicine at Mount Sinai, Biomechanics Core, New York, United States of America, 4Icahn School of Medicine at Mount Sinai, Comparative Medicine and Surgery, New York, United States of America and 5 The Cooper Union, New York, United States of America

**Background and Aims:** There are several complications associated with hemodialytic vascular that arise from the incorrect cannulation, including aneurysms, infection, vessel damage, and uncontrolled bleeding. These risks severely limit treatment opportunities for self-cannulation by patients, which is necessary step for home hemodialysis. To improve quality of life and reduce complications, we developed a novel access port, called Safe Entry Port for AV fistulae (SEAL), that integrates with fistulae, guides cannulation, and uses an internal colinear valve to prevent aneurysms with minimal risk of back-bleeding and infections (Figure 1A-C).

**Method:** The device was additively manufactured using direct metal laser sintering of FDA-approved Ti-6Al-4V. It was then polished and coated with silver-doped titanium nitride (TiN/Ag). The operation of the valve was tested in a mock circulation system using a peristaltic pump and Tyvek tubing to produce a pulsatile hydrostatic pressure gradient. The antimicrobial properties of the valve coating were evaluated in vitro against biofilm formation using standard assays for bacterial spreading area and turbidity. A custom computer-controlled robotic cannulation system was created to fatigue test the port as well as to determine the needle force required to open the valve. Finally, the device was implanted subdermally on a mature brachiophedic arteriovenous fistula of an adult sheep and cannulated biweekly for six weeks.
Device integration and host tissue reaction were evaluated using standard histopathological methods and micro-CT scanning.

**Results:** SEAL is engineered to integrate directly over a fistula via a Ti matrix (a mesh of small holes covering the sides of the device for interaction with host tissue). No fluid leaked through the valve during *in vitro* testing even under physiologically high circulatory pressure. In repeated cannulations of the device during *ex vivo* simulations with 14G dialysis needles, the peak force required to engage the valve recorded in our dialysis fatigue cycling simulation was $160.5 \pm 0.02$ mN (Figure 1D, E). The device withstood cannulation cycles equivalent to 14 years of dialysis. Furthermore, the colinear valve smoothly opened for continuous flow through the needle guide (Figure 1F-I) and closed automatically under the tensile force similar to that of subcutaneous tissue. Antimicrobial TiN/Ag coating showed significant reduction in bacterial growth in both biofilm assays (Figure 1J,K). In preclinical trials, no signs of infection or backbleeding were observed during the continuous six-week cannulation period; vascular access was continuous with no resistance or complications.

**Conclusion:** We show that SEAL nearly eliminates backbleeding risk both *in vitro* and *in vivo*. The TiN/Ag coating of the colinear valve significantly limits bacterial biofilm formation *ex vivo*. Preclinical studies in the sheep model show that the device implanted on a mature fistula can easily be cannulated twice a week without any infection, cannulation complications, or backbleeding for an extensive period. SEAL has the potential to change the future of dialysis treatments, improve the quality of life for patients due to the reduction of complications, and allow improved access to home hemodialysis.
#6345 HIGH BRACHIAL ARTERY BIFURCATION AND CLINICAL IMPLICATIONS UPON HEMODIALYSIS VASCULAR ACCESS PLANNING
Pilar Simões, Juliana Francisca Da Costa e Silva Barbosa Damas, Tiago Assis Pereira, Catarina Maruço, Mafalda Sobral, Sofia Corado, Sofia Carellha, Ana Pena, Bernardo Do Sacramento Marques Da Costa and Cristina Jorge
Centro Hospitalar Universitário de Lisboa Central, Portugal

Background and Aims: Preoperative ultrasound mapping provides information about overall vessel, caliber, flow and anatomic variations, useful for hemodialysis (HD) vascular access planning. High bifurcation of the brachial artery (HBBA) is one of such variations, established early upon fetal development. Its implications in arteriovenous HD access creation are fairly unknown. The present work aims to characterize the prevalence and demographic characteristics of patients presenting with HBBA and study its impact upon HD vascular access planning, construction and patency.

Method: We developed a retrospective study focusing on 457 patients accessed from 2018 to 2021. Demographic data and presence of HBBA were registered as well as vessel diameter and peak systolic velocities (PSV) for brachial and radial arteries. Theoretical feasibility for each specific access (i.e., radiocephalic, brachiocephalic, brachiobasilic and prosthetic fistulae, according to ultrasound evaluation), final choice of access and 30-day patency were also gathered. Categorical variables are presented as frequencies and percentages and continuous variables as means and standard deviations or medians and interquartile ranges, as appropriate. Logistic regressions were adjusted considering sex, race, arm dominance and HBBA as independent variables.

Results: From a total of 457 patients, 193 (42.2%) were women and 264 (57.8%) were men. Mean age was 65.4 ± 15.3 years. 383 (83.8%) were Caucasian and 427 (93.4%) were right-handed. High bifurcation of the brachial artery was present on both arms of 6 (1.3%) patients, only one arm on 62 (13.6%) and on none of the remaining 389 (85.1%) patients. We found an association between being non-Caucasian and presenting with HBBA (27% vs 12.5%, p-value = 0.01) but not with sex or arm dominance. Considering all patients, female sex was associated with smaller radial artery diameter, (2.0 ± 0.7 mm vs 2.2 ± 0.6 mm, p < 0.01). HBBA was not associated with a significant difference on arterial diameters (adjusted for sex and race) and there were also no significant differences when comparing dominant vs non-dominant arms. We found no association between HBBA and the theoretical feasibility of a radiocephalic fistula but rather with the choice of arteriovenous graft as the only possible access (26.5% vs 19.5%, p-value = 0.044). A total of 379 (77.0%) patients proceeded to vascular access construction: 59 (15.6%) radiocephalic fistulas, 229 (60.4%) brachioccephalic fistulas, 31 (8.2%) brachiobasilic fistulas and 60 (15.8%) arteriovenous grafts were created, with no differences between HBBA and non-HBBA groups. There was, however, an association between non-Caucasian patients and the choice for a more proximal access (p = 0.001) as well as the need for surgical or angiographic reintervention within 45 days after access creation (11% [95% CI: 6.0% - 16.7%], p-value = 0.002).

Conclusion: Our study suggests that presenting with HBBA is not necessarily associated with lower quality vessels and less distal access construction. However, this variation seems to be more frequent among non-Caucasians, who appear to receive more proximal accesses, in greater need for early intervention than their counterparts. Further investigation is necessary to understand if apart from diameter or PSV, HBBA could influence other determinants of access placement choice, such as distance from brachial artery to cephalic or basilic vein or risk of distal hypertension syndrome.

#6792 VASCULAR ACCESS SURVIVAL OUTCOME IN ELDERLY HEMODIALYSIS PATIENTS: A SINGLE-CENTER RETROSPECTIVE STUDY
Bongkok Surattichaiyakul
Bhumiranjagarindra Kidney Institute Hospital, Bangkok, Thailand

Background and Aims: Elderly hemodialysis patients usually have lower life expectancy of vascular access than another age-group. Our center, elderly patients are the most of population of hemodialysis patients. Prior to initiate hemodialysis, planning of first vascular access has been established by patients, nephrologist, and vascular surgeon. The calculation technique for arteriovenous fistula (AVFs) has been determined by experienced hemodialysis-nurse and patient preferences. The aim of this study was to analyze the survival outcome of the access depending on the vascular type in the elderly.

Method: The study was collected retrospective data between Jan 1, 2013, and December 31, 2022. We identified elderly patient (age ≥65) who initiate in-center hemodialysis and first-use vascular access in our center, including arteriovenous fistulas, graft, tunnel-catheter. Outcomes were vascular access patency and subgroup analysis for non-extreme elderly group and extreme (age ≥80) elderly group. A χ2 test, Kaplan-Meier analysis were performed.

Results: Overall number of elderly patients who initiated hemodialysis are 170: 63 AVFs-first (74% buttonhole cannulation technique), 21 grafts-first and 86 forter nal-catheters. Mean survival of vascular accesses are higher in AVFs group (78 months in AVFs, 52.5 months in grafts, 53.3 months in tunnel-cather P = 0.012). The outcome was consistency in the subgroup age 65-80 (89.0 months in AVFs, 47.3 months in grafts, 47.2 months in tunnel-cather P = 0.005). However, mean vascular access survival did not differ in subgroup age ≥80 (56.3 months in AVFs, 58.4 months in grafts, 56.4 months in tunnel-cather P = 0.98).

Conclusion: In our single center data, vascular access patency of elderly patients was highest in AVFs-first group and AVFs should be the first choice for elderly patients who would initiate hemodialysis especially non-extreme elderly group.

#3179 PREDICTORS OF VASCULAR ACCESS THROMBOSIS IN MAINTENANCE HEMODIALYSIS PATIENTS – QA, KT/V AND CONVEXTIVE VOLUME
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Background and Aims: Vascular access (VA) is vital for hemodialysis (HD) treatments and should allow to achieve the recommended dose of dialysis. Thrombosis is the primary cause of VA failure in grafts (AVG) and fistulas (AVF) and should be avoided as it can lead to significant patient morbidity and mortality. However, despite its importance, predictors of VA thrombosis are not completely established. Even if large randomized controlled trials are lacking to clearly identify the ideal surveillance strategies and benefits of surveillance, evidence suggests that when combined with preemptive interventions, prospective monitoring and surveillance and early detection of dysfunctional VA may reduce the thrombosis rate and improve its long-term patency. Several monitoring and surveillance techniques of VA can be used, from unexplained drop in dialysis adequacy (Kt/V and convective volume) to the noninvasive estimation of VA blood flow (Qa). The aim of this study was to assess whether these parameters can predict VA thrombosis.

Method: We retrospectively evaluated all episodes of VA thrombosis admitted in our Vascular Access Centre (VAC) between July 2019 and December 2022. Patients’ demographics, VA characteristics and data from dialysis sessions were collected. Descriptive statistics were calculated and expressed as mean (standard deviation) or median (IQR) or count (%), as adequate. Values were compared using Mann-Whitney for independent samples and Pearson chi-squared test with 95% confidence intervals (CI). The predictors of VA thrombosis studied were Qa, Kt/V and convective volume (CV), in the case of thrombosis on hemodiafiltration. Qa was measured using the thermodilution method called blood temperature monitoring (BTM®), and Kt/V and CV with Online Clearance Monitoring (OCM®). In this study, we evaluated the ratio between the last measured value of Qa prior to the thrombosis episode and the average of the previous three months (Qa trend), and the ratio between the last measured value of Kt/V and CV before the thrombosis episode and the average of the previous month (Kt/V trend and CV trend, respectively) as predictors of VA thrombosis.

Results: From July 2019 and December 2022, we treated, in our VAC, 386 VA thrombosis episodes in 226 patients. In our study population, mean age was 71.1 (± 13.2) years, 64% were male, 31% had diabetes. The dialysis vintage was 51 (69) months and the VA vintage was 42 (62) months. 70.2% of the VA thrombosis were on AVF. Prior to thrombosis the median of Qa obtained by BTM was 650 (495) mL/min, the median of k/t/V was 1.63 (0.62) and the median of CV was 22.4 (6.3). The average of the previous values for Qa, Kt/V and CV were 658 (333) mL/min, 1.53 (0.35) and 23.5 (3.9) L. The median (IQR) trend of Qa trend, Kt/V trend and CV trend were -8.5 (33.3) %, -6.0 (28.2) % and -2.5 (17.0)%. We found no statistical significance for Qa trend and CV trend between AVF and AVG as predictors of VA thrombosis, but the reduction in Kt/V values was significantly more pronounced in AVF (-6.8%; Q1 -20.1% to Q3 0.7%) than in AVG (-3.8%; Q1 -18.0% to Q3 -5.0%) (p = 0.007) as predictor of thrombosis. In 68.9% of VA thrombosis, we noticed a reduction in Kt/V value before the episode (73.8% in AVF and 57.5% in AVG, p = 0.002). We found no statistically significance in the reduction of Qa and CV values between AVF and AVG thrombosis episodes.
Conclusions: Our study showed that Ki/V trend was a better predictor of VA thrombosis than Qa trend and CV trend, especially in AVF.

#5014

VALIDATION AND APPLICABILITY OF A MONITORING SYSTEM FOR VASCULAR ACCESS IN HAEMODIALYSIS: A MULTICENTRE STUDY

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Background and Aims: Routine systems for monitoring vascular access (VA) performance are lacking. We recently showed that with a VA triage system it is possible to improve the average value of a number of VA efficiency parameters and that the VA triage score was associated with clinical outcomes. The triage categorization is generated monthly by a scoring system which is based on a number of parameters (blood flows, VA pressure values, end HD circuit clots and a dedicated score of the external VA examination, Ki/V) recorded at each session by the staff on a dedicated electronic spreadsheet. According to threshold values, triage classified each VA in Green (G), Yellow (Y) or Red (R), thus indicating the VA performance and the clinical risk of complication linked to VA. In our open label single centre study, with three years of follow-up, the average VA score improved significantly and G VA associated with lower mortality, compared to the Y and R VA. Aims: To validate the ability of the triage system to early identify VA with increased risk of complications.

Methods: In this interventional prospective, blinded multicentre study, each centre used the VA triage electronic spreadsheet without knowledge of the generated triage. After six months of system implementation, two years of follow-up (01/01/2020 - 01/12/2021) were planned to record VA related events. Two external reviewers evaluated the records. A minimum of three months VA follow up was necessary for patients enrollment.

Results: From 18 HD centres we enrolled 757 patients, aged 64.5±15.5 y.o.; 27% diabetics; HD since 24.4±2.4 months; 369 (48.7%) with arteriovenous fistula (AVF) and 388 (51.3%) with permanent central venous catheter (CVC). During 11.4±5.6 months of follow-up (range 3-23), 10853 are HD sessions were recorded on the triage electronic spreadsheet, with 214 total clinical events and an event free time of 224.5±172 days (range 4-713). The VA related events were 130 (70.1%) during 16.3±2.2 months of follow-up (range 3-23) with an event free time of 230±160 days (range 11-713). The VA Triage was: 60% Green, 35% Yellow and 5% Red. In the 369 patients with AVF the VA Triage was: 61% Green, 36% Yellow and 3% Red; The AVF Triage Green group showed: lower incidence of VA related events respect to the AVF Triage Yellow and Red group (30% vs 48%; P: 0.05; higher time-free from VA events (AVF Green vs AVF Yellow-Red: log-rank test: 0.04). Similar results were confirmed in the CVC groups: VA events incidence Triage Green 15% vs Triage Yellow-Red 40% (p: 0.001; time-free from VA events log-rank Test 0.001).

Conclusion: Our VA triage system identifies 40% of vascular accesses as yellow-red triage. These VA were not identified as at elevated clinical risk by the dialysis staff and only the Triage system was able to highlight them as critical. Notably the VA access with Yellow and Red Triage independently from the VA typology had an higher risk of clinical complications that according to the time survival curve could be detectable roughly 237.8 days before the event developed. The Triage system was able to identify early the VA with increased clinical risk and it may be a useful tool to prevent VA complication.

#4500

IMPLEMENTATION OF A NEW GENERATION DIGITAL STETHOSCOPE FOR ARTERIOVENOUS FISTULA MONITORING IN HEMODIALYSIS PATIENTS

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“Magna Graecia” University of Catanzaro, Catanzaro, Italy

Background and Aims: The management of complications of arteriovenous fistula (AVF) for hemodialysis, principally stenosis, remains a major challenge for clinicians with a substantial impact on health resources. Stenosis not infrequently preludes to thrombotic events with the loss of AVF functionality. A frequent monitoring with physical examination is at the basis for an appropriate clinical care. It includes a regular inspection, palpation and auscultation of the arm. A normally functioning AVF, when listened by a stethoscope, has a continuous systolic-diastolic low-frequency murmur while with stenosis the frequency of the murmur increases and the duration of diastolic component decreases, disappearing in severe stenosis. These evidences are strictly subjective and dependent from operator skill and experience. New generation digital stethoscopes are able to record sound and subsequently dedicated software allows to extract quantitative variables (amplitude and frequency) that characterize the sound in an absolutely objective and repeatable way. The aim of our study was to analyze with an appropriate software listenable sound from AVFs taken by a commercial digital stethoscope and to investigate the potentiality to develop an objective new monitoring system to detect stenosis.

Method: Between September 2022 and January 2023, we screened forty-eight patients from two hemodialysis centers in Catanzaro (Italy). Patients were screened from two blinded experienced examiners for recognized criteria for stenosis by doppler ultrasound (DUS). We recorded the sound coming from the AVFs using a 3M™ Littmann® CORE Digital Stethoscope 8570 (Figure 1-A), in standardized sites: on the anastomosis chamber, at a distance of 5 and 10 cm from it, on the site of stenosis and immediately after. The sound waves were transformed into quantitative variables (amplitude and frequency) using a sound analysis software.

Figure 1:
Results: Based on doppler evaluation, 14/48 patients (29%) were classified as stenotic of which three were hemodynamically significant. The sounds detected in the stenosis sites had a significant higher average frequency compared to non-stenotic sites (Figure 1-B). Characteristics of sound waves were significant different for stenotic and non-stenotic patients in term of average power, mean amplitude and mean frequency. Analysis of waves permitted us to determine peculiar shape for stenosis and another for normal AVF (Figure 1-C,D).

Conclusions: The analysis of sound waves by a digital stethoscope permitted us to distinguish between stenotic and no stenotic AVFs. The standardization of this technique and the introducing of data in a deep learning algorithm could allow an objective and fast method for a frequent monitoring of AVF.

HEMODIALYSIS CATHETER-RELATED RIGHT ATRIAL THROMBOSIS AND PULMONARY EMBOLISM: ANTICOAGULANT THERAPY MAY NOT BE REQUIRED

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Background and Aims: Though tunneled cuffed catheters (TCCs) are frequently inserted for treating thrombotic malfunction, it is unclear whether such exchanges are associated with an increased risk of pulmonary embolism (PE). This study sought to investigate the incidence of PE among patients with hemodialysis catheter-related right atrial thrombosis (CRAT).

Method: We conducted a retrospective cohort study on 180 hemodialysis (HD) patients treated in the West China Hospital with a diagnosis of CRAT between May 2018 and March 2020. All cases with CRAT were treated with catheter replacements (guidewire exchange or insertion at new sites) and the tip of new catheters were adjusted to be away from the original position and close to the right atrial. Antiplatelet therapy was started after the surgery with dipyridamole. All patients maintained routine hemodialysis without any thrombolysis or thrombectomy. We investigated the PE incidence and mortality among them.

Results: Of the 180 patients undergoing catheter replacement and with CART, 10 patients had asymptomatic PEs pre-operation and 3 additional patients developed PE post-operation. During follow-up, two patients died of pneumonia and acute myocardial infarction, respectively, but no patients died due to PE or other thrombosis complications.

Conclusion: The incidence of PE among HD patients with CRAT is low (5.6%), and there does not appear to exist an elevated risk of fatal PE. Combined catheter.

<table>
<thead>
<tr>
<th>Table 1: Demographic and clinical variables.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>Age, y (mean ± SD)</td>
</tr>
<tr>
<td>Male, n(%)</td>
</tr>
<tr>
<td>BMI, kg/M² (mean ± SD)</td>
</tr>
<tr>
<td>Cause of ESRD, n(%)</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td>Duration of TCC, months [Q1-Q3]</td>
</tr>
<tr>
<td>Antiplatelet</td>
</tr>
<tr>
<td>Comorbidities, n(%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>PVD</td>
</tr>
<tr>
<td>Cancer</td>
</tr>
<tr>
<td>Functional class (NYHA), n(%)</td>
</tr>
</tbody>
</table>

| Abbreviations: BMI, body mass index; PVD, peripheral vascular disease; |

<table>
<thead>
<tr>
<th>Table 2: Characteristics of the thrombi and central venous abnormalities.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>Type of CRAT, n(%)</td>
</tr>
<tr>
<td>Catheter-tip thrombus</td>
</tr>
<tr>
<td>Mural thrombus</td>
</tr>
<tr>
<td>Diameter of thrombus, n (%)</td>
</tr>
<tr>
<td>&lt;2cm</td>
</tr>
<tr>
<td>2-6cm</td>
</tr>
<tr>
<td>&gt;6cm</td>
</tr>
<tr>
<td>Sites, n(%)</td>
</tr>
<tr>
<td>RA</td>
</tr>
<tr>
<td>SVC/RA</td>
</tr>
<tr>
<td>Type of obstruction, n(%)</td>
</tr>
<tr>
<td>I-III</td>
</tr>
</tbody>
</table>
Table 3: Characteristics of patients with asymptomatic PE.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>Cause of ESRD</th>
<th>Duration of TCC, months</th>
<th>No. of thrombi</th>
<th>Sites</th>
<th>Thrombus size (cm × cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>Male</td>
<td>Urologic disease</td>
<td>72</td>
<td>2</td>
<td>SVC, RA</td>
<td>5.6*0.6</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>Female</td>
<td>Glomerulonephritis</td>
<td>12</td>
<td>2</td>
<td>SVC, RA</td>
<td>2.3*0.8</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>Female</td>
<td>Diabetic nephropathy</td>
<td>72</td>
<td>2</td>
<td>SVC, RA</td>
<td>5.7*1.0</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
<td>Female</td>
<td>Diabetic nephropathy</td>
<td>72</td>
<td>1</td>
<td>RA</td>
<td>3.2*0.7</td>
</tr>
<tr>
<td>5</td>
<td>77</td>
<td>Female</td>
<td>Glomerulonephritis</td>
<td>15</td>
<td>1</td>
<td>RA</td>
<td>5.6*0.8</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>Female</td>
<td>Diabetic nephropathy</td>
<td>12</td>
<td>2</td>
<td>SVC, RA</td>
<td>4.9*1.3</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>Male</td>
<td>Glomerulonephritis</td>
<td>60</td>
<td>2</td>
<td>SVC, RA</td>
<td>5.6*0.8</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>Female</td>
<td>Diabetic nephropathy</td>
<td>7</td>
<td>1</td>
<td>RA</td>
<td>4.9*0.9</td>
</tr>
<tr>
<td>9</td>
<td>47</td>
<td>Female</td>
<td>Glomerulonephritis</td>
<td>36</td>
<td>1</td>
<td>RA</td>
<td>2.5*1.4</td>
</tr>
<tr>
<td>10</td>
<td>54</td>
<td>Female</td>
<td>Diabetic nephropathy</td>
<td>36</td>
<td>2</td>
<td>SVC, RA</td>
<td>3.2*0.9</td>
</tr>
</tbody>
</table>

Table 4: Catheter replacement procedures details.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N = 180 n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure indication, n(%)</td>
<td>141 (78.3%)</td>
</tr>
<tr>
<td>Restricted blood flow</td>
<td></td>
</tr>
<tr>
<td>Cuffed catheter exposed to air</td>
<td>17 (9.4%)</td>
</tr>
<tr>
<td>Damaged catheter</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>SVC</td>
<td>20 (11.1%)</td>
</tr>
<tr>
<td>Surgical strategy, n(%)</td>
<td></td>
</tr>
<tr>
<td>In situ replacement</td>
<td>161 (89.4%)</td>
</tr>
<tr>
<td>Ectopic replacement</td>
<td>19 (10.6%)</td>
</tr>
<tr>
<td>PTA</td>
<td>61 (33.9%)</td>
</tr>
<tr>
<td>PTS</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Catheter tip position, n(%)</td>
<td></td>
</tr>
<tr>
<td>SVC</td>
<td>10 (5.6%)</td>
</tr>
<tr>
<td>RA</td>
<td>124 (68.9%)</td>
</tr>
<tr>
<td>IVC</td>
<td>43 (23.9%)</td>
</tr>
<tr>
<td>SVC/RA</td>
<td>3 (1.7%)</td>
</tr>
</tbody>
</table>

SVCS, Superior vena cava syndrome. SVC/RA, the junction of superior vena cava and right atrium.

#3139

PREVALENCE OF INFECTIONS ASSOCIATED WITH THE HEMODIALYSIS CATHETER IN MEXICO CITY

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Background and Aims: In hemodialysis, intravenous catheter is the most frequent vascular access to begin treatment in patients with chronic kidney disease. Infectious complications are a frequent adverse effect of the vascular access, they may cause vascular access retreat and serious diseases like septic shock, bacterial endocarditis, septic arthritis, venous thromboembolism and death (between 5 and 10%). Leading microorganisms of hemodialysis infection are Gram positive bacteria, while Gram negative are less common.

Method: Study type and design: Used a descriptive, retrospective, open, observational and analytical cross-sectional study. Sampling type: Non-probabilistic of consecutive cases. Population: Patients diagnosed with CKD 5 KDIGO on renal function replacement therapy with hemodialysis through a temporary or permanent catheter in a private kidney care unit in Mexico City from October 2014 to September 2022.

Results: We identified 168 cases of CRBSI throughout the 8 years of the study. We found a prevalence of 0.86% for every 100 hemodialysis and a cumulative incidence of 4.97% for every 100 hemodialysis. Leading etiology pathogens of CRBSI in the kidney care unit were Gram negative bacteria (76.8%), mainly Enterobacter cloacae (20.8%), Escherichia coli (13.7%), Stenotrophomonas maltophilia (11.9%) and Burkholderia cepacia (4.2%). We found that 51.8% of the Gram negative CRBSI were due to multiresistant bacteria, which led to 5 directly related deaths. On the other hand, Gram positive bacteria caused 23.2% of CRBSI. Staphylococcus aureus and Staphylococcus epidermidis were the most frequent with 8.9% and 8.3%, respectively, with no related deaths.

Conclusion: Unlike international literature, in our study, gram negative bacteria were the main agents of CRBSI. The prevalence of CRBSI in our study was high, however, infection directly related mortality remained low. These results led us to investigate the origin of the vascular access infection. In an attempt to reduce the number of CRBSI, we emphasized preventive measures,
especially hand hygiene of healthcare professionals within the kidney care unit and with the patient’s personal environment at home. We would like to recall that empirical therapy should be based on the results of the kidney care unit microbiology and antibiotic sensitivity, to reduce CRBSI episodes and bacterial resistance.

#3226
DEVELOPMENT AND USABILITY ASSESSMENT OF AN AI-ENHANCED DASHBOARD SUPPORTING AVF MANAGEMENT IN CLINICAL PRACTICE
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1Fresenius Medical Care Italia SpA, Italy, 2FMC - Dialysis Services, Slovakia, 3Fresenius Medical Care, United States of America, 4Fresenius Medical Care Italia SpA, Italy, 5Fresenius Medical Care, Czech Republic, 6Fresenius Medical Care, Singapore and 7Fresenius Medical Care, Germany

Background and Aims: Despite the rise in publications reporting Artificial Intelligence (AI) solutions in healthcare, their usage in clinical practice remains limited. Prominent barriers for their implementation in clinical practice are the lack of integration of AI-based tools in the hospital health information system and clinical workflows. We previously developed an AVF Failure risk score to assess the expected incidence of AVF failures within 3 months based on routinely collected dialysis data. The risk score showed high accuracy (AUC = 0.81) and calibration. Based on this risk score, we developed an AI-enhanced dashboard supporting the management of AVF in hemodialysis patients. The usability and usefulness of the AI-enhanced AVF management dashboard was evaluated in a pilot quality improvement program.

Method: A quality improvement framework was used to evaluate the usability of an AI-enhanced dashboard for AVF management (Fig. 1A). First, healthcare professionals (HCP) were involved to provide inputs for model design, endpoint definition, and potential predictors through various qualitative interview techniques such as brainstorming sessions and focus groups (Phase I). A machine learning model was then developed to assess the expected incidence of AVF failure within 3 months. The model used routinely collected clinical data to minimize additional burden on clinical workflow. (Phase II). After developing and validating the model, a model error analysis was conducted using case studies methodology to improve model performance (Phase III). Once the model reached a good accuracy, think-aloud interview was used to abstract HCP needs and to design a user interface for model output. A user-friendly dashboard was developed to display the risk of AVF failure within 3-months and patient’s vascular access history (Phase IV). This solution was integrated in the health record system and updated monthly with the latest risk score and medical information. A pilot quality improvement program was conducted in 15 clinics across 4 countries (IT, CZ, SK, SG) from May to December 2022. HCP were asked to evaluate their agreement with the risk score using a 5-point Likert scale (completely disagree to agree) and assess the usefulness of the dashboard in clinical decision making. At this stage the dashboard is not used for medical decision making (Phase V). The evaluation results were compiled into a monthly report and shared with all the HCP involved in the project to promote awareness and engagement. After 3 months of usage, a round-table discussion was held with all participants to gather their feedback and discuss clinical cases (Phase VI).

Results: Access to the AI-enhanced dashboard increased during the evaluation period. In the first two months of the pilot quality improvement program, the AI-enhanced dashboard was evaluated for 20% patients with an AVF, a proportion that doubled by the end of the program (Fig. 1B). HCP reported 90% agreement with risk model rating (Fig. 1C), suggesting that the model capture relevant physiological status of the patient and its output is understandable by the healthcare staff. Qualitative analysis of round-table discussions showed that the dashboard is perceived as useful and clear. HCP suggested few changes in the user interface to enhance actionability and improve clinical workflow integration.

Conclusion: Our results support the usefulness and intelligibility of the AI-enhanced AVF management dashboard. The advance of AI-models highlighted the importance to develop new strategies for their integration and evaluation in clinical practice. The engagement of HCP in the early phases of AI-model design and development grants a continuous feedback loop bringing clinical and AI world together. A clinical perspective in dashboard design reflects the needs of healthcare professionals and enhance consideration of patient medical needs. The synergy between theoretical and clinical perspective is crucial to improve model performance, usability, and implementation in clinical practice.

Figure 1: A) Workflow of the improvement framework. B) Percentage of evaluated dashboard’s entry C) Percentage of agreement reported by HCP.
#4046 ADVANCED CHRONIC KIDNEY DISEASE, PREOPERATIVE ISOMETRIC EXERCISE AND VASCULAR ACCESS: LET’S CLEAR THE DOUBTS

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1Hospital Terrassa, Consorci Sanitari Terrassa, Barcelona, Nephrology, Terrassa, Barcelona, Spain and 2Hospital Terrassa, Consorci Sanitari Terrassa, Barcelona, Vascular Surgery, Terrassa, Barcelona, Spain

Background and Aims: Arteriovenous fistula (AVF) is the best vascular access for hemodialysis. However, the role of preoperative isometric exercises in patients with advanced chronic kidney disease (CKD) who are candidates for AVF is unclear and not well reported in the literature. The main objective of this study was to evaluate the effect of preoperative isometric exercise on vascular territory in advanced CKD prior to AVF creation.

Method: An 8 months prospective single-center study. We performed an isometric preoperative exercise program for 4 weeks on the non dominant arm (exercise arm) and was compared with the dominant arm (control arm) performing usual activity in our advanced CKD patients. Demographic data, upper limb muscle strength (ULMS), Doppler ultrasound (DUS) measurements (forearm and distal cephalic vein (FCV, DCV) diameter, basilic vein (BV) diameter and depth, peak systolic velocities (PSVs) and diameters in the radial artery (RA) and braquial artery (BA), as well as percentage of patients candidates to AVF in both arm (exercise and control arm) according to Spanish Clinical Guidelines of Vascular Access (VA) and possible medical complications were analyzed.

Results: 27 patients. 67.7%men. Mean age 70.3±10.4years. Mean cardiovascular risk factors: HBP (93.5%) and DM (64.5%). Exercise arm was left side in 87.1%. A significant increase was observed in ULMS only in exercise arm at the end of study (23.8±6.8=7Kgs vs 27.6±9.5Kgs, p = 0.001). Related to DUS measurements, there were not differences between groups on vein diameter. However, a significant increase was observed in RA PSV (57.2±15.3 vs 62.6±17.4cm/sec, p = 0.044), BA diameter (4.6±1.0 vs 4.9±0.9mm, p = 0.029) and percentage of patients who could be candidates to AVF (70.4 vs 92.6%, p = 0.034) in exercise arm at the end of the study. We did not observe any related complications (pain, hypotension or muscle injury).

Conclusion: Preoperative isometric exercises would increase the percentage of performing a native AVF in those advanced CKD patients candidates for HD. Similarly, our results suggest that preoperative isometric exercise could be a useful tool to improve the vascular territory, mainly arterial, in our patients. However, more studies are required to confirm our results.

#6597 THE EFFECT OF PATHOGEN ON THE OUTCOME OF HEMODIALYSIS CATHETER-RELATED BLOODSTREAM INFECTIONS IN HOSPITALIZED PATIENTS: A SINGLE CENTER ANNUAL RECORD

Petros Kalogeropoulos, Ourania Tsetsorou, Ioanna Tsoympy, Petros Nikolopoulos and Sophia Lionaki

Department of Nephrology, 2nd Propaedeutic Internal Medicine, Medical School, National and Kapodistrian University of Athens, “Attikon” University Hospital, Athens, Greece

Background and Aims: Tunneled double-lumen catheters are increasingly used as permanent vascular access in hemodialysis patients, particularly in those with limited vascular access options. Catheter-related bloodstream infection (CRBSI) is a major cause of hospitalization with increased mortality and cost. The purpose is to study the effect of the pathogen on the clinical course of the hemodialysis patients with CRBSI.

Method: Patients hospitalized in our department from 11/2021 to 12/2022 with established CRBSI were retrospectively studied. Their demographics, duration of hospitalization, microbiological data, central venous catheter management and hospital outcome were recorded.

Results: A total of 27 patients with median age (SD) 68.03 (16.93) years were treated, 12 (44.4%) were men. The following pathogens were isolated from the blood cultures: Staphylococcus aureus in 7 (25.9%) patients, coagulase-negative Staphylococcus in 10 (37%) patients, Gram-positive bacteria in 4 (14.8%) patients, Gram-negative bacteria in 3 (11.1%) patients, candida in one (3.7%) patient, and 2 (7.4%) patients had negative cultures. Mean SD duration of hospitalization was 16.85 (13.15) days for all patients. Patients in whom Staphylococcus aureus and Candida were isolated had longer hospital stay than other infections with a mean (SD) 29 (18) days and 41 days respectively (p = 0.014). Metastatic infections occurred in 4 (14.8%) patients, of whom 2 had endocarditis, one endocarditida and pulmonary abcess, and one endocarditis, lung abscess and brain abcess. All 4 patients isolated Staphylococcus aureus in blood culture out of a total of 7 (57,1%) patients with this pathogen (p = 0.02). 3 of 7 (42,8%) patients with Staphylococcus aureus, 1 of 10 (10%) with coagulase-negative Staphylococcus, and 1 of 3 (33,3%) with Gram-negative bacteria died (p = 0.385). In 26 of the 27 patients (96.3%) central venous catheter was removed.

Conclusion: The majority of patients in the present sample required central venous catheter removal. The type of pathogen seems to play an important role both in the duration of hospitalization and in the occurrence of metastatic infections.

#6656 PATIENTS’ PERSPECTIVES ON HAEMODIALYSIS ACCESS: A QUANTITATIVE STUDY

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Background and Aims: Vascular access is an essential requirement for hemodialysis (HD). There is strong evidence that an arteriovenous fistula (AVF) is preferable to access via a central venous catheter (CVC) for long term haemodialysis, yet many patients opt for access via a CVC. We performed a cross-sectional study to assess patient preferences regarding vascular access. The quantitative component of this work is presented here.

Method: Questionnaires were administered to patients attending dialysis at four sites in the East Anglia region of the UK (n = 380). Additional patient data was collected from medical records. Analysis was performed using the R software.

Results: 63% (n = 238) of patients completed the survey. The median age of respondents was 75 years (range 24-95 years), 64% were male (n = 153), the median length of time on dialysis was 23 months, and 64% (n = 152) were using an AVF. There was no significant association between age and form of access (p = 0.11). 65% of respondents believed that an AVF was the best access route for health, 10% believed a CVC was the best route, and 25% were unsure. This was not significantly affected by the participant’s access route at the time of the study (p = 0.91) or self-reported pre-dialysis education (p = 0.09). Respondents who believed that the health professional caring for them preferred AVFs were significantly more likely to believe that AVFs were best for their health (p < 0.0001 for both medical and nursing staff preference). However, overall, there was uncertainty about the preferred haemodialysis access of health professionals, with 40% and 47% of respondents unsure regarding the preference of medical and nursing staff, respectively. These patients were also more likely to respond as ‘unsure’ as to which access type was better for their health. We asked participants to rate 16 possible concerns they may have about access on a 1-9 scale (Figure 1). The most highly rated concerns were related to sleeping, pain, bleeding and access longevity, each receiving a rating of ≥2 in nearly 40% of participants. Notably, infection risk was rated as the lowest priority concern, only receiving a rating of ≥2 in 5% of participants. Concerns were similar regardless of the active form of access. 63% (n = 54) of respondents with a CVC would not consider changing to an AVF. The decision to switch from CVC to AVF was not significantly associated with age (p = 0.69), or the number of AVF operations a patient had undergone in the six years prior to the study year (p = 0.94). The decision was also not associated with respondent belief regarding the best access type for health (p = 0.84). Differences in access concerns could not significantly explain the decision to or not to switch from CVC to AVF. However, analysis of free-text responses identified peer experiences as a strong influence on the decision to switch.

Conclusion: Most HD patients are aware that an AVF is associated with better health outcomes than a CVC. Despite this, a large proportion of patients dialysing via a CVC do not wish to change their access, with many reporting concerns of bleeding, needling pain, and difficulty sleeping. Infection risk was not a consideration for most patients. Additionally, we found that patients reported significant uncertainty about doctor and nurse preference for haemodialysis access. These findings are mirrored by analysis of the free text responses to the questions in this study. In particular, peer experiences were a significant determinant of the decision to switch from a CVC to AVF. The findings suggest that when we discuss vascular access with patients, a broad scope of topics should be addressed, beyond health outcomes alone, to allow for effective decision making. They also suggest that there is room to improve the communication of our perspectives as healthcare workers, both from a nursing and medical perspective.
Figure 1: Patients’ rating of haemodialysis-access related concerns on a scale of 1-9, with 1 being the lowest concern and 9 the highest concern. No patient rated any concern above 5.

Figure 2: Response of patients with a CVC for haemodialysis access when asked if they would consider an AVF.
PERCUTANEOUS ARTERIOVENOUS FISTULA CREATION: A DUBAI HOSPITAL EXPERIENCE

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Background and Aims: Targeting to improve the quality of care for chronic kidney disease patients (CKD) a non-surgical creation of native arteriovenous fistulae (AVF) with potentially cosmetic advantages, was offered for CKD patients in Dubai. The procedure started in January 2021 and the follow up continued till January 2023. The goal of this report is to share the original first experience in Dubai for this technique using 4F WavelinQ EndoAVF System.

Method: Fourteen patients underwent sonographic vascular mapping for endovascular AVF creation using 4F WavelinQ EndoAVF System. Nine patients were deemed suitable for Endovascular AVF creation and underwent the procedure under regional anaesthesia. Concomitant ulnar artery and ulnar vein or the concomitant radial artery and radial vein was used for the procedure.

Results: In this case series, the patients have a mean age of 53 ± 17 years, majority of the cases were men (77.8%). All cases were hypertensives (100%) with 2 cases (22.2%) have biopsy proven Glomerulonephritis and 5 cases (55.5%) were diabetics. The technique succeeded (defined by blood flow from used artery to concomitant deep vein and through perforator vein to superficial vein) in all patients (100%). Maturation success (defined as estimated fistula flow rates exceeded 500 mL/min and access vessel diameter was more than 4 mm) with multiple venous outflows was achieved in 8 cases (88.1%). One case (11.1%) showed primary maturation failure. Five cases (55.5%) achieved successful cannulation with excellent blood flow and reliable arterial and venous pressure during dialysis. Time to maturation was 35 ± 17 days and time to successful cannulation averaged 63 ± 45 days. Among patients achieving maturation success, one patient requested AVF closure (using coil embolization) due to mild to moderate upper limb oedema that required reintervention, one case underwent pre-emptive kidney transplantation and did not require to use the AVF and one patient refused using the AVF. In our study 3 cases (33.3%) required reintervention to facilitate maturation. It worth mention that among the 3 cases underwent reintervention, one case requested closure of the fistula and one case refused to use the fistula and only one case of the successful cannulation group underwent single reintervention.

Conclusion: In our limited experience, AVF creation using Endovascular technique resulted in dependable haemodialysis access with reliable maturation time, achieving excellent patency in the successful cannulation group with high blood flow rate and accepted arterial and venous pressure during dialysis. It also showed that the procedure was safe with better cosmetic shape and no scars. However more studies with bigger sample size are needed for better evaluation of the technique and to confirm the endovascular AVF creation proper position in the guidelines for vascular access creation in haemodialysis.
Background and Aims: Central tunnelled catheter (CVC)-related infections are a leading cause of catheter lost and being the source of significant morbidity and mortality of end stage kidneys disease (ESKD) patients. The study aimed to evaluate the impact of the implementation of the own REDS/MEWS scale for combined assessment of ESKD patients dialyzed with the CTC on the frequency of infective complication.

Method: A group of 52 ESKD patients dialysed through a CTC were evaluated, pre-dialysis on every session, using the REDS/MEWS scale for 24 months years and results as well as follow up of participants were compared with a two years period of time before the tool was introduced.

Figure 1: REDS/MEWS scale chart (sample).
MEWS – modified early warning score, CTC – central tunnelled catheter.
Results: Two-years cumulative incidence of CTC exit site infection (ESI) has dropped significantly (log-rank \( p < 0.001 \)) from 0.87 episode per 1000 catheter days (52.3%, CI95 [34.2%; 67.3%]) in time before REDS/MEWS was used to 0.28 episode per 1000 catheter days (19.3%, CI95 [7.3%; 30.1%]) in REDS/MEWS time. There were also significantly less episodes of ESI complicated with catheter related blood stream infection (CRBSI) requiring CTC removal (0.8 episode per 1000 catheter days; 20.6%, CI95 [8.4%; 33.2%]) vs. 0.4 episode per 1000 catheter days; 5.4%, CI95 [1.1; 8.7%]; log-rank \( p = 0.05 \), in pre – REDS and REDS time respectively. There was no serious complications as infective endocarditis, vertebral disc abscess among patients due to early detection and treatment of possible CTC related infection.

Conclusion: The REDS/MEWS scale appears to be a simple, cost-effective tool reducing frequency of the CTC related infective complication and the type of vascular access loss.

#6934

INFLAMMATORY STATUS PRIOR TO THE CREATION OF ARTERIOVENOUS FISTULAS FOR HEMODIALYSIS: IS IT DETERMINING?

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Background and Aims: Clinical practice guidelines recommend an arteriovenous fistula (AVIF) as the preferred vascular access for hemodialysis and is associated with a lower incidence of morbidity and mortality. However, primary vascular access (VA) failure is not uncommon. Low-grade inflammation is present in ERCT. We identified the inflammatory parameters that influence the primary patency of the vascular access for hemodialysis.

Method: Cross-sectional study; We included all VAs made between October 2009 and April 2022. We evaluated the initial performance after the creation of the VAs. Demographic variables (age, sex), CKD etiology, and associated comorbidity were collected. Statistical analysis with SPSS 25.0. Categorical variables are expressed as percentages and compared using the Chi2 test. Quantitative variables are expressed as mean ± standard deviation and the t-student test was used to compare them. Statistical significance for a value of \( p<0.05 \).

Results: 712 VA performed in 546 patients were reviewed between October 2009 and April 2022. 617 autologous VA (86.7%) and 95 prosthetic VA (13.3%) were performed. The mean age of the patients was 65.4 ± 14.1 years and 67.4% were male. The most frequent etiology of CKD was diabetic nephropathy (30.5%), followed by unknown (17.3%) and glomerulonephritis (16.4%). 91.4% of the patients presented arterial hypertension (HTA), diabetes mellitus (DM) 47.5%. 72.6% of the VA presented primary permeability. In the univariate analysis using Chi2 and T student, AHT (p<0.001), treatment with statins (p<0.001), antaggregation (p<0.001), normal fibrinogen levels (p = 0.003), and CRP (p<0.001) reached statistical significance. = 0.039. When recoding the PCR in relation to its normal values, the pathological levels were associated with primary failure after the creation of AVFs.

Conclusion: In our study, inflammatory states with elevated CRP and ferritin were associated with primary failure in initial functioning after the creation of AVFs. On the contrary, arterial hypertension and treatment with statins prior to the creation of AVFs are associated with their primary permeability.

#6572

FLUORINATED GRAPHENE REDUCES PLATELET ACTIVATION AND ADHESION ON HEMODIALYSIS CATHETER

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Background and Aims: Catheter thrombosis remains one of the major complications of hemodialysis. Superhydrophobic surfaces are suggested to be capable of creating an energy barrier that prevents cells and proteins from contacting with the catheter surface directly, making catheter less thrombotic. Fluorinated graphene (FG) is a superhydrophobic material. It has been applied to create self-cleaning surfaces. It also shows good biocompatibility. Based on these features of FG, we prepared an FG coating on hemodialysis catheter attempting to reduce clinical thrombotic events.

Method: FG suspension was made in a solution of 95 wt.% ethanol, 5 wt.% deionized water and 3 wt.% 1H,1H,2H,2H-Perfluorooctyltriethoxysilane (POTS, C14H15F17O3Si). Immediately following the plasma activation, catheter segments of 1 cm\(^2\)(Gamcat, GDHK1325) were spray coated with FG suspension both inside and outside the catheter lumen. Samples were air-dried for later use. We tested the hemolysis rate, platelet activation and adhesion performances, and the partial thromboplastin time (PTT) of the FG-coated samples. Test for hemolysis was performed with FG-coated catheter and the isotonic extract of the FG coating in direct contact with fresh rabbit blood respectively. Platelet activation and adhesion was performed according to the ASTM F2388-19 standard and also assessed by scanning electron microscope. PTT assay was performed according to the ASTM F2382-18 standard.

Results: FG-coated catheter is hydrophobic and shows a water contact angle of 150° (Figure 1a). It reduced 83.5% of platelet adhesion per 100 μm\(^2\) catheter surface area and avoided 53.86% of platelet loss from the blood when compared to uncoated catheter (Figure 1b, 1c). It has a hemolysis rate of less than 2% in both direct blood contact test and the extract test (Figure 1d). The PTT of FG-coated sample was 88.92±1.31s versus 83.03±4.94s of the uncoated catheter yet with no statistical significance (P>0.05) (Figure 1e).

Conclusion: FG coating has great hemocompatibility. Though no significant improvement was observed in the PTT assay, FG coating still significantly reduced the adherent and activated platelet on catheter, which seems promising to reduce thrombotic events. Yet, more tests needed to be performed, and the antithrombotic ability of FG coating in the fluid state needs to be further confirmed in the following study.
The effect of acupressure applied to different fistula area on fistule needle entry pain

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Background and Aims: This study was conducted to determine the effectiveness of acupressure application on Hegu point on the severity of acute pain caused by fistula needle in patients with brescia-cimino, snuff-box and antecubital fistula.

Method: This study was randomized control study which was conducted with 66 intervention and 65 control participants, recruited from a dialysis centre of a foundation university in Turkey between October 2021 and February 2022. Simple randomization was used for sample selection in the study. The participants in the intervention group were divided into 3 groups according to the fistula area. The first group was consisted of participants with brescia-cimino fistula, the second group was consisted of participants with snuff-box fistula, and the third group was consisted of participants with antecubital fistula. The of all 22 participants were assigned to each group in the intervention group. Acupressure was applied 3 minute before needle placement in the fistula area of the participants in the intervention group. No intervention was made in the control group in the study. Data were collected using Descriptive Information Form and pain scale (Numeric Analog Scale-NRS). NRS was used to determine the severity of acute pain experienced by patients during fistula needle insertion. Since the data of the study showed normal distribution, the data were analyzed with parametric tests. The independent sample t-test was used to examine the homogeneity of the data between the two groups. Spearman correlation analyses were used to compare categorical variables. Statistical significance was assumed at p < 0.05.

Results: In the study, the groups are similar to each other (p>0.05). In the study, the mean age of the participants in the intervention group was 60.50±15.19, and 40.9% of them were in the 61-75 age group. The mean duration of hemodialysis was 7.31±3.31 (min:1-max:20). Of the participants, 43.9% had antecubital, 33.3% had a brescia-cimino fistula and 27.7% had a snuff-box fistula. The mean age of the participants in the control group was 60.84±15.34 years, and 33.8% of them were in the 61-75 age group. The mean duration of hemodialysis was 7.27±4.29 (min:1-max:20). 35.4% of the participants had antecubital, 30.8% had brescia-cimino fistula and 33.8% had snuff-box fistula. While there was no decrease in the severity of acute pain during fistula needle insertion in the participants in the control group, a significant decrease was found in the mean acute pain severity scores experienced by the patients in the intervention group, where acupressure was applied to the Hegu (LI4) acupuncture point (p<0.05, Table 1). In the study, there was a difference within the groups in terms of the mean acute pain severity scores of different fistula areas in the intervention group but, there was no difference in acute pain severity scores between the groups in three different fistula areas.

Conclusion: The results of this study support that acupressure applied to the Hegu acupuncture point was effective in reducing acute pain at fistula needle insertion in different dialysis fistula area. In addition, the results of the study provide a practical and cost-effective reference for dialysis nurses in acute pain management.
Table 1: Distribution of NRS pain scores in each three session follow-ups of the participants in the intervention and control groups (n = 131).

<table>
<thead>
<tr>
<th>Groups</th>
<th>In-group scores of the Intervention Groups</th>
<th>Control Groups</th>
<th>Test</th>
<th>Intervention groups (n = 65)</th>
<th>Control Groups (n = 66)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antecubital fistula (n = 22)</td>
<td>Brescia-cimino fistula (n = 22)</td>
<td>Sauff-box fistula (n = 22)</td>
<td>F</td>
<td>p</td>
<td>Mean±SD (min-max)</td>
<td>Mean±SD (min-max)</td>
<td>t</td>
</tr>
<tr>
<td>First Session</td>
<td>2.14±1.08 (1-5)</td>
<td>2.18±0.20 (1-3)</td>
<td>1.82±0.13 (0-3)</td>
<td>0.765</td>
<td>0.470</td>
<td>2.75±1.27 (1.6)</td>
<td>2.05±1.19 (1-5)</td>
</tr>
<tr>
<td>Second Session</td>
<td>1.59±0.66 (1-3)</td>
<td>1.36±0.84 (0-3)</td>
<td>1.54±0.91 (0-3)</td>
<td>0.479</td>
<td>0.622</td>
<td>2.78±1.33 (1-6)</td>
<td>1.50±0.80 (0-5)</td>
</tr>
<tr>
<td>Third Session</td>
<td>1.13±0.46 (0-2)</td>
<td>0.81±0.20 (0-2)</td>
<td>1.09±0.86 (0-3)</td>
<td>1.598</td>
<td>0.210</td>
<td>2.88±1.35 (0-5)</td>
<td>1.01±0.54 (0-4)</td>
</tr>
</tbody>
</table>

- Fisher test, *p < 0.001, One-Way ANOVA, Independent Sample-t test.

REFERENCES


#4520

THE USE OF FAR INFRARED LIGHT DURING HEMODIALYSIS SEEMS TO MAINTAIN ARTERIOVENOUS FISTULA BLOOD FLOW BETTER THAN USING A HEAT PAD - A PILOT STUDY

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Background and Aims: The use of the native arteriovenous fistula (AVF) in chronic hemodialysis (HD) patients yields great challenges to keep a patent AVF, especially among those with diabetes mellitus and cardiovascular disease. Often repeated radiological interventions or surgery of the AVF is necessary. Accumulation of advanced glycation end products (AGE) in tissue is shown to contribute to the complications of diabetes mellitus and uremia [1]. Far infrared light (FIR) irradiation of the AVF have shown protective effects in maintaining AVF blood flow [2,3]. Using a heat pad (HP) to stimulate vascular flow is another alternative. Primary aim of the study was to compare if the use of a HP is as good as FIR to maintain AVF blood flow. Secondary aim: Evaluate change in AGE accumulation in tissue after FIR and HP treatment.

Method: This pilot study included HD patients with a native lower arm AVF. Eighteen patients were randomly assigned to treatment during HD: Ten patients to FIR and another group of eight patients to use HP (Two of the HP-patients refused to fulfill the study). Before and after a period of 15 HD treatments each, blood tests, AVF blood-flow measured with a Transonic® were performed. FIR-exposure during 15 HD treatments was better maintained among patients treated with FIR than with HP SAF as a predictor for atherosclerosis was not changed. Long-term exposure to FIR may be necessary.

#4664

GENDER DIFFERENCES IN VASCULAR ACCESS FOR INCIDENT HAEMODIALYSIS PATIENTS: A REGISTRY-BASED STUDY

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Background: Gender disparities of some aspects of vascular access (VA) for haemodialysis (HD) have been reported. Aims: To analyze the VA profile of incident HD patients (pts) depending on gender in Catalonia.

Method: Data from the Catalan Renal Registry of 22,859 end-stage kidney disease (ESKD) pts older than 18 years of age starting HD therapy was examined over a 24-year period (1997-2021). Results: Male (n = 14,921) and female (n = 8038) characteristics were different regarding age (66.2±14.2 vs 67.2±14.4 years), normal functional status (40.2% vs 33.2%), cardiovascular disease (58.3% vs 48%) and obesity rate (body mass index BMI 30 kg/m²; 16.1% vs 25.7%) (for all comparisons, p<0.001). The distribution of the first VA used for starting HD was different in men vs women: fistulae AVF (46.1%, n = 6308 vs 41.3%, n = 3088), graft AVG (0.8%, n = 108 vs 1.7%, n = 129) and tunnelled catheter (20.4%, n = 2789 vs 23%, n = 1719) (for all comparisons, p<0.001); without differences for non-tunnelled catheter (32.8%, n = 4488 vs 34%, n = 2537) (p = 0.083). Percentage of both men and women starting HD by AVF it decreased progressively from 1997 (53.4% and 41.8%, respectively) to 2021 (37.3% and 33.2%, respectively) (p<0.001 and p=0.032, respectively). Percentage of incident men with AVF: it was higher than women in 1997 (53.4% vs 41.8%, p = 0.002) but this difference decreased over time and was no longer significant in 2021 (37.3% vs 33.2%, p = 0.22). Probability of starting HD by AVF: it was independently associated with male gender (odds ratio 1.32 [95% confidence interval: 1.23–1.41], p<0.001) after adjusting for age, primary kidney disease, functional status, BMI, cardiovascular disease and ESKD presentation (multivariate logistic regression analysis). By using a competing risk model, the hazard ratio (HR) for receiving a kidney graft (KG) within five years from starting HD, depending...
on the first VA used to start HD (AVF vs catheter), was: 1.82 (95% CI: 1.69-1.95, p < 0.001) for men and 2.32 (95% CI: 2.11-2.55, p < 0.001) for women. In comparison with men that started HD by AVF, the HR of women for receiving a KG within five years from starting HD by AVF was 1.12 (95% CI: 1.04-1.21, p = 0.002). In comparison with women that started HD by catheter, the HR of men for receiving a KG within five years from starting HD by catheter was 1.13 (95% CI: 1.03-1.24, p = 0.007). The HR of death within five years from starting HD, depending on the first VA used to start HD (catheter vs AVF), was: 1.55 (95% CI: 1.47-1.63, p < 0.001) for men and 1.95 (95% CI: 1.81-2.11, p < 0.001) for women. In comparison with men that started HD by catheter, the HR of death for women within five years from starting HD by catheter was 1.01 (95% CI: 0.95-1.06, p = 0.81). In comparison with women that started HD by AVF, the HR of death for men within five years from starting HD by AVF was 1.26 (95% CI: 1.17-1.36, p < 0.001).

Conclusions: 1) Although AVF was the main type of VA used for starting HD in both sexes, the percentage of AVF was significantly lower in women at the expense of AV and tunneled catheter. 2) Male gender was an independent factor associated with a 32% greater probability of starting HD by AVF than female. 3) Women initiating HD by AVF were more likely to receive a KG over time than men with an AVF. 4) Men and women shared the same probability to die over time after starting HD with a catheter. 5) Men starting HD by AVF were more likely to die over time than women with an AVF. 6) Regardless of gender, initiating HD by catheter was associated with a lower probability of receiving a KG and a higher probability of dying over time compared to AVF.

#2787

HOSPITAL MANAGEMENT OF AN INTEGRATED CLINICAL PRACTICE UNIT OF VASCULAR ACCESS FOR HEMODIALYSIS: A CHALLENGE FOR IMPROVING HEALTHCARE QUALITY?

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Background and Aims: Vascular access (VA) for haemodialysis (HD) is essential for renal patients due to its high morbimortality and economic cost. Integrated Clinical Practice Units (ICPU) allows health organizations to establish comprehensive care, improve the quality and safety of care processes, as well as favor the accessibility of health care. The VA multidisciplinary teams for HD are crucial in the proper management of VA, although their implementation in daily clinical practice is not fully consolidated. The aim of this study was to analyze the effectiveness of the healthcare processes in patients with VA for HD after the creation of our ICPU focused in the multidisciplinary management of the VA (FUVA) through quality of care indicators.

Method: 12 years retrospective uncinicentric study analyzed in two periods: first period (2010-2015) and second period (2016-22) after FUVA creation. The indicators include sociodemographic data, processes activities (first and successive visits, endovascular procedures, type and number of surgical interventions, delayed time for interventions, mean hospitalisation stay, and successive visits, endovascular procedures, type and number of surgical interventions). The local Ethics and Research Committee has approved the conduct of the retrospective study. In this study, the definition of a CRBSI is taken from Kidney Disease Outcomes Quality Initiative (KDOQI) Vascular Access-2019 update as 1) clinical manifestations (fever ≥ 37.5°C or rigors or presence of clinical signs of infection); 2) confirmation of bacteremia (blood cultures growing the same organism from the dialysis catheter and a peripheral vein), with either positive semiquantitative (>15CFU/catheter segment), or quantitative (>10^6 CFU/catheter segment), differential period of catheter culture versus peripheral blood culture (BC) positivity of 2 hours; 3) exclusion of another source of infection. Information including patient demographics, causes of kidney failure, and duration of TDC was obtained.

#3349

METICULOUS CATHETER CARE CAN REDUCE CATHETER-RELATED BLOODSTREAM INFECTIONS SIGNIFICANTLY IN HEMODIALYSIS PATIENTS – A 5-YEAR SINGLE CENTRE STUDY

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Background and Aims: The use of central venous catheters as hemodialysis (HD) vascular access is a leading contributor to a high rate of bloodstream infection. Our dialysis unit in China has followed the China National Infection Control Policy for HD unit as well as developed its own specific dialysis catheter care protocol using the Centre for Disease Control and Prevention (CDC) guidelines as a template. By doing so, our HD unit has achieved a tunnelled catheter death rate of 0.0229 per 1000 catheter days in the past 5 years. This report, aims to share our experience with the other units.

Method: We have undertaken a retrospective analysis to determine our catheter-related bloodstream infection (CRBSI) rate, The Local Ethics and Research Committee has approved the conduct of the retrospective study. In this study, the definition of a CRBSI is taken from Kidney Disease Outcomes Quality Initiative (KDOQI) Vascular Access-2019 update as 1) clinical manifestations (fever ≥ 37.5°C or rigors or presence of clinical signs of infection); 2) confirmation of bacteremia (blood cultures growing the same organism from the dialysis catheter and a peripheral vein), with either positive semiquantitative (>15CFU/catheter segment), or quantitative (>10^6 CFU/catheter segment), differential period of catheter culture versus peripheral blood culture (BC) positivity of 2 hours; 3) exclusion of another source of infection. Information including patient demographics, causes of kidney failure, and duration of TDC was obtained.
Results: The Covidien Palindrome chronic catheters have been used in the majority of our patients during the study period. All tunnelled dialysis catheters were placed by the nephrologists under radiological guidance in the Hospital’s sterile Digital Subtraction Angiography (DSA) Suite. In the study period (2017-2021), an average of 235 prevalent patients were receiving dialysis in the HD unit. A total of 212 tunnelled dialysis catheters have been inserted and managed according to our local dialysis access pathway and catheter care protocol. The TDC days have been calculated by adding all the catheter days until the catheters have been removed or the patients have been transferred out of our HD unit. There was a total of 43,585 catheter days. The average waiting time for arteriovenous fistula (AVF) surgery was two weeks. The mean duration of TDC use was 107.8±14.8 days, range 1-1827 days. The incidence of confirmed tunnelled CRBSI was 0.0229/1000 catheter days.

Conclusion: Our local catheter care protocol is similar to the CDC's “scrub-the-hub” protocol. 2% chlorhexidine with 70% alcohol has been used for the scrubbing and disinfection but we have a few additional steps. In our practice, great attention is given to the cleansing of the clamps. 1) Prior to removal of the caps, the clamps are opened and the surroundings are cleaned and disinfected thoroughly. 2) Two nurses are assigned to connect the bloodlines to the hubs, hence the risk of hub contamination is reduced. 3) The point of connection between the hubs and the bloodlines is protected with a gauze dressing in 3 layers during the entire duration of the dialysis. We believe our success with a very low rate of CRBSI has been the result of strict adherence to 1) good and general hygiene, 2) a well-designed dialysis catheter care protocol, 3) good use of a vascular access nurse, 4) short-duration of TDC days, and 5) short waiting time for AVF. Limitations: We may have underestimated the true rate of CRBSI because of the inherent nature of the diagnostic criteria as mentioned above. Although it is unlikely that a blood culture would have been missed before the onset of symptoms, we cannot exclude the possibility that asymptomatic bacteria may have been present before the onset of symptoms. In conclusion, we believe our success with a very low rate of CRBSI has been the result of strict adherence to 1) good and general hygiene, 2) a well-designed dialysis catheter care protocol, 3) good use of a vascular access nurse, 4) short-duration of TDC days, and 5) short waiting time for AVF.

Method: Prospective analysis of all adult patients with CKD who were referred for VM, at a tertiary center, between March 2021 and August 2021. No patients were excluded. Preoperative DUS by a single experienced nephrologist was carried out. HGS was measured using a Hand Dynamometer and PAD was defined as ABI<0.9. According to distal vasculature size (<2mm) sub-groups were analyzed.

Results: 80 patients were included and 67.5% were male, mean age 65.7±14.7 years and 51% were on Renal Replacement Therapy (RRT). Twelve (15%) participants had PAD. HGS was higher in dominant arm (20.5±12.0 kg vs 18.8±11.2 kg). Fifty-eight (72.5%) patients had vessels smaller than 2 mm in diameter. There were no significant differences between groups concerning demographic and comorbidities (diabetes, PAD). HGS was significantly higher in patients who had vessels greater than or equal to 2 mm in diameter (26.1±15.5 kg vs 18.4±9.7 kg, p = 0.010).

Conclusion: Greater HGS was associated with more developed distal vessels. Low HGS might be an indirect sign of poor vascular characteristics, which might help predict the outcomes of VA creation and maturation.

#4047
ULTRASOUND-GUIDED RIGHT INTERNAL JUGULAR TUNNELED CATHETER INSERTION FOR HAEMODIALYSIS: PRACTICES AND OUTCOMES FROM A SINGLE CENTRE
Chittesh Ramgobin, Bilal Khurshid, Sharmilee Renganarajan, Adele Green, Dimitrios Poullakos, Maharajan Raman, David New, David Lewis and Rajkumar Chinnadurai
Salford Royal Infirmary, Northern Care Alliance Foundation Trust, Department of Renal Medicine, Salford, United Kingdom

Background and Aims: Internal jugular vein tunnelled catheters are important vascular access for haemodialysis (HD). In our practice, Left-sided internal jugular (IJ) catheter insertion is performed in radiology under direct X-ray screening. Most right-side internal jugular (RIJ) catheters are inserted under ultrasound guidance in dedicated renal procedure rooms. Vascular access can become challenging with the potential for venous stenosis and thrombosis with catheter use. The aims of this study are to evaluate our practices and outcomes of non-radiologically inserted RIJ tunnelled HD catheters and to investigate the predictors of procedure failure.

Method: 200 successive RIJ tunnel HD catheters inserted from June 2016 under ultrasound guidance at our centre were included in this analysis. Data including demographics, co-morbidities, first or higher order insertion, outcome (success or failed attempt), and immediate complications were collated from electronic patient records. Binary logistic regression analysis was conducted to investigate the predictor for failure in catheter insertion.

Results: Of the 200 patients, 152 (76%) were first-time insertions and 48 (24%) were second or higher order insertions. The median age of our cohort was 58 years, with a predominance of males (68%) and white ethnicity (82%). 36.5% were diabetic, with 37.5% having a history of cardiovascular disease. Nearly 30% of patients were on an antplatelet agent, and 8% were on anticoagulants, which were appropriately managed before line insertion. Pre-operative median haemoglobin was 93 g/dl, with clotting screen and platelet counts in the target range. There was a statistically significant difference in the success of insertion, depending on the insertion being first or subsequent (96.1% vs 81.2%; p = 0.001). The reason for failure in insertion included on-table observation of a small calibre vein on ultrasound or failure to thread wire/dilator due to possible stenosis or thromboses. All line rewire (12/48) procedures were performed successfully. Immediate complication (<1 week) was recorded in 9% of patients, predominantly tunnel bleeding (n = 7) and malposition (deep or high; n = 7) (Table 1). Second or higher-order RIJ catheter insertion showed a higher risk for failure in a multivariable binary logistic regression analysis. (OR: 6.4; CI: 2.1-20.5; P = 0.002) (Figure 1). Of the higher-order insertions, the longer duration between the first and subsequent catheters showed a higher risk for failure (OR:1.19; CI:1.04-1.4; p = 0.010).

Conclusion: Second or higher-order catheter insertions with a longer duration between the first and the subsequent insertion carry a significant risk of failure due to vein stenosis and thrombosis. Therefore, a careful case-to-case triaging of patients based on previous access history is warranted before listing patients for routine ultrasound-guided insertion.

#3866
PREOPERATIVE ASSESSMENT FOR VASCULAR ACCESS: VASCULAR MAPPING AND HANDGRIPT STRENGTH
João Fortes, Bernardo Marques Da Silva, João Fernandes, Hugo Silva, Alice Fortes, José António Lopes and Joana Gameiro
Portugal

Background and Aims: A reliable vascular access (VA) is required for patients receiving chronic haemodialysis (HD) treatment. VA choice is complex and must consider patient characteristics, predicted patency and risk of primary failure. Vascular mapping (VM) by duplex doppler ultrasonography (DUS) can aid in the planning of which VA to place. Peripheral artery disease (PAD) is associated with higher AVF failure and can be assessed by calculating the ankle-brachial index (ABI). Muscle strength is independently associated with mortality risk and can be evaluated with handgrip strength (HGS). This study aims to describe and analyze clinical anthropometric and laboratory characteristics of patients referred for vascular mapping prior to VA creation and to correlate VM data, HGS, and ABI.

Method: Prospective analysis of all adult patients with CKD who were referred for VM, at a tertiary center, between March 2021 and August 2021. No patients were excluded. Preoperative DUS by a single experienced nephrologist was carried out. HGS was measured using a Hand Dynamometer and PAD was defined as ABI<0.9. According to distal vasculature size (<2mm) sub-groups were analyzed.

Results: 80 patients were included and 67.5% were male, mean age 65.7±14.7 years and 51% were on Renal Replacement Therapy (RRT). Twelve (15%) participants had PAD. HGS was higher in dominant arm (20.5±12.0 kg vs 18.8±11.2 kg). Fifty-eight (72.5%) patients had vessels smaller than 2 mm in diameter. There were no significant differences between groups concerning demographic and comorbidities (diabetes, PAD). HGS was significantly higher in patients who had vessels greater than or equal to 2 mm in diameter (26.1±15.5 kg vs 18.4±9.7 kg, p = 0.010).

Conclusion: Greater HGS was associated with more developed distal vessels. Low HGS might be an indirect sign of poor vascular characteristics, which might help predict the outcomes of VA creation and maturation.

<table>
<thead>
<tr>
<th>Vessels ≥ 2 mm (n = 22)</th>
<th>Vessels &lt; 2 mm (n = 58)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.1 ± 15.3</td>
<td>65.9 ± 14.5</td>
</tr>
<tr>
<td>Gender (male) – n (%)</td>
<td>15 (68.2)</td>
<td>39 (67.2)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus – n (%)</td>
<td>6 (27.3)</td>
<td>21 (36.2)</td>
</tr>
<tr>
<td>Hypertension – n (%)</td>
<td>18 (81.8)</td>
<td>50 (86.2)</td>
</tr>
<tr>
<td>Laboratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.2 ± 1.7</td>
<td>10.5 ± 1.5</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.7 ± 0.5</td>
<td>3.7 ± 0.8</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>4.2 ± 1.6</td>
<td>4.3 ± 2.1</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m2)</td>
<td>15.6 ± 5.7</td>
<td>14.5 ± 4.0</td>
</tr>
<tr>
<td>RRT status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RRT – n (%)</td>
<td>15</td>
<td>26</td>
</tr>
<tr>
<td>Anthropometric characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral artery disease – n (%)</td>
<td>6 (27.3)</td>
<td>6 (10.3)</td>
</tr>
<tr>
<td>Handgrip strength dominant arm (kg)</td>
<td>26.1 ± 15.5</td>
<td>18.4 ± 9.7</td>
</tr>
</tbody>
</table>
Figure 1: Multivariable binary logistic regression analysis- risk factors for failure of insertions.

Table 1: Demographics and outcomes of line insertion.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (200)</th>
<th>First catheter (152)</th>
<th>Second and above (48) 2nd-42, 3rd-4, 4th-2</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58.5 (45.4-71.4)</td>
<td>58.7 (49.1-72.7)</td>
<td>54.6 (41.1-70)</td>
<td>0.135</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>136 (68%)</td>
<td>107 (70.4%)</td>
<td>29 (60.4%)</td>
<td>0.196</td>
</tr>
<tr>
<td>Ethnicity (White)</td>
<td>164 (82%)</td>
<td>125 (82.2%)</td>
<td>39 (81.2%)</td>
<td>0.877</td>
</tr>
<tr>
<td>Diabetes</td>
<td>73 (36.5%)</td>
<td>55 (36.2%)</td>
<td>18 (37.5%)</td>
<td>0.869</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>75 (37.5%)</td>
<td>59 (38.8%)</td>
<td>16 (33.3%)</td>
<td>0.494</td>
</tr>
<tr>
<td>Antiplatelet agent</td>
<td>59 (29.5%)</td>
<td>49 (32.2%)</td>
<td>10 (20.8%)</td>
<td>0.131</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>16 (8%)</td>
<td>15 (9.9%)</td>
<td>1 (2.1%)</td>
<td>0.083</td>
</tr>
<tr>
<td>Haemoglobin, g/dl</td>
<td>93 (81-109)</td>
<td>97 (82.5-112)</td>
<td>88 (80.5-97)</td>
<td>0.016</td>
</tr>
<tr>
<td>Platelet count, x 10⁹/L</td>
<td>230 (175-309)</td>
<td>225 (176-300)</td>
<td>273 (161-329)</td>
<td>0.245</td>
</tr>
<tr>
<td>Prothrombin time, sec</td>
<td>11.8 (11-12.6)</td>
<td>12 (11-12.5)</td>
<td>11.7 (11.4-12.5)</td>
<td>0.929</td>
</tr>
<tr>
<td>APTT, sec</td>
<td>31.1 (28.2-34)</td>
<td>30.8 (28.1-34)</td>
<td>32.3 (29.3-34.3)</td>
<td>0.157</td>
</tr>
<tr>
<td>Urea, mmol/L</td>
<td>23.3 (14.4-32.2)</td>
<td>23.3 (14.5-32.9)</td>
<td>22.8 (14.3-27.7)</td>
<td>0.712</td>
</tr>
<tr>
<td>Successful insertion</td>
<td>185 (92.5%)</td>
<td>146 (96.1%)</td>
<td>39 (81.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Immediate complication</td>
<td>18 (9%)</td>
<td>16 (10.5%)</td>
<td>2 (4.2%)</td>
<td>0.180</td>
</tr>
</tbody>
</table>

Continuous variables expressed as median and interquartile range and p-value by Mann-Whitney U test. Categorical variables are expressed as numbers and percentages with p-values by Chi-square test.

#2543
NEPHROFLOW FOR ESTIMATION OF VASCULAR ACCESS FLOW FOR HEMODIALYSIS: WHEN TO MEASURE?
Pablo Alejandro Sarduy Coronado¹, José Luis Merino Rivas², Cecilia Peña Peña², Noelia Abad², Blanca Bueno Antúnez², Beatriz Espejo Marchante², Jesús Martin-Centellas² and Vicente Paraíso²

¹Hospital Virgen de la Luz, Cuenca, Spain and ²Hospital Universitario del Henares, Coslada, Spain

Background and Aims: Current guidelines emphasize the need for surveillance of vascular access (VA) for hemodialysis (HD), especially arteriovenous fistulas (AVF). Detecting a reduction in VA flow is a useful tool to anticipate the complications of VA such as thrombosis. The DMed NephroFlow (NIPRO®) system, based on ultrasound dilution (UD) methods, has been shown to be comparable to the classic Transonic® measurement system for estimating VA flow and can be applied for VA surveillance. Our objective is to determine if there are significant differences when performing flow measurements with NephroFlow® between the first hour and the second hour of the HD session, as well as between any of the three days in which the patient attends HD.

Method: For two consecutive weeks, patients with AVF or graft (gAVF) on HD in our unit underwent VA flow measurements using the NephroFlow® system at the first and second hour of HD, on the 3 days that they attended HD sessions. Interspersing the first hour with the second each week to avoid significant loss in HD quality. For the study, we proceeded according to the usual recommendations of stable flow at 250 ml/min, corresponding ultrafiltration rate, needles in the same vein, without change in dry weight, with the same nurse staff, and transferring all patients to conventional HD.

Results: Twenty-one patients have been included, 13 male and 8 female, mean age 68±12.3 years. The mean time on HD was 36±23 months. The type of VA was: 10 patients presented a radiocephalic AVF, 5 brachiocephalic AVF, 2 patients a brachio basilic AVF, and 4 patients a gAVF. The estimated mean flow obtained by NephroFlow® in the first hour of all sessions and in the second hour was 1056±754 and 1130.16±769 ml/min, respectively; intraclass correlation index was 0.737 and K-W Test H 0.349 (p<0.05). The mean flow on the first day was 1129±794.5 ml/min, ICC = 0.662; second day 1027.5±729 ml/min, ICC = 0.812; third day 1121.5±42 ml/min, ICC = 0.774. In all cases p<0.05.
Conclusion: No significant differences have been observed in the VA flow estimated with the NephroFlow® ultrasound dilution system, neither at measurement time (the first or the second hour of HD session) nor day of performance (first, second or third day of HD session of the week). NephroFlow® UD system may be a useful tool for VA surveillance and could be applied when is necessary.

#6728
ALCOHOL LOCK FOR PROPHYLAXIS AGAINST PERMCATH CRBSI: IS IT A BOON?
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Primus Super Speciality Hospital, Nephrology, New Delhi, India

Background and Aims: Introduction: Catheter related blood stream infection (CRBSI) is a dreaded complication in patients with tunneled dialysis catheter and often results in catheter loss. Antibiotic lock, a preventive strategy, is not followed for fear of emergence of resistant strains. We have reported usefulness of 70% alcohol lock in cases of established CRBSI. The present study was aimed to find usefulness of alcohol lock for CRBSI prophylaxis.

Method: This is a single centre observational pilot study. Dialysis patients with Permcath as vascular access were randomised into two groups. Both groups were similar in age, sex and comorbidities. Both groups received routine heparin lock after each dialysis session. Group A in addition also received 70% alcohol lock, once a fortnight. Patients with minimum follow up of 60 days were included in the study. Diagnosis of CRBSI was made by IDSA criteria.

Results: Forty five patients with permcath were divided in Group A (29 patients) and Group B (16 patients). In Group A, 21 and in Group B, 12 patients completed the study. In Group A, during a mean follow up of 2988 catheter days, 5 patients (23%, 1/600 days) developed CRBSI (2 pseudomonas, two staphylococcus aureus and 1 Klebsiella) and in group B, 4 patients (33%) with mean follow up of 1611 catheter days (1 in 403 catheter days) developed CRBSI (p = 0.69) (2 Klebsiella, two staphylococcus). There was no case of catheter leak, crack or block in either group. Results showed a trend towards better outcome in alcohol lock group though because of small number, statistical significance couldn’t be reached.

Conclusion: This pilot study found usefulness of alcohol lock in preventing CRBSI. Alcohol lock is cheap and there was no apparent catheter damage with alcohol over 6 months period. A larger study can confirm our findings.

#3597
MONOCLONAL GAMMOPATHY AS A RISK FACTOR FOR ARTERIOVENOUS FISTULA PRIMARY FAILURE
Catarina Almeida1, João Peixoto2, Vítor Martins3, Clara Nogueira4, Susana Pereira4, Ana Ventura4 and Maria Clara Almeida1
1Centro Hospitalar Vila Nova de Gaia / Espinho, Nephrology, Portugal and 2Centro Hospitalar Vila Nova de Gaia / Espinho, Angiology and Vascular Surgery, Portugal

Background and Aims: Arteriovenous fistula (AVF) is the preferred vascular access for hemodialysis (HD) in most patients. However, postoperative complications such as primary failure (PF) with a reported incidence between 20-60% remain a major problem. Patients diagnosed with monoclonal gammopathy (MG) are at increased risk of thrombotic events, either due to the disease itself or the chemotherapy used for its treatment. The aim of this study was to evaluate whether the presence of MG was associated with primary AVF failure.

Method: We performed a retrospective single-center case-control study including 103 patients observed in our vascular access consultation for planning their first HD access. Demographic and clinical data were collected, such as the presence of diabetes, hypertension, cardiovascular disease and MG. Distal AVF was the access of choice when possible. Primary failure was defined as incapacity to use AVF for HD because of failure to mature or thrombosis. Univariate analysis was performed, and a logistic regression was applied to access predictors of PF. A p-value inferior to 0.05 indicated statistical significance.

Results: In total 14 (13.6%) patients had MG (11 multiple myeloma, 1 light-chain deposition disease, 1 proliferative glomerulonephritis with monoclonal immunoglobulin deposits and 1 amyloid light-chain amyloidosis). Regarding the AVF location, 13 patients constructed a constructed a distal AVF and 1 patient a proximal AVF. When compared to the group of 89 patients who did not have MG, there were no significance differences in sex, age, prevalence of diabetes and cardiovascular disease neither in AVF construction site. Arterial hypertension was more frequent in the group of patients without MG (93.2% versus 64.3%, p = 0.007). PF occurred in 57.1% (8/14) of patients with MG and in 27% (24/89) of those without MG (p = 0.032). In logistic regression, the presence of MG was the only predictor of primary AVF failure (OR 4.39 95% CI: 1.23-15.75).

Conclusion: In our study, we found that a patient with monoclonal gammopathy has a 4-fold increased risk for primary AVF failure comparing to the general chronic kidney disease patients. Therefore, a careful evaluation must be made when planning for AVF placement in these patients, balancing individual life’s expectancies and monoclonal gammopathy prognosis.

#4245
CATHETER-ASSOCIATED BLOODSTREAM INFECTIONS IN A HOSPITAL DIALYSIS UNIT – SEASONAL INFLUENCE AND COVID-19 PANDEMIC
Irene Galindo Marin, Carmen Mon Mon, Milagros Ortiz, Maria Sanchez, Rosa Camacho, Carolina Lentisco, Irene Oñate, Juan Carlos Herrero Berron and Aniana Oliet
Hospital Severo Ochoa, Nephrology, Spain

Background and Aims: Catheter-associated bloodstream infections (CRBSI) are an important source of morbidity and mortality among patients receiving hemodialysis through a central venous catheter (CVC). Despite of the efforts to choose the arteriovenous fistula as the first vascular access, a large proportion of end stage kidney disease population initiates dialysis using these catheters. Thus, efforts to prevent catheter-associated bloodstream infections remain important. The aim of our study is to analyze the outcomes of the episodes of CRBSI in our dialysis unit. Secondly, we evaluated the seasonal distribution
and the possible impact of infection-control measures implemented during COVID-19 pandemic.

Method: We conducted a single-center retrospective observational study of all cases of tunneled dialysis catheter-associated bacteremia that need hospitalization during a nine-year period (January 2013 – December 2022).

Results: A total of 67 episodes of catheter-associated bloodstream infections in 52 hemodialysis patients were registered. This translates into a total of 2 episodes per 1000 catheter-days. Among all patients, the mean age was 68.5 years, 74.6% were men and 25.4% women. Five patients (9.6%) had any type of immunosuppressive treatment. Nearly 88% used a tunneled jugular catheter as definite vascular access and the remainder used a femoral one. Eighteen of all episodes (26.9%) occurred during the first thirty days of catheter implantation. Ten of all patients (19.2%) suffer at least a second infection during the follow-up period, without differences in clinical and demographic characteristics. The microbial etiology of the infections were Gram-positive organisms in 67.2% and, within these, 83% were Staphylococcus Aureus. The catheter had to be removed in 65.7% of all cases and there were significant difference (p<0.01) between Gram negative infections (preservation of 70%, successfully treated with prolonged antibiotic therapy) and Gram positive ones (preservation 12%, 3 cases of S. epidermidis and 2 cases of S. Aureus due to limited vascular tree). Admission to the intensive care unit was required in five patients and there were only two cases of endocarditis as metastatic complication. There was no death related to CRBSI. About the seasonal distribution, the majority of episodes occurs in summer and spring (43.3% and 23.9% respectively), whereas in autumn and winter there were fewer cases registered (16.4% and 16.4% in both). Despite of the increasing use of CVC as definite vascular access in our dialysis unit (almost 60%), the rate of CRBSI has been declining in parallel over the years. Since 2018, we reported less than 0.5 episodes per 1000 catheter-days. Conclusion: This study shows a low frequency of CRBSI compared to previous studies. Among all episodes, the predominant infecting organism was methicillin-sensitive Staphylococcus Aureus (14.7% were methicillin-resistant). The early catheter removal, especially in aggressive strains as S. Aureus, reflects a low number of serious complications, with uncommon metastatic infections and no death directly related to CRBSI. A large proportion of infections were in summer; it may be attributable to hiring of less experienced professionals. We identified a substantial decline in rates of CRBSI coincident with COVID-19 pandemic. Nevertheless, this reduction was apparent beginning nearly two years before pandemic. This suggests that factors other than changes in infection-control practices during the pandemic are partially responsible of that.

OUTBREAK OF RALSTONIA SPP AND BURKHOLDERIA SPP CATHETER-RELATED BLOODSTREAM INFECTION IN A HAEMODIALYSIS UNIT

Mauro Valente1, Francesca Orecchioni1, Fabiana Brigante1, Maria Ilaria Moretti1, Marcello Derrico1, Marco Moretti2, Marcello Tavio1, Maria Soledad Ferreiro Cotorrelo1, Veronica Pasquali1, Massimo Marchi2 and Andrea Ranghino1

1AOU delle Marche, Nephrology, Dialysis and Renal Transplantation Unit, Ancona, Italy; 2AOU delle Marche, Laboratory Medicine, Ancona, Italy; 3Polytechnic University of the Marche Region, Department of Biomedical Sciences and Public Health, Section of Hygiene, Preventive Medicine and Public Health, Ancona, Italy; 4AOU delle Marche, Unit of Emerging and Immunosuppressed Infectious Diseases, Department of Gastroenterology and Transplantation, Ancona, Italy; 5AOU delle Marche, Health Care Medical Directory, Ancona, Italy and 6Fresenius Medical Care, Crema, Italy

Background and Aims: Ralstonia (RB) and Burkholderia (BB) species are environmental Gram-negative bacilli responsible for several nosocomial infections in immunocompromised or frail patients. RB and BB may contaminate medical devices because of their ability to survive in a biofilm and with low nutrient requests. Reports of infection outbreaks due to RB and BB are very few and only in sporadic cases, the source of contamination was identified. We describe here: i) how we managed an outbreak of bacteremia caused by RB and BB occurred in our dialysis unit, ii) what we have done to identify the source of infection and iii) the countermeasures we adopted to reduce the risk of new events.

Method: From 7 to 16 April 2021, 6 out of 39 (15.4%) hemodialyzed (HD) patients with a long-term indwelling central venous catheter (CVC) developed symptoms related to infection. Blood cultures revealed the presence of RB and BB. Thus, a prompt check of the blood cultures of all HD patients with CVC was performed. Blood samples were inoculated in an automated microbial detection system (VIRTUO BIOMERIEUX) and subsequently, blood positive samples were inoculated in Chocolate and Columbia blood Agar plates. In addition, a microbiological analysis of disinfectants, drugs used in dialysis unit and samples collected from the reverse osmosis water unit (ROW) and from the ROW delivery line were performed. None of the samples obtained from the ROW and from the ROW delivery line resulted positive. Thus, a microbiological analysis of the biofilm attached on the loading pipes (LP) and on the loading plastic tubes (LPT) that connect the hemodialyzer consoles (HC) to the ROW delivery line were performed. Briefly, LPT were subjected to ultrasound sonication at 30–40 KHz (BactoSonic-Bandelin), to disrupt the bacterial biofilm. The material obtained from sonication was cultured. Bacteria was identified by an automated mass spectrometry (MALDI-TOF VITEK® MS, Biomerieux).

Results: Bacteremia due to RB and BB was confirmed in 7 out of 39 (17.9%) of the hemodialyzed patients with a long-term indwelling CVC. 1 out of 7 was asymptomatic. Baseline characteristics of the 6 symptomatic patients were: mean age 68±16 years; mean C-reactive protein 4.48±1.3 mg/dl; mean procalcitonin 13.27±11.07 ng/ml; mean body temperature 37.9±1.4°C. The antibiotic therapy was decided according to antibiogram and included meropenem and ciprofloxacin. CVC were removed in all infected patients between 6 to 11 days from the diagnosis. Concomitantly, a new one was placed. None of the HD patients with arterio-venous fistulae developed bacteremia. RB and BB were isolated in the biofilm of 11 out of 37 LPT. Thus, we modified the ROW delivery line in order to set up a scheduled chemical and physical disinfections of the ROW delivery line with the hemodialysis consoles connected avoiding the risk of new contamination of the LPT and loading pipes. Briefly, on alternate months the whole system that include ROW delivery line (PE-Xa Medical Device, Fresenius Medical Care), loading pipes, LPT and hemodialysis consoles are disinfected by hot water (90°C) produced by a water heater (AquaB plus HF, Fresenius Medical Care) and by chemical disinfectant, 5% peracetic acid according to the protocols made by the console fabricant. In addition, we added to the reverse osmosis system a filtration module of 0.01 μm (Aquapor, Fresenius Medical Care) prior to the ROW delivery line. Figure 1. Awaiting for the modification of the ROW delivery line, the patients with CVC

Figure 1: Hemodialysis water treatment system scheme.
were dialyzed using a portable water treatment unit. After more than 14 months from the modification of the whole system for production and delivery of ROW none of the hemodialyzed patients developed infection by RB and BB.

**Conclusion:** Our experience suggests that infection outbreak by unusual bacteria such as RB and BB could be successful treated using antibiotic therapy. Nevertheless, in dialysis unit the source of infection should be investigated in order to adopt the countermeasures necessary to reduce the risk of new infections.

**ARTIFICIAL INTELLIGENCE APPLIED TO VASCULAR DOPPLER ULTRASOUND MODELS FOR PREDICTING UNDERDEVELOPMENT OF VASCULAR ACCESS IN NEPHROLOGY**

Alfonso Lara Ruiz, María Jesús Moyano Franco, Fernando Bertomeu Moreno, Javier Burgos Martín, Melissa Cintra and Mercedes Salguiera Lazo

Hospital Universitario Virgen Macarena, Nephrology, Sevilla, Spain

**Background and Aims:** The vascular access of choice for hemodialysis patients is the arteriovenous fistula (AVF). There is a high rate of early primary failure and loss of primary AVF patency. Monitoring of vascular access is essential for early diagnosis of complications and prolonging survival. Models based on Artificial Intelligence (AI) and Machine Learning (ML) can be used for this.

**Method:** Retrospective descriptive study of the Vascular Doppler Ultrasound (VDU) in adults carried out since January 2019 to January 2022 in our AVF follow-up nephrology clinic. We analyze the results and create AI-based AVF underdevelopment prediction models. We included clinical, demographic and ultrasound variables. Patients were undergoing AVF post-surgery follow-up (VDU by protocol at 3-4 weeks after AVF surgery) or were referred to the clinic with signs of AVF dysfunction. The insufficient development of the vascular access is established as an objective variable. SPSS 20 Statistical Package. Automated Learning Analysis (ML) with Orange ML and BigML.

**Results:** 243 VDU were performed. Of the total, 139 (57%) were follow-up post-surgical VDU per protocol and 104 (43%) were AVF dysfunction VDU. Using supervised ML Analysis techniques with random sampling of 80% of the instances for Training and 20% for Test, we obtain prediction models for the underdevelopment (UD) attribute of AVF. Decision tree algorithm, Area under the curve (AUC) 89%, Classification accuracy (CA) 90%, Precision 90%. Random Forest Algorithm (RF) (AUC) 95%, (CA) 86%, Accuracy 81%. Near Neighbor Algorithm (K-NN) (AUC) 88%, CA 82%, Accuracy 78%. Convolutional Neural Networks (NNC) (AUC) 82%, CA 74%, Accuracy 60%. Algorithm with unsupervised technique of clustering in k-Means 3 clusters are obtained. The variables that best correlate with the objective variable are access flow, vein diameter, resistance index (RI) proximal, (RI) distal, and diameter of the anastomosis.

**Conclusion:** The vascular ultrasound systematized by the nephrologist facilitates the early diagnosis of complications that lead to early intervention. Analysis of the data with techniques (ML) can facilitate early diagnosis AVF poor development requiring close monitoring or intervention. The development of a nephrology clinic for monitoring vascular access could avoid invasive and unnecessary procedures for the patient.

**EARLY EXPERIENCE OF ENDOVASCULAR CREATION OF ARTERIOVENOUS FISTULA IN SOUTHEAST ASIA**

Kok Pan Loo1, Ru Yu Tan1, Chee Woon Tan1, Tze Tec Chong1, Kiang Hiong Tay1, Hsien Tsung Tan1, Kun Da Zhuang3, Apoorva Gogna1 and Chieh Suai Tan1

1Department of Renal Medicine, Singapore General Hospital, Singapore,
2Department of Vascular Surgery, Singapore General Hospital, Singapore and
3Department of Vascular and Interventional Radiology, Singapore General Hospital

**Background and Aims:** Creation of native arteriovenous fistulae(AVF) has been traditionally through open surgical technique. Endovascular creation of AVF (EndoAVF) has been shown to be an effective alternative to open surgery in Europe and North America. In Asia, EndoAVF creation is a novel technique and we report our early experience of EndoAVF creation in a case series of 18 patients.

**Method:** Between Nov 2021 to Aug 2022, ultrasound vein mapping was performed in a total of 39 patients. Eighteen patients were deemed suitable for EndoAVF and proceed for the procedure. EndoAVF creation was attempted by multidisciplinary team comprising of vascular surgeon, interventional radiologists and nephrologists. The patients were prospectively followed-up for at least 6-months. Baseline demographics, vascular characteristics, unassisted maturation, functional patency and freedom from intervention were studied.

**Results:** Table 1 shows the baseline demographics of the participants. Twelve patients (67%) were already initiated on hemodialysis via tunneled dialysis catheters during the procedure. EndoAVF was successfully created in 16 (89%) patients. Of which, 13 (72%) were WavelinQ while the remaining 5 (28%) were Ellipsys EndoAVF. The reasons of failures were inability to cannulate artery (n = 1) and vein (n = 1). Minor complications occurred in 6 patients: extravasation in 5 cases and hematoma in 1 patient. The brachial artery flow rates at creation and 1-month post-creation were 558 ± 328 and 583 ± 215 mls/min, respectively. Two participants (11%) underwent interventions to facilitate maturation of the EndoAVF. The median time to maturation was 70 (IQR 49 – 106) days while the median time to first successful 2-needle cannulation was 77 (56 – 127) days. At 6-months, 8 (50%) of EndoAVFs that were successfully created required further intervention to maintain patency, while 1 EndoAVF was abandoned from failure to mature despite intervention.

**Conclusion:** EndoAVF can be created successfully in a Southeast Asian population. Further studies with more patients and longer follow-up periods are needed to assess long-term outcomes.

<table>
<thead>
<tr>
<th>Table 1: Demographics</th>
<th>Number of patients (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 (38.88%)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (61.11%)</td>
</tr>
<tr>
<td>Race</td>
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<tr>
<td>Chinese</td>
<td>16 (88.89%)</td>
</tr>
<tr>
<td>Malay</td>
<td>2 (11.11%)</td>
</tr>
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<td>Age</td>
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<tr>
<td>40-49</td>
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<tr>
<td>50-59</td>
<td>7 (38.88%)</td>
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<td>60-69</td>
<td>4 (22.22%)</td>
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<td>70-79</td>
<td>6 (33.3%)</td>
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<tr>
<td>Etiology of CKD</td>
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<tr>
<td>DM</td>
<td>10 (55.5%)</td>
</tr>
<tr>
<td>HTN</td>
<td>0 (0%)</td>
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<tr>
<td>cGN</td>
<td>6 (33.3%)</td>
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<tr>
<td>ADPKD</td>
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<tr>
<td>Obstructive uropathy</td>
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<tr>
<td>Others</td>
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<tr>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>11 (61.11%)</td>
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<tr>
<td>HTN</td>
<td>15 (83.33%)</td>
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<tr>
<td>Hyperlipidemia</td>
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<td>Ischemic Heart Disease</td>
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<td>Cerebrovascular Accident</td>
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<td>Peripheral arterial disease</td>
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<tr>
<td>Usage of antplatelet</td>
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<tr>
<td>Aspirin</td>
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<tr>
<td>Plavix</td>
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<tr>
<td>Dual antplatelet</td>
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<tr>
<td>Other antplatelet agent</td>
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<tr>
<td>Not on antplatelet agent</td>
<td>9 (50%)</td>
</tr>
<tr>
<td>Use of anticoagulation</td>
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<td>Warfarin</td>
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<tr>
<td>Enoxaparin</td>
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<tr>
<td>Direct Oral anticoagulation</td>
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<tr>
<td>Not on anticoagulation</td>
<td>14 (77.78%)</td>
</tr>
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</table>
Abstracts

MONOCENTRIC EXPERIENCE (ENDOAVF) FOR HEMODIALYSIS ACCESS: A RETROSPECTIVE #5918

Table 2:

<table>
<thead>
<tr>
<th>EndoAVF</th>
<th>Number of pts (Percentage)</th>
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<tbody>
<tr>
<td>Types of EndoAVF</td>
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<tr>
<td>Wavelinq</td>
<td>13 (72.2%)</td>
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<tr>
<td>Ellipsys</td>
<td>5 (27.7%)</td>
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<tr>
<td>Successful Creation of AVF</td>
<td>16 (88.88%)</td>
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<tr>
<td>Minor complications</td>
<td>6 (33.33%)</td>
</tr>
<tr>
<td>Extravasation</td>
<td>5 (27.78%)</td>
</tr>
<tr>
<td>Hematoma</td>
<td>1 (5.5%)</td>
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<tr>
<td>Time to maturity (Days)</td>
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<tr>
<td>Median (Days)</td>
<td>70</td>
</tr>
<tr>
<td>Interquartile Range (Days)</td>
<td>49-106</td>
</tr>
<tr>
<td>Time to first successful 2-needle cannulation (Days)</td>
<td>77</td>
</tr>
<tr>
<td>The brachial artery flow rates (mls/min)</td>
<td>558 ± 328</td>
</tr>
<tr>
<td>at creation (mls/min)</td>
<td></td>
</tr>
<tr>
<td>1-month post-creation (mls/min)</td>
<td>583 ± 215</td>
</tr>
<tr>
<td>EndoAVFs that were successfully created required further intervention to maintain patency in 6 months</td>
<td>8 (50%)</td>
</tr>
<tr>
<td>Device-Related Serious Adverse Events</td>
<td>0</td>
</tr>
<tr>
<td>Procedure-Related Serious Adverse Events</td>
<td>0</td>
</tr>
<tr>
<td>EndoAVF abandoned</td>
<td>1 (5.5%)</td>
</tr>
</tbody>
</table>

ENDOVASCULAR CREATION OF AN ARTERIOVENOUS FISTULA (ENDOAVF) FOR HEMODIALYSIS ACCESS: A RETROSPECTIVE MONOCENTRIC EXPERIENCE

Ludovica Odone1, Jacopo Gianassi1, Egrina Dervishi1, Roberta Cutruzzula1, Costanza Gaudio1, Giacomo Gabbani2, Gianmarco Falcone2, Fabrizio Fanelli2 and Calogero Cirami2

1 AOUCareggi, Nephrology Dialysis and Transplantation, Firenze, Italy and 2 AOUCareggi, Vascular and Interventional Radiology, Firenze, Italy

Background and Aims: Functioning vascular access is an essential element for life-saving hemodialysis therapy. Surgical creation of a radiocephalic arteriovenous fistula (AVF) is the gold standard of vascular access for hemodialysis. However, an endovascular approach to arteriovenous fistula creation (endoAVF) has increasingly gained acceptance over the last years as an alternative to the conventional surgical method. It offers a minimally invasive method for the formation of arteriovenous shunts and allows the creation of fistulas with minimal vessel trauma. There are currently two technologies available for this purpose, the Ellipsys Vascular Access System (Medtronic, Avenu Medical, San Juan Capistrano, Calif) and the Wavelinq endoAVF System (BD Medical, Franklin Lakes, NJ). At our centre (Careggi University Hospital, Florence), we developed an integrated service, based on a multidisciplinary approach between Interventional Radiology and Interventional Nephrology available for this purpose, the Ellipsys Vascular Access System (Medtronic, Avenu Medical, San Juan Capistrano, Calif) and the Wavelinq endoAVF System (BD Medical, Franklin Lakes, NJ). At our centre (Careggi University Hospital, Florence), we developed an integrated service, based on a multidisciplinary approach between Interventional Radiology and Interventional Nephrology for percutaneous arteriovenous fistulas utilizing both Ellipsys and Wavelinq. We describe our experience with a case series of 39 patients, showing feasibility and outcome of this treatment option.

Method: Between December 2020 and January 2023 we created an endoAVF in 39 patients. Patients were suitable for the procedure after a pre-therapeutic ultrasound vascular mapping showed adequate brachial, radial and ulnar vessels and no ipsilateral central venous stenosis. After procedure, we performed a regular clinical and ultrasound monitoring. Therefore, we collected data regarding patient characteristics, initial technical success rate, number of access lost and number of endoAVF meeting primary and secondary patency.

Results: Of the total of 39 patients treated with endoAVF, 29 (74.3%) were male, with a mean age of 60.1 ± 33.9 years. The Wavelinq procedure was performed in 32 patients (82.0%) and the Ellipsys procedure in 7 patients (17.9%). Initial technical success was achieved in 38 (97.4%) cases, while in 1 case we had a primary failure of the fistula (Figure 1). Among these 38 patients, 4 (10.5%) were lost to follow-up because of death from other causes (3 patients) and because of kidney transplantation (1 patient), while 2 other patients (5.2%) have not required hemodialysis yet. Of the remaining 32 patients, we had 2 fistulas lost because of complications and a cumulative functional patency of 93.7% (30 fistulas), with a primary patency rate of 76% (23 fistulas).

Conclusion: The endoAVF appears to be feasible and safe for the creation of arteriovenous fistula suitable for hemodialysis access. Our data show an high functional cumulative patency of the endoAVF and a good primary patency, reducing the necessity of further interventions. Furthermore, in the prevalent hemodialysis population, the minimally invasive endovascular arteriovenous fistula procedure should help improving long wait times for vascular access creation. Further studies with more patients and multicentric data are needed to assess long-term outcomes.

ALCOHOL LOCK IN CRBSI: A PANACEA

Prem Varma and Mahak Singla

Primus Super Speciality Hospital, Nephrology, New Delhi, India

Background and Aims: CRBSI is a dreaded complication of permcath, with a reported incidence of 1.1 – 5.5 episodes/1000 days. Many of these patients especially those infected with Staphylococcus aureus, Pseudomonas aeruginosa or fungal growth require catheter removal. 70% alcohol possibly breaks the biofilm in the catheter and exposes hidden bacteria to antibiotics. This study was done to find the usefulness of 70% alcohol lock in patients with established CRBSI.

Method: All dialysis patients in our centre with permcath as vascular access were the subjects of the study. All patients were given heparin lock after each dialysis session. CRBSI was diagnosed as per CDS/IDSA criteria. All patients with CRBSI in addition to antibiotics were also given 70% alcohol lock (2 ml in each port) for 3 consecutive days. Outcome of these patients in term of clinical response and need for catheter removal was studied. The catheter outcome of this group was compared with our patients (retrospective controls) who were given only antibiotics and not given alcohol lock.

Results: Over last two years 166 permcaths were placed in our institution. Eighty nine of them continued dialysis in our centre. Their total follow up period was 12028 days (30-720 days). There were 18 episodes of CRBSI in 14 of these patients (1.5 episodes per 1000 catheter days). Three of these patients (16.67%) required catheter removal, rest all improved with antibiotics and alcohol lock. Over a follow up of 150 days (30 –420 days), these patients have been doing well and there has been no episode of catheter leak or break or block. On comparing with our retrospective control of 22 patients with CRBSI, who were not given alcohol lock, 15 (68.18%) required catheter removal (P = 0.001).
Conclusion: The present study though on small numbers, shows that alcohol lock works as a boon in the setting of established CRBSI. It avoids catheter removal in majority of patients.

#3438

OUTCOME OF HEMODIALYSIS TUNNELED CUFFED CATHETER PLACEMENT BY THE NEPHROLOGIST AT THE DIALYSIS UNIT Sander Camp1,2, Dieter De Clerck1,2, Wilfried Cools1,2 and Patricia Van Der Niepen2

1UZ Brussels, Jette, Belgium and 2Vrije Universiteit Brussel Campus Jette, Jette, Belgium

Background and Aims: A large proportion of patients starts dialysis treatment with a temporary catheter which is afterwards replaced by a tunneled cuffed catheter (TCC) by the surgeon or interventional radiologist. This implies a certain dependency on the availability of the surgeon or radiologist. During this waiting time, the patient is exposed to a temporary catheter, which is accompanied by a higher risk of infection. At the UZ Brussels, until 2017 TCCs were placed at the operating room by the surgeon. In September 2017 nephrologists at the UZ Brussels started to place TCCs at the dialysis unit, without the use of fluoroscopy, to lower the time of exposure to a temporary catheter.

Method: We did a retrospective analysis of 100 patients who got a TCC placed at the dialysis unit from September 2017 until February 2021 (nephrologist group); as a control group we evaluated the last 100 patients who got a TCC by the surgeon before this period. We evaluated complications (during procedure and within the first month), catheter function during the second week and after three months, and waiting time to get a TCC. Logistic regression analysis was performed to detect differences in complication rate and catheter function. Two-way analysis of variance was performed on the log transformed waiting times.

Results: In both groups, comorbidities such as diabetes mellitus, history of cardiac surgery and presence of a pacemaker or port-a-cath at the time of catheter insertion were comparable. In both groups almost half of the patients were taking antplatelet therapy. In the nephrologist group more patients got a catheter because of AKI (32% versus 15%) and less patients had a planned admission (19% versus 42%). More patients had a TCC placement after an ICU admission (33% versus 18%) and only few of the catheter placements were replacements of in situ TCC’s (3% versus 35%). In the nephrologist group, catheters were inserted in the right (93%) and left jugular vein (7%). In the surgeon group, catheters were inserted in the right (71%) and left jugular vein (23%) and in the subclavian vein (6%). In the nephrologist group there were no failed procedures, but 2 left jugular vein catheters were not in the correct position (turning upwards in the superior vena cava). In 3 patients the carotid artery was punctured and 3 patients had a significant exit site bleeding. In the surgeon group, 3 patients had a failed procedure and 2 patients had a carotid puncture. Analysis of late complications in the nephrologist group showed a bleeding from the exit site in 8 patients, development of bacteremia in 2 patients and the neck wound opened up in 2 patients. In the surgeon group 9 patients had an exit site bleeding, 4 patients had an exit site infection, 2 patients had a bacteremia, 1 patient had a catheter cuff becoming visual at the exit site, 1 patient had a catheter dislocation, 1 patient had a vena cava superior syndrome and 1 patient had a large hematoma. The presence of AKI and the use of antplatelet therapy were found to be risk factors of getting a late complication. Getting a catheter placed by the nephrologist lowered the risk, even after correction for AKI and antplatelet therapy, with an odds ratio of 0.414 (p = 0.044). In the nephrologist group, 92% of catheters had a good early function, compared to 84% in the surgeon group. At three months, about half of the catheters were still in use. Catheter function was correct in 87% in the nephrologist group versus 77% in the surgeon group. In patients who first started with a temporary catheter, the mean waiting time to get a TCC in the nephrologist group was 1.6 days compared to 4.5 days in the surgeon group (p < 0.001). In patients who got immediately a TCC the mean waiting time was 0.6 days in the nephrologist group compared to 2.4 days in the surgeon group (p < 0.001).

Conclusion: In patients who have to start dialysis urgently, TCC’s can be placed without fluoroscopy by the nephrologist at the dialysis unit in a safe and efficient manner. This lowers the need for temporary catheters, and shortens the waiting time for getting a TCC.

#6848

DIABETES AND HEMODIALYSIS ARTERIOVENOUS ACCESS CONSTRUCTION – A RETROSPECTIVE STUDY IN A SINGLE CENTER

Catarina Marouço1, Juliana Francisa Da Costa e Silva Barbosa Damas1, Tiago Assis Pereira1, Miguel Bigotte Vieira1, Sofia Carellha2, Ana Pena2, and Cristina Jorge1

1Hospital Curry Cabral, Nephrology Department, Lisboa, Portugal and 2Hospital Curry Cabral, General Surgery, Portugal

Background and Aims: The preferred vascular access for patients with end-stage renal disease is native arteriovenous fistula (AVF). However, in some patients, given their co-morbidities, vascular access (VA) construction is not feasible. Diabetes Mellitus (DM) is described as one of the main factors associated with vascular access failure. The aim of this study is to characterize in a non-diabetic versus diabetic population the pre-surgical vascular mapping by doppler ultrasound (DUS), as well as analyze which VA could theoretically be constructed, what VA was effectively were constructed and its patency between the two groups.

Method: We present a retrospective study of a cohort of patients that were evaluated by DUS for pre-surgical planning and VA construction from 2018 to 2021. We collected demographic, clinical and DUS parameters. The feasibility for VA construction was classified in pre-surgical evaluation as possible, non-advisable or as borderline. The patency after surgery was observed until day 45.

Results: We analyzed a total of 355 patients. Almost half of the population had diabetes (n = 161, 45.4%). The demographics and clinical parameters are summarized in Table 1. Concerning pre-surgical vascular mapping, we observed that patients with diabetes had more severe calcifications than the non-diabetic group. Table 2 summarizes the doppler characteristics of right and left radial and brachial arteries in both groups. Regarding the feasibility of VA construction, the non-diabetic group was more likely to receive a radiocephalic fistula than the diabetic fistula (33% vs 23.6%, pvalue 0.12). Surprisingly, in our study the non-diabetic group had also more patients that could only sustain a prosthetic fistula (15.5% vs 12.4%, pvalue 0.41). Diabetic patients showed more likelihood to construct proximal fistulae (67.4% vs 56.8%, p = 0.06). In terms of what type of VA was effectively created, more radiocephalic fistulas were performed in the non-diabetic group (13.9% vs 7.5%, pvalue 0.17). In the diabetic group more brachiocephalic fistulas (65.6% vs 62.4%, pvalue 0.17) and more prosthetic fistulae (19.4% vs 14.4%, pvalue 0.17) were constructed.

Concerning VA patency at 45 days the diabetic group demonstrated higher rates but with no statistical significance (88.4% vs 83.2%, pvalue < 0.18). Only 2 patients in the non-diabetic group were on dialysis treatment within 45 days. The demographics and clinical parameters are summarized in Table 1. Concerning pre-surgical vascular mapping, Table 2 summarizes the doppler characteristics of right and left radial and brachial arteries in both groups. Regarding the feasibility of VA construction, the non-diabetic group was more likely to receive a radiocephalic fistula than the diabetic fistula (33% vs 23.6%, pvalue 0.12). Surprisingly, in our study the non-diabetic group had also more patients that could only sustain a prosthetic fistula (15.5% vs 12.4%, pvalue 0.41). Diabetic patients showed more likelihood to construct proximal fistulae (67.4% vs 56.8%, p = 0.06). In terms of what type of VA was effectively created, more radiocephalic fistulas were performed in the non-diabetic group (13.9% vs 7.5%, pvalue 0.17). In the diabetic group more brachiocephalic fistulas (65.6% vs 62.4%, pvalue 0.17) and more prosthetic fistulae (19.4% vs 14.4%, pvalue 0.17) were constructed.

Concerning VA patency at 45 days the diabetic group demonstrated higher rates but with no statistical significance (88.4% vs 83.2%, pvalue < 0.18). Only 2 patients in the non-diabetic group were on dialysis treatment within 45 days.

Table 1: Demographic and clinical parameters of the study population.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non Diabetic</th>
<th>Diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.0 ± 16.1</td>
<td>68.5 ± 14.2</td>
</tr>
<tr>
<td>Male (%)</td>
<td>53.6</td>
<td>64.6</td>
</tr>
<tr>
<td>Melanodermic (%)</td>
<td>16.5</td>
<td>12.4</td>
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<tr>
<td>Hypertension (%)</td>
<td>90.2</td>
<td>96.9</td>
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<td>Obesity (%)</td>
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<td>Peripheral artery disease (%)</td>
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<tr>
<td>Active or past smokers (%)</td>
<td>38.1</td>
<td>35.4</td>
</tr>
<tr>
<td>Pre-dialytic stages (%)</td>
<td>56.2</td>
<td>62.1</td>
</tr>
<tr>
<td>First vascular access (%)</td>
<td>76.8</td>
<td>82.0</td>
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</table>

Table 2: Doppler ultrasound artery characterization.

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<tr>
<th>Parameter</th>
<th>Non-diabetic</th>
<th>Diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left brachial PSV (cm/s)</td>
<td>65.5 ± 18.9</td>
<td>75.6 ± 19.0</td>
</tr>
<tr>
<td>Left brachial diameter (mm)</td>
<td>4.1 ± 0.9</td>
<td>4.1 ± 0.8</td>
</tr>
<tr>
<td>Brachial right PSV (cm/s)</td>
<td>66.0 ± 18.6</td>
<td>75.5 ± 20.6</td>
</tr>
<tr>
<td>Brachial right diameter (mm)</td>
<td>4.1 ± 0.9</td>
<td>4.3 ± 0.8</td>
</tr>
<tr>
<td>Lef radial artery PSV (cm/s)</td>
<td>49.3 ± 15.6</td>
<td>56.2 ± 18.8</td>
</tr>
<tr>
<td>Lef radial artery diameter (mm)</td>
<td>2.1 ± 1.2</td>
<td>2.0 ± 0.5</td>
</tr>
<tr>
<td>Right radial arterial PSV (cm/s)</td>
<td>51.3 ± 17.2</td>
<td>59.5 ± 18.8</td>
</tr>
<tr>
<td>Right artery (mm)</td>
<td>2.1 ± 0.5</td>
<td>2.1 ± 0.5</td>
</tr>
<tr>
<td>Moderate to severe calcification (%)</td>
<td>22.2</td>
<td>44.7</td>
</tr>
</tbody>
</table>
arterial hypertension, showed to be predictive for VA patency, in the univariate and multivariate analysis that included age, sex, diabetes and ethnicity (OR 0.3, p-value <0.09 and OR 0.32, p-value <0.019 respectively).

Conclusion: We found that diabetic patients had significantly more comorbidities (older age, obesity and peripheral artery disease). Regarding the construction of a VA, in diabetic patients there was a lower probability of creating a radiophlebic fistula but a similar possibility of constructing a proximal fistula. Besides that, after VA construction, no differences were found between the two groups in terms of vascular patency. Although diabetic status reduced the probability for radiophlebic fistulas, once VA construction was successful no differences in VA survival at 45 days was verified.

#5737
THE ASSOCIATION OF SERUM IRISIN WITH EARLY PATENCY LOSS OF ARTERIOVENOUS FISTULA
Xiejia Li, Hong Wu, Zheng Li, Lingzi Yang and Hong Liu
The 2nd Xiangya Hospital of Central South University, Department of Nephrology, Changsha, P.R. China

Background and Aims: In patients receiving hemodialysis (HD), arteriovenous fistula (AVF) is the preferred form of vascular access owing to its long-term patency and low risk of infection. Early patency loss of AVF (<1 year) is associated with higher risk of mortality and morbidity. Irisin is thought to play a protective role in the regulation of endothelial function and vascular calcification. However, the relationship between serum irisin level and early patency loss of AVF is unclear.

Method: In 73 end-stage kidney disease (ESKD) patients, including pre-dialysis patients who receive AVF placement for the first time (n = 10), HD patients with early patency loss of AVF (n = 24), HD patients that lose AVF function more than 1 year (n = 39), fasting (>8 hours) serum irisin levels and other biochemical parameters (hemoglobin, serum albumin, calcium, phosphate, intact parathyroid hormone, triglyceride, total cholesterol, D-dimer, fibrinogen, FGF23, C-reactive protein) were measured before receiving placement or after AVF thrombosis. All patients had radial-cephalic fistula.

Results: Among 73 patients (median age 58 years, 60.3% male, 31.5% diabetes mellitus (DM)), patients with early patency loss of AVF had significantly higher serum irisin levels compared with pre-dialysis patients and HD patients whose AVF patency maintained more than 1 year. The increase of irisin may be related to its putative role in compensatory mechanisms against vascular injury, which is then lost with longer dialysis duration and aggravated vascular damage.

Table 1: Comparison of clinical and biochemical characteristics for the 73 ESKD patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All (N = 73)</th>
<th>Pre-dialysis (N = 10)</th>
<th>AVF patency ≤ 1 year (N = 24)</th>
<th>AVF patency &gt; 1 year (N = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.0 (51.0-68.0)</td>
<td>56.5 (35.0-60.0)</td>
<td>59.5 (51.5-69.5)</td>
<td>58.0 (50.0-69.0)</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>44 (60.3%)</td>
<td>8 (80.0%)</td>
<td>12 (50.0%)</td>
<td>24 (61.5%)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>23 (31.5%)</td>
<td>3 (30.0%)</td>
<td>7 (29.2%)</td>
<td>13 (33.3%)</td>
</tr>
<tr>
<td>Systolic blood pressure, (mmHg)</td>
<td>140 (124-155)</td>
<td>156 (128-163)</td>
<td>140 (132-154)</td>
<td>136 (120-148)</td>
</tr>
<tr>
<td>Diastolic blood pressure, (mmHg)</td>
<td>87 (72-94)</td>
<td>89 (82-99)</td>
<td>90 (80-97)</td>
<td>82 (70-90)</td>
</tr>
<tr>
<td>Hemoglobin, (g/L)</td>
<td>111 (95-123)</td>
<td>85 (77-100)</td>
<td>112 (94-124)</td>
<td>111 (99-122)</td>
</tr>
<tr>
<td>Albumin, (g/L)</td>
<td>40.2 (37.4-44.0)</td>
<td>39.0 (30.6-45.6)</td>
<td>39.6 (36.5-45.7)</td>
<td>40.5 (38.8-43.9)</td>
</tr>
<tr>
<td>Triglyceride, (mmol/L)</td>
<td>1.68 (1.24-2.27)</td>
<td>1.41 (0.98-1.82)</td>
<td>1.76 (1.31-2.30)</td>
<td>1.67 (1.23-2.24)</td>
</tr>
<tr>
<td>Total cholesterol, (mmol/L)</td>
<td>3.65 (3.13-4.28)</td>
<td>4.07 (3.24-4.57)</td>
<td>3.92 (3.32-4.64)</td>
<td>3.49 (2.99-3.81)</td>
</tr>
<tr>
<td>Calcium, (mmol/L)</td>
<td>2.01 (1.84-2.18)</td>
<td>2.05 (1.80-2.19)</td>
<td>1.96 (1.83-2.14)</td>
<td>2.01 (1.85-2.20)</td>
</tr>
<tr>
<td>Phosphorus, (mg/L)</td>
<td>1.92 (1.55-2.35)</td>
<td>1.80 (1.47-1.99)</td>
<td>1.73 (1.44-2.44)</td>
<td>2.07 (1.74-2.47)</td>
</tr>
<tr>
<td>iPTH, (pg/mL)</td>
<td>293.5 (183.8-537.5)</td>
<td>326.5 (161.0-503.4)</td>
<td>228.1 (180.2-433.9)</td>
<td>344.8 (188.2-579.6)</td>
</tr>
<tr>
<td>CRP, (mg/L)</td>
<td>7.71 (2.95-13.10)</td>
<td>4.88 (2.62-8.93)</td>
<td>8.49 (3.01-12.70)</td>
<td>9.43 (2.95-25.30)</td>
</tr>
<tr>
<td>D-Dimer, (ug/L)</td>
<td>0.50 (0.32-1.12)</td>
<td>0.84 (0.44-2.31)</td>
<td>0.52 (0.36-1.53)</td>
<td>0.44 (0.24-0.99)</td>
</tr>
<tr>
<td>Fibrinogen, (g/L)</td>
<td>3.85 (3.31-4.55)</td>
<td>4.61 (3.85-6.39)</td>
<td>3.52 (3.08-4.18)</td>
<td>3.95 (3.31-4.55)</td>
</tr>
<tr>
<td>FGF23, (pg/mL)</td>
<td>5.59 (3.33-12.44)</td>
<td>6.39 (3.59-18.30)</td>
<td>4.41 (3.61-6.43)</td>
<td>7.06 (2.69-16.39)</td>
</tr>
<tr>
<td>Irisin, (ng/mL)</td>
<td>519.4 (226.7-1578.0)</td>
<td>409.0 (207.8-663.5)</td>
<td>1350.6 (393.1-2699.1)</td>
<td>397.0 (156.2-848.0)</td>
</tr>
</tbody>
</table>
Table 1: Characteristics of the study population with comparison between the CRBI and non-CRBI groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>CRBI (n = 27)</th>
<th>Non-CRBI (n = 67)</th>
<th>Total (n = 94)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>Ultrasound guided</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (25.9)</td>
<td>18 (26.9)</td>
<td>25 (26.6)</td>
<td>0.926</td>
</tr>
<tr>
<td>No</td>
<td>20 (74.1)</td>
<td>49 (73.1)</td>
<td>69 (73.4)</td>
<td></td>
</tr>
<tr>
<td>Insertion site</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right jugular vein</td>
<td>20 (74.1)</td>
<td>48 (71.6)</td>
<td>69 (72.3)</td>
<td>0.185</td>
</tr>
<tr>
<td>Left jugular vein</td>
<td>2 (7.4)</td>
<td>11 (16.4)</td>
<td>13 (13.8)</td>
<td></td>
</tr>
<tr>
<td>Right subclavian vein</td>
<td>4 (14.8)</td>
<td>2 (3.0)</td>
<td>6 (6.4)</td>
<td></td>
</tr>
<tr>
<td>Left subclavian vein</td>
<td>1 (3.7)</td>
<td>5 (7.5)</td>
<td>6 (6.4)</td>
<td></td>
</tr>
<tr>
<td>Right femoral vein</td>
<td>0</td>
<td>1 (1.5)</td>
<td>1 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Left femoral vein</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Catheter duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 30 days</td>
<td>3 (11.1)</td>
<td>35 (52.2)</td>
<td>38 (40.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td>24 (88.9)</td>
<td>32 (47.8)</td>
<td>56 (59.6)</td>
<td>0.189</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20 (74.1)</td>
<td>40 (59.7)</td>
<td>60 (63.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7 (25.9)</td>
<td>27 (40.3)</td>
<td>34 (36.2)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Organism causing CRBI.

<table>
<thead>
<tr>
<th>Organism</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram negative organism</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>5</td>
<td>18.51</td>
</tr>
<tr>
<td><em>Pseudomonas</em></td>
<td>4</td>
<td>14.81</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>2</td>
<td>7.40</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>1</td>
<td>3.70</td>
</tr>
<tr>
<td><em>Cronobacter sakazakii</em></td>
<td>1</td>
<td>3.70</td>
</tr>
<tr>
<td><strong>Gram positive organism</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative <em>Staphylococcus</em></td>
<td>9</td>
<td>33.32</td>
</tr>
<tr>
<td>Methicillin-sensitive <em>Staphylococcus aureus</em></td>
<td>3</td>
<td>11.11</td>
</tr>
<tr>
<td>Methicillin-resistant <em>Staphylococcus aureus</em></td>
<td>2</td>
<td>7.40</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>27</td>
<td>99.95</td>
</tr>
</tbody>
</table>

**D3 - EPIDEMIOLOGY & OUTCOME**

#2559
**THE EFFECT OF INTRADIALYTIC EXERCISE ON CARDIAC OUTCOMES IN HEMODIALYSIS PATIENTS**

Mei Huang1, Aiili LV2, Honghong LV3, Feng Yang3, Yan Li1, Yan Hua1 and Chunping Ni1

1Air Force Medical University, School of Nursing, P.R. China, 2Xi’an Jiaotong University, Health Science Center, P.R. China and 3Second Affiliated Hospital of Air Force Medical University, P.R. China

**Background and Aims:** Cardiovascular disease is the main cause of death of hemodialysis patients, accounting for 42% of all deaths. Because exercise can reduce many risk factors of cardiovascular disease in these patients, we observed the effect of intradialytic exercise on left ventricular structure and function.

**Method:** A randomized controlled trial was used. Participants were randomly divided into control group and exercise group. Among them, the exercise group carried out intradialytic aerobic and resistance exercise for 3 months, 5-6 times every two weeks, according to their dialysis frequency. The left ventricular end-diastolic volume, mass and ejection fraction were measured by echocardiography before and 12 weeks after the intervention. (ClinicalTrial registration number: NCT05718765).

**Results:** At first, 60 people were recruited and completed the baseline assessment (30 people in each group). The average age of patients in the intervention group was 47.81-11.76 years old, and the average hemodialysis vintage was 17.23-3.09 months. There were 18 men in total. The average age of patients in the control group was 48.56-16.83 years old, and the average hemodialysis period was 17.67-2.83 months. There were 25 men in total. Before the intervention, the two groups of patient indicators were balanced, and the difference was not statistically significant (P>0.05). Finally, 53 patients completed the trial protocol (27 control group and 26 exercise group). After 3 months of intervention, there were significant differences in left ventricular mass, left ventricular end diastolic volume and left ventricular ejection fraction between the two groups (P<0.05). Moreover, the cardiac outcomes of the intervention group were lower than those of the control group, as shown in Table 1.

**Conclusion:** The exercise for 3 months can effectively reduce the left ventricular mass and significantly improve the left ventricular function and structure of hemodialysis patients. This will help to improve the research and development of exercise on cardiac in hemodialysis patients.

#2606
**SARS-COV-2 ANTIBODIES IN PATIENTS ON HEMODIALYSIS AFTER THE MRNA VACCINATION**

Takayasu Taira

Yokohama Daiichi Hospital, Nephrology, Yokohama, Japan

**Background and Aims:** Strategies to minimize the transmission risk of the coronavirus disease 2019 (COVID-19) in patients on hemodialysis (HD) have been implemented worldwide. We investigated the levels of SARS-CoV-2 neutralizing antibodies in Japanese patients.

**Method:** Study (1) We measured the SARS-CoV-2 nucleocapsid antibodies in the serum samples of 55 patients who had undergone HD between August 1 and December 14, 2020. We included 42 patients who had two doses of SARS-CoV-2 nucleocapsid antibodies in Japanesepatients. Neutralizing antibodies in Japanese patients.

**Results:**
- **SARS-CoV-2 Antibodies:** We measured the SARS-CoV-2 nucleocapsid antibodies in the serum samples of 55 patients who had undergone HD between August 1 and December 14, 2020. We included 42 patients who had two doses of...
the mRNA vaccine BNT162b2 between August 1 and November 30, 2021. We measured the levels of SARS-CoV-2 spike antibodies in their plasma and the SARS-CoV-2 nucleocapsid antibodies. We included 33 patients who had three doses of the mRNA vaccine, BNT162b2, between April 1st and July 30th, 2022. We measured the levels of SARS-CoV-2 spike antibodies in their plasma and the SARS-CoV-2 nucleocapsid antibodies. Study (2) We tested the serum samples of 8,982 Japanese adults with normal renal function for SARS-CoV-2 nucleocapsid antibodies between July 1 and November 18, 2020 as the control group. We tested 10 adults who had two doses of the mRNA vaccine BNT162b2, for SARS-CoV-2 spike antibodies at 4, 8, 12, 16, and 20 weeks after vaccination between May 1 and November 30, 2021.

**Results:** Two of 35 patients on HD were positive for SARS-CoV-2 nucleocapsid antibodies, while 54 were asymptomatic. One had SARS-CoV-2 nucleocapsid antibodies. The seropositivity of SARS-CoV-2 nucleocapsid antibodies was negative in 42 patients after the second dose of the BNT162b2 mRNA vaccine. No patients were infected with COVID-19. Of the 42 patients, 41 tested positive for SARS-CoV-2 spike antibodies after the second dose. The median titer of SARS-CoV-2 spike antibodies after vaccination was 253.5 (0.4-5,116) U/mL. All 33 HD patients tested positive for SARS-CoV-2 spike antibodies after the third dose. The mean titer of SARS-CoV-2 spike antibodies after the third vaccination was significantly higher than after the second BNT162b2 vaccination (N = 33: 9,745 U/mL vs. 221 U/mL, respectively; p<0.0001). The mean SARS-CoV-2 spike antibodies titer of patients aged 56–92 years (266.7 U/mL) was lower than of patients aged 28–53 years (1,320.4 U/mL). The seropositivity of SARS-CoV-2 nucleocapsid antibodies was negative after the BNT162b2 mRNA vaccine. No patients were infected with COVID-19. Study 2 Serological testing showed that 47 of the 8,982 Japanese adults with normal renal function tested positive for SARS-CoV-2 nucleocapsid antibodies. The prevalence was significantly higher in the Japanese HD population than in adults with normal renal function (p<0.01). The mean SARS-CoV-2 spike antibodies in the older group (55-73 years) were 1006, 643, 520, 464, and 390 U/mL at 4, 8, 12, 16, and 20 weeks post-vaccination. Contrasting, the mean SARS-CoV-2 spike antibodies the younger group (26–45 years) were 2685, 2032, 1731, 1609, and 1527 U/mL at 4, 8, 12, 16, and 20 weeks post-vaccination.

**Conclusion:** Japanese HD patients had SARS-CoV-2 neutralizing capacities after the BNT162b2 vaccination. Most developed spike antibodies after the three doses. The mean titer of spike antibodies after the third vaccination was significantly higher than after the second vaccination (p<0.0001).

#5510

**CKD-ASSOCIATED PRURITUS SEVERITY AND ITS ASSOCIATION WITH BODY DISTRIBUTION AND EQ-5D HEALTH-RELATED QUALITY OF LIFE IN HAEMODIALYSIS PATIENTS**

Pann Ei Hynnn S1, Monica Hernandez2, Alessandro Sasso2, Matthew Gittus1, Richard Powell1, Louise Dunn1 and James Fotheringham1,2

1Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom, 2School of Health and Related Research, United Kingdom and 3Royal Devon and Exeter Hospital, United Kingdom

**Background and Aims:** Chronic Kidney Disease associated pruritus (CKD-aP) is common affecting 40% of people with kidney disease receiving dialysis. It is associated with decreased health-related quality of life (HRQoL) as assessed using disease-specific instruments. A better understanding of how the severity of CKD-aP is related to the distribution of affected body parts and generic of HRQoL assessed using the EQ-5D instrument could improve the identification, assessment, and treatment of CKD-aP including advocating for access to new therapies.

**Method:** Prevalent in-centre haemodialysis patients from five centres prospectively completed the EQ-5D-5L HRQol questionnaires, the severity-based worst itch numeric rating scale (WI-NRS) and multi-dimensional 5-D itch pruritus disease specific quality of life instruments. Latent class mixture models were used to identify clusters of patients with similarly affected body parts as assessed through the 5-D itch and map the pruritus measures to the EQ-5D utility value (1 being perfect health and 0 being dead, heavily skewed). Patient demographics, comorbidities, dialysis prescription and anti-pruritus medications were collected.

**Results:** Pruritus data on 485 respondents were obtained. No pruritus was reported in 164 (33.8%), with 117 (24.1%) reporting mild, 123 (25.4%) reporting moderate and 81 (16.7%) reporting severe pruritus. Commonly affected body parts included groin (22%), upper arms (21%), forearms (11%), and back (10%). Anti-pruritus medication use across CKD-aP severity (none to severe) was 40.6%, 38.3%, 36.6% and 55.6%, and varied by body part with 38.8%, 21.0% and 14.5% use in those affected in the upper limbs, groin and lower legs respectively. Latent class analysis identified three groups of patients who had progressively worsening severity and number of body parts affected, but the distribution of affected body parts was relatively constant (left-hand figure) and reduction in EQ-5D by affected body part was similar. Although the WI-NRS and 5-D itch instruments correlated with each other, only the 5-D itch had a strong relationship with EQ-5D-3L. Controlling for age, sex, diabetes, and years receiving dialysis, predicted EQ-5D-3L utility dropped linearly from 0.69 to 0.41 (right-hand figure).

**Conclusion:** Contemporary UK data shows CKD-aP remains highly prevalent amongst people with kidney failure on dialysis. Severe CKD-aP was commonly reported despite half of the patients with severe CKD-aP receiving antipruritic medication, illustrating a high unmet need and likely undertreated. Although there were similar reductions in HRQoL, medication use varied by body part and those whose groin is affected may be reporting other body parts to access therapies. High use of CKD-aP medications in none or mild severity may represent more severely affected individuals benefiting from these drugs as the cross-sectional nature of the study means those who reported no pruritus may have had pruritus in the past which resolved in response to the medications prescribed and reported in these analyses. Overall, as it worsens CKD-aP appears to affect a similar distribution of body parts. Pruritus instruments that include domains that are broader than just pruritus severity more closely approximate the EQ-5D generic HRQoL measure and therefore more strongly advocate for the value of treating this unpleasant condition. Funded by CSL Vifor.

*Figure 1: Response of patients with a CVC for haemodialysis access when asked if they would consider an AVF.*
QUALITY OF LIFE IN FAMILY CAREGIVERS OF END STAGE KIDNEY DISEASE PATIENTS: A PROSPECTIVE STUDY

Stavroula Vovlianou1,2, Vasilios Koutlas3, Fani Papoulidou2, George Tsigaras2, Haralampos Milionis4, Petros Skapinakis5 and Evangelia Ntounousi1,3

1Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannina, Greece, Internal Medicine, Greece, 2General Hospital of Kavala, Nephrology, Kavala, Greece, 3University Hospital of Ioannina, Ioannina, Greece, Department of Surgery and Transplant Unit, Ioannina, Greece, 4Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannina, Greece, Nephrology, Greece and 5Faculty of Medicine, School of Health Sciences Ioannina, Greece, Psychiatry, Greece

Background and Aims: Family caregivers of patients with end stage kidney disease (ESKD) face the challenge of demanding patients’ care, in addition to their own daily tasks, which affect their well-being and quality of life (QoL). The aim of this prospective study was to assess and describe the QoL of family caregivers of ESKD patients at the beginning of kidney replacement therapy (KRT) and one year later.

Method: Sixty - two ESKD patients and their caregivers were recruited. Caregivers' QoL was assessed with the Short Form-36 questionnaire and EuroQol-5Dimension-3Level. QoL of caregivers and patients was measured twice, three months after initiation of KTR (T0) (53 patients started hemodialysis and 9 peritoneal dialysis) and after the first 12 months of KTR (T1), in order to investigate the possible changes of QoL during this crucial period.

Results: The mean value (Table 1) of caregivers’ physical component summary (PCS) subscale was found to change significantly during study period (T0: M = 54.21, SD = 8.06 vs T1: M = 51.58, SD = 10.46, t(61) = 2.02, p = .048). Caregivers presented a statistically significant decrease (p <.05) in physical health after one year of KRT. Likewise, the EQ-5D Index and the EQ-5D visual analogue scale (VAS) showed a statistically significant decline (p = .046 and p<.001 respectively). Finally, correlation of means of QoL dimensions between ESKD patients and their caregivers did not yield statistical significance in the particular longitudinal study.

Conclusion: The results provide evidence that the overall caregivers’ QoL scores deteriorated over the one-year period of KTR. Further studies of larger sizes and with a longer duration will probably better define the QoL variations of ESKD patients’ caregivers. Both groups may benefit from an educational program before patients initiate KTR.

ALTERNATIVES TO DAYTIME IN-CENTER HEMODIALYSIS AND EMPLOYMENT AMONG PATIENTS WITH KIDNEY FAILURE

Jose Perez1, Jingbo Niu1, Wolfgang Winkelmayer1, Kerri Cavanaugh2, Monique Pappadis3 and Kevin Erickson1

1Baylor College of Medicine, Houston, United States of America, 2Vanderbilt University School of Medicine, Nephrology, Nashville, United States of America and 3University of Texas Medical Branch, Galveston, United States of America

Background and Aims: Maintaining employment is a priority for many patients with kidney failure. In addition to its economic benefits, employment is associated with physical and psychological wellbeing. Yet, only 30-35% of working aged patients with advanced chronic kidney disease in the United States (US) report employment prior to starting dialysis and many patients stop working at the onset of kidney failure. While access to a dialysis treatment schedule outside of working hours may help patients to remain employed, the effects of alternative dialysis options on employment after starting dialysis are not well understood.

Method: We analyzed data from the US National Dialysis Registry to determine whether access to nearby facilities offering evening dialysis shifts and home dialysis increases the likelihood that patients are able to continue working after they start dialysis. Our cross-sectional analysis included working-aged patients (ages 18-54) receiving dialysis in US facilities in 2016. We combined information reported at the levels of individual patients and dialysis facilities. In a negative binomial regression model, we examined the

Figure 1: Plot of longitudinal PCS, MCS, EQ5D Index, and EQ5D VAS of caregivers.

Table 1: Correlation of SF-12 PCS and SF-12 MCS, EQ-5D Index and EQ-5D VAS in patients’ caregivers at T0 (initiation of treatment) and at T1 (one year later).

<table>
<thead>
<tr>
<th>Caregivers</th>
<th>Patients</th>
<th>Paired Difference (Mean)</th>
<th>Test Statistica</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-12 PCS</td>
<td>T0 (n = 62)</td>
<td>54.21 (±8.06)</td>
<td>51.58 (±10.46)</td>
<td>2.63</td>
<td>2.02</td>
</tr>
<tr>
<td>SF-12 MCS</td>
<td>T0 (n = 62)</td>
<td>38.23 (±13.7)</td>
<td>37.02 (±13.23)</td>
<td>1.21</td>
<td>.634</td>
</tr>
<tr>
<td>EQ-5D Index</td>
<td>T0 (n = 62)</td>
<td>.70 (±.17)</td>
<td>.65 (±.19)</td>
<td>0.047</td>
<td>2.03</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>T0 (n = 62)</td>
<td>80.39 (±14.56)</td>
<td>72.26 (±14.25)</td>
<td>8.129</td>
<td>5.712</td>
</tr>
</tbody>
</table>

(a) Paired samples t-test
associations among exposures of interest (the presence of facilities offering home dialysis and/or evening dialysis shifts in a patient’s locality) and the number of employed working-aged adults at each dialysis facility. The multivariable regression model adjusted for observed patient, dialysis facility, and geographic characteristics, including patient health and demographic characteristics, information about individual patient employment at the onset of dialysis, local unemployment rates, and the number of working-aged patients at a given dialysis facility.

Results: We identified 4,860 US dialysis facilities with information about patient employment in 2016. Median employment among working-aged adults at these facilities was 17.9% (interquartile range 8.8% to 28.6%). In multivariable, fully adjusted, regression models, the presence of at least one facility offering an evening dialysis shift in a county was associated with a 3% increase in the relative rate of maintaining employment among all working-aged patients receiving dialysis in the county (risk ratio (rr) 1.03; 95% Confidence Interval (CI) 1.01 to 1.05; p = 0.02). The presence of at least one facility offering home dialysis in a county was associated with a 26% increase in the relative rate of maintaining employment (RR 1.26; 95% CI 1.18 to 1.34; p < 0.001). The likelihood of employment did not increase with additional facilities in a county offering home dialysis.

Conclusions: Access to dialysis schedules outside of regular working hours – evening dialysis shifts and home dialysis – is associated with increased employment among patients with kidney failure. Efforts to increase access to alternative dialysis treatments could help patients to continue working.

#2600
INCIDENCE RATE, OUTCOMES, AND RISK FACTORS ASSOCIATED WITH COVID-19 INFECTION IN FULLY MRNA-VACCINATED HEMODIALYSIS PATIENTS
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Background and Aims: Despite the high efficacy of vaccines against coronavirus disease (COVID-19), some people continue to become infected with SARS-CoV-2 after vaccination. Older age, immunosuppression, and severe comorbidities are associated with the occurrence of COVID-19 and adverse outcomes in the general population of vaccinated patients. However, because of the above factors, hemodialysis (HD) patients may be at higher risk for postvaccination SARS-CoV-2 infection than the general population, and risk factors associated with COVID-19 in fully vaccinated HD patients have never been studied. The present study aimed to determine the incidence rate, outcomes, and risk factors for SARS-CoV-2 infection in fully vaccinated HD patients.

Method: In this multicenter case-control cohort study, we followed HD patients for 1 year after SARS-CoV-2 vaccination and compared incidence rates and outcomes of COVID-19 with unvaccinated patients selected by propensity score matching based on potentially confounding variables (age, diabetes, and dialysis vintage). Patients who had been fully vaccinated against COVID-19 with either Pfizer-BNT-162b2 or Moderna-mRNA-1273 vaccine and had at least one positive SARS-CoV-2 PCR test >14 days after the second dose were defined as cases. Unvaccinated HD patients who had not been infected with COVID-19 before study enrollment and had at least one positive test thereafter were defined as controls. The outcomes studied were COVID-19-related hospitalizations, oxygen maintenance, and death. Demographic data and routine blood tests (the last measurements before COVID-19) were analyzed as possible risk factors for COVID-19 infection in vaccinated HD patients. Data were presented as incidence rate or proportion and compared with the chi-square (χ2) test. Univariate logistic regression analysis was used to determine risk factors for SARS-CoV-2 infection after vaccination and presented as odds ratio (OR) and 95% confidence interval (CI).

Results: Among a total cohort of HD patients (n = 327) aged 52 ± 9.4 years with a dialysis vintage of 44 (21-76.6) months, 133 (40.7%) HD patients were fully vaccinated. During the 12-month follow-up period, the incidence rate of SARS-CoV-2 infection was significantly lower in the vaccinated group compared with the matched unvaccinated group: 0.29 (95% CI: 0.18; 0.42) vs 0.59 (95% CI: 0.46; 0.74) per patient-year (p < 0.0001). Proportions of COVID-19-associated hospitalization (χ2 = 20.1, p < 0.0001), oxygen demand (χ2 = 27.8, p < 0.0001), and death (χ2 = 7.6, p = 0.004) were also significantly lower in the case group compared to unvaccinated matched controls. In risk factor analysis, older age, obesity, dialysis duration of more than 5 years, arterial hypertension, elevated C-reactive protein, anemia, and low levels of parathyroid hormone and high-density lipoprotein cholesterol were associated with postvaccination SARS-CoV-2 infection (Fig. 1).

Conclusion: Vaccinated HD patients had a significantly lower incidence of SARS-CoV-2 infection and associated adverse outcomes compared to the unvaccinated group. HD patients aged ≥65 years with Kt/V <1.2, obesity, dialysis duration of more than five years, arterial hypertension, elevated C-reactive protein, and low levels of hemoglobin, parathyroid hormone, and high-density lipoprotein cholesterol had a higher risk of infection following vaccination.

#3463
MULTINATIONAL COMPARATIVE EFFICACY OF 6 DIFFERENT COVID-19 VACCINES FOR THE PREVENTION OF BREAKTHROUGH INFECTION AND MORTALITY IN HD PATIENTS
Mathias Haahrhaus1,2, Rainer Peter Woitas3, Pedro Mota Veiga4, Carla Santos5, Mohammed Alhomrani5, Eliana Silva5, Carlos Lucas3 and Fernando Macário5
1Karolinska Institutet, Dept of Renal Medicine, Stockholm, Sweden, 2Diaverum Sweden, Malmö, Sweden, 3Diaverum Deutschland GmbH, München, Germany, 4Polytechnic Institute of Viseu, School of Education, Viseu, Portugal, Viseu, Portugal and 5Diaverum Saudi Arabia, Riyadh Front - Building N8, Riyadh, Saudi Arabia

Background and Aims: COVID-19 vaccines induce specific immune responses to reduce COVID-19 infections and severe complications. Dialysis patients exhibit increased COVID-19-related incidence rates and mortality due to poor immune responses. We studied retrospectively the efficacy of 6 different COVID-19 vaccines as well as the combination of vaccines for the prevention of new COVID-19 infections and related mortality in a large multi-national hemodialysis cohort.

Method: All patients from 22 countries in Europe, Asia, Africa, and South America, 18 years or older, registered within in the network of a multi-national dialysis provider on January 31th, 2021, were included into the study. We analyzed the incidence of symptomatic COVID-19 in HD patients with vaccination status after 2 doses of 6 different SARS-CoV-2 vaccines in comparison to HD patients who did not receive any vaccine. Patients were screened for COVID-19 symptoms at each dialysis visit and SARS-CoV-2 PCR tests were performed in all symptomatic patients. All PCR-confirmed COVID-19 infections, and deaths occurring between January 31th, and July 15th, 2021 were analyzed. Results were stratified by vaccine type and compared to unvaccinated patients. Data are presented as incidence rate ratios per 1000 patient days and odds ratios vs. no vaccine (95% CI).

Results: Of 38342 eligible patients registered on the index date, 2413 were excluded due to a positive SARS-CoV-2 PCR within 3 months before baseline and 26 were excluded due to unclear vaccination data. The remaining 35903 patients were analyzed. 7816 patients (21.7%) had received a single vaccine dose and 18853 patients (52.5%) had received two doses of any COVID-19 vaccine (Vaxzevria 3180 and 1321, Comirnaty 2823 and 13116, Spikevax 185 and 1521, Sputnik V 1194 and 432, Sinovac 266 and 1722, Sinopharm 168 and 416, or any combination of two different vaccines 325). The 9119 patients (25.4%) who remained unvaccinated during the observational period showed
Figure 1: Flowchart of the study.

### Table 1: Incidence rates after 2 doses of vaccine.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>All patients (N = 27,972)</th>
<th>COVID-19 during follow-up</th>
<th>Total follow-up (person days)</th>
<th>Incidence rate / 1000 person days</th>
<th>Incidence rate ratio vs. no vaccine (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No vaccine</td>
<td>9,119</td>
<td>954</td>
<td>1,298,162</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>Vaxzevria</td>
<td>1,321</td>
<td>13</td>
<td>76,527</td>
<td>0.17</td>
<td>0.23 (0.12-0.4)</td>
</tr>
<tr>
<td>Comirnaty</td>
<td>13,116</td>
<td>141</td>
<td>1,324,644</td>
<td>0.11</td>
<td>0.15 (0.12-0.17)</td>
</tr>
<tr>
<td>Spikevax</td>
<td>1,521</td>
<td>5</td>
<td>110,740</td>
<td>0.05</td>
<td>0.06 (0.02-0.14)</td>
</tr>
<tr>
<td>Sputnik V</td>
<td>432</td>
<td>11</td>
<td>21,871</td>
<td>0.5</td>
<td>0.68 (0.34-1.23)</td>
</tr>
<tr>
<td>Sinopharm</td>
<td>416</td>
<td>7</td>
<td>18,126</td>
<td>0.39</td>
<td>0.53 (0.21-1.09)</td>
</tr>
<tr>
<td>Sinovac</td>
<td>1,722</td>
<td>50</td>
<td>149,140</td>
<td>0.34</td>
<td>0.46 (0.34-0.61)</td>
</tr>
<tr>
<td>Different vaccines</td>
<td>325</td>
<td>5</td>
<td>19,402</td>
<td>0.26</td>
<td>0.35 (0.11-0.82)</td>
</tr>
</tbody>
</table>

Table 2: Effect of 2 doses of vaccine on all-cause mortality vs. no vaccine.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Odds ratio (95% confidence interval)</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaxzevria</td>
<td>0.034 (0.017-0.067)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Comirnaty</td>
<td>0.079 (0.067-0.093)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spikevax</td>
<td>0.091 (0.062-0.133)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sputnik V</td>
<td>0.188 (0.095-0.372)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sinopharm</td>
<td>0.037 (0.015-0.091)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sinovac</td>
<td>0.043 (0.030-0.061)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Different vaccines</td>
<td>0.046 (0.017-0.125)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Logistic regression with no vaccine as reference, adjusted for country, age, gender, diabetes mellitus, Charlson comorbid. index, and dialysis vintage.

an incidence rate of 0.74/1000 patient days. In the cohort of patients vaccinated two times, 232 developed Covid-19. The lowest incidence rate ratio was observed in patients that had received Spikevax 0.06 (0.02-0.14). By contrast, patients after Sinopharm, Sinovac, and Sputnik V exhibited highest incidence rate ratios 0.53 (0.21-1.09), 0.46 (0.34-0.61), 0.68 (0.34-1.23), respectively. The largest sub-cohort of 13116 patients, who had received Comirnaty, however, had an incidence rate ratio of 0.15 (0.12-0.17). Albeit incidence rates and ratios were heterogeneous, all vaccines including Sputnik V showed a significant efficacy to reduce mortality compared to no vaccine. Conclusion: Combinations of different vaccines and two doses of mRNA-based vaccines very effectively prevented breakthrough infections. Despite considerable differences in preventing COVID-19 infections, all vaccines effectively reduced mortality, compared to no vaccines, in this high-risk dialysis patient cohort.

Conclusion: Physical activity is associated the lower risk of developing dementia in ESRD patients with hemodialysis.

### Table 2: Effect of 2 doses of vaccine on all-cause mortality vs. no vaccine.

**Method:** A total 19,877 hemodialysis patients aged ≥ 40 years who underwent health check-ups were identified from the Korean National Health Insurance Service database and were analysed in this study. Individuals with physical activities were defined as meeting following criteria: (i) three or more days/week of vigorous activity of at least 20 min per day or (ii) five or more days/week of moderate-intensity activity of at least 30 min per day. The occurrence of dementia was monitored through the end of 2018 by the ICD-10 codes.

**Results:** During the 4.6-year follow-up, 1,755 patients with hemodialysis developed dementia. Physical activity was associated with the lower risk of any dementia (hazard ratio [HR], 0.779, 95% confidence interval (CI), 0.7-0.867) even after adjusting for several confounding factors. Risk of developing dementia was still lower in hemodialysis patients with physical activity when we analyse the risk of Alzheimer’s dementia and vascular dementia separately (HR 0.817 and 0.685, respectively). In subgroup analyses, the risk of dementia tended to lower in hemodialysis patients with physical activity than without physical activity in all subgroups.

**Conclusion:** Physical activity is associated the lower risk of developing dementia in ESRD patients with hemodialysis.

#5394

**PHYSICAL ACTIVITY AND THE RISK OF DEMENTIA IN END-STAGE RENAL DISEASE PATIENTS WITH HEMODIALYSIS: A NATIONWIDE POPULATION-BASED STUDY**

Hong Sang Choi, Minah Kim, Tae Ryon Oh, Sang Heon Suh, Chang Seong Kim, Eun Hui Bae, Seong Kwon MA and Soo Wan Kim

Chonnam National University Medical School, Department of Internal Medicine, Rep. of South Korea

**Background and Aims:** Several studies have reported that dementia has a high prevalence in patients with end-stage renal disease (ESRD) patients. However, the relationship between physical activity and the risk of developing dementia has not been elucidated in ESRD patients with hemodialysis.
Background and Aims: Since the beginning of the industrial era, human activities have led to a significant increase in the concentration of greenhouse gases (GHGs) in the atmosphere and are the cause of climate change, the negative effects of which on human health are already visible (1). Paradoxically, the health sector also exerts a major pressure on the environment through carbon-based care activities that emit GHGs (2). In this context, a few studies have highlighted the significant carbon footprint associated with hemodialysis (3). However, to date, no similar study has been conducted in France.

Method: The objective of this work was to evaluate the carbon footprint of a hemodialysis unit in France using the Bilan Carbone ® approach developed by The French Agency for Ecological Transition and the Bilan Carbone Association. Activity data associated with hemodialysis provision at the Charles De Gaulle facility in 2021 was collected and converted to a common measurement unit of tonnes of CO2 equivalents (tCO2-eq) via established emissions factors. This facility, that belongs to the ARTIC 42 association, is located in the town of Saint-Priest en Jarez and provides hemodialysis through a total of 56 hemodialysis generators.

Results: Over the year 2021, the Charles de Gaulle facility provided a total of 25270 hemodialysis treatments ensuring the care of approximately 162 patients (at a rate of 3 sessions per week). The associated annual carbon footprint for the facility was 1436 t CO2-eq. Annual carbon footprint amounted to 8.9 t CO2-eq/patient/year corresponding to 57 kg CO2-eq /treatment. Emissions were essentially indirect, with more than 90% coming from scope 3. The main sources of emissions were: products and services purchase (30% of total emissions, that is 437 t CO2-eq), patients and staff travels (25% of total emissions, that is 361 t CO2-eq), and fixed assets (21% of total emissions, that is 299 t CO2-eq). Energy consumption (particularly electricity) and waste treatment accounted for a small proportion of GHG emissions (respectively 8% and 6%).

Conclusion: Our results confirm the high carbon footprint associated with in-center hemodialysis, showing that it is mainly attributable to indirect emissions. These empirical data will serve as a basis for reflection in the development of a strategy to reduce GHG emissions associated with hemodialysis. This work will hopefully be paving the way for the necessary ecological transition of medical practices, focused on the patient and the ecosystems on which he/she depends.

REFERENCES

Figure 1: The cumulative probability of any dementia development among the hemodialysis patients with physical activity and without physical activity.

Figure 1: Hemodialysis activity and associated GHG emissions for the Charles de Gaulle facility over the year 2021.
COVID-19 in their original dialysis units and were therefore transferred for further HD treatment to the first hospital in Serbia transferred to exclusively admit COVID-19 patients at the onset of the epidemic. According to the local protocol, all patients were hospitalized while being dialedy. Data were collected from clinical charts and patient histories for the period between March 19, 2020, and March 19, 2022, and analysed with SPSS software, version 22 (IBM Corporation, New York, USA).

Results: A total of 1384 HD treatments were performed in 226 patients (6.1±2.4, range 1 – 34 per patient). Most patients (98.5%) had at least one comorbidity: hypertension (68.1%), diabetes (26.1%), cardiovascular disease (16.4%), cerebrovascular disease (7.5%), malignancy (9.3%), chronic respiratory disease (4.0%) or autoimmune disease (1.8%). The average number of comorbidities was 1.9±1.0 (range 0 – 4). Only 2.2% of all patients were vaccinated. Most patients (78.0%) had bilateral pneumonia upon admission, 15.3% had normal pulmonary X-ray, 5.1% had unilateral pneumonia and 1.7% had ARDS. 34% of the patients required mechanical ventilation. Fifty-seven patients (25.2%) received corticosteroid therapy, 5.3% were treated with chloroquine, 2.7% received antiviral therapy and 1.8% were administered IL6 antagonist. The overall mortality rate was 39.4%. Patients who died were significantly older (67.6±12.4 vs 63.6±12.7, p = 0.012), more often had cardiovascular disease (p = 0.046) and bilateral pneumonia (p≤0.01), had worse CT severity score (13.0±5.1 vs 9.2±5.0; p<0.001) and required invasive mechanical ventilation (p<0.001) and had fewer HD treatments performed during hospitalization (5.1±4.8 vs 6.8±4.2; p = 0.007). They also had significantly higher white blood cells count (8.3±5.3 vs 5.6±2.9; p<0.001), serum urea (24.9±12.0 vs 21.1±8.4 mmol/L; p = 0.01), LDH (111.0±65.9 vs 63.9±72.9 IU/L; p<0.001), CRP (157.2±91.1 vs 61.1±98.4 mg/dL; p = 0.008), IL-6 (14.9±16.3 vs 2.8±7.3 pg/mL; p = 0.004), and Ddimer (372.3±294.1 vs 240.7±101.5 ng/mL; p<0.001). Multiple logistic regression showed a significant association between mortality and older age (OR 1.11, 95% CI 1.04-1.18, p = 0.001), need for mechanical ventilation (OR 43.1, 95% CI 9.5-198.6; p<0.001), higher CT severity score (OR 1.16, 95% CI 1.07 - 1.25; p<0.001), fewer HD procedures performed (OR 0.80, 95% CI 0.69-0.93; p = 0.003) and higher D-dimer levels (OR 1.00, 95% CI 1.00 - 1.01; p = 0.012).

Conclusion: Maintenance HD patients are considered a high-risk population for contracting COVID-19 and developing a severe form of the disease. Older age, higher CT severity score

### #2613

**DIETARY FIBER INTAKE, THEIR SOURCES AND MORTALITY IN ADULTS ON HEMODIALYSIS: THE DIET-HD STUDY**

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**Background and Aims:** Higher fiber intake is associated with lower cardiovascular and all-cause mortality in the general population, but their benefits and which sources of fiber are healthier in patients on hemodialysis are uncertain.

**Method:** Daily fiber intake (DFI) and their sources (vegetable and fruit, staple food and other sources) were ascertained by the Global Allergy and Asthma European Network food frequency questionnaire within the DIET-HD study, a multinational cohort study of adults on hemodialysis. Adjusted Cox regression analyses were conducted to evaluate the association of DFI and fiber sources (vegetable and fruit, staple foods, others) with cardiovascular and all-cause mortality. Estimates were calculated as hazard ratio (HR) with 95% confidence interval (CI).

**Results:** 8,110 patients were followed for median of 3.8 years (26,074 person-years). There were 2,953 deaths, of which 1160 cardiovascular-related. The median (interquartile range) DFI was 12.0 (8.1-17.5) gram per day and vegetables and fruits (49%) were the major sources. Each unit increase in total DFI was not associated with either all-cause (hazard ratio [HR], 0.99; 95%CI 0.99-1.00, p = 0.379) or cardiovascular mortality (HR, 0.99; 95%CI 0.99-1.00, p = 0.98). Compared with the lowest DFI tertile (<9.5mg/day), the adjusted HRs for cardiovascular mortality among those in the middle (9.5-15.3 g/day) and highest tertiles (≥15.3 g/day) were respectively 0.97 [95% CI, 0.84-1.13] and 0.79 [95% CI, 0.65-0.96] (P for trend = 0.02). Each unit increase in fraction of DFI from vegetable and fruit was associated with lower all-cause (HR, 0.70;95%CI: 0.57-0.86, p = 0.001) but not with cardiovascular mortality
(HR 0.75-95%CI 0.54-1.04, p = 0.08). Each unit increase in the fraction of DFI from other sources (including dressing sauce etc.) was associated with higher all-cause mortality (HR 1.66; 95%CI 1.22-2.27, p = 0.001) but not with cardiovascular mortality (HR, 1.63; 95%CI, 0.83-2.24, p = 0.23). No association were observed between fiber from staple food and all-cause or cardiovascular mortality.

Conclusion: Fiber intake in the hemodialysis population is low. A higher fiber intake from vegetable and fruit, and a lower fiber intake from other sources (including dressing sauce etc.) is associated with lower all-cause death.

### #3595

**DIALYSIS MODALITY AFFECTS SENESCENCE-RELATED PHENOTYPE OF T AND B LYMPHOCYTES**

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1Aristotle University of Thessaloniki, Hippokration Hospital, Department of Nephrology, Thessaloniki, Greece and 2Hippokration Hospital, Department of Immunology, National Peripheral Histocompatibility Center, Thessaloniki, Greece

**Background and Aims:** Hemodialysis (HDF) is characterized by enhanced clearance of middle molecular weight toxins and therefore, it is considered superior to hemodialysis (HD), especially in higher hemofiltration volumes. Although proinflammatory cytokines are lower in HDF, its impact on immune phenotype has not been studied, so far. In this study we compared the lymphocytes’ senescent phenotype between HD and HDF patients.

**Method:** Senescent and exhausted related lymphocyte markers, including CD45RA, CCR7, CD28 and CD57 on T cells and CD27 and IgD on B cells, were assessed by flow cytometry in 35 ESRD patients on HD and 25 ESRD patients on HDF, respectively, p = 0.006. CD28-CD57 T cells were also lower in HDF patients, without reaching statistical significance [17.4 (8.5-41) vs 34 (12.7-52.9) % for HDF and HD respectively, p = 0.06]. Hemofiltration volume was negatively correlated to effector memory CD8+ T cells re-expressing CD45RA count (CD8+ EMRA), (r = -0.46, p = 0.027) and positively correlated to total B cells count (r = 0.46, p = 0.025). However, not all B cell subtypes were equally affected, with only naïve IgD+CD27- B cells and switched memory IgD-CD27+ B cells count showing positive correlation with hemofiltration volume (r = 0.53, p = 0.008 and r = 0.5, p = 0.015, respectively).

**Conclusion:** Hemodialfiltration and high filtration volumes may have beneficial effects on adaptive immunity, predisposing to less senescent and exhausted T and B cell phenotypes.

### #5439

**HOME DIALYSIS DOES NOT HAVE THE MONOPOLY ON LOW COST**

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1AUB Santé, Rennes, France, 2AUB Santé, Saint Malo, France, 3Agence de la biomédecine, REIN registry, Saint Denis La Plaine, France and 4EHESP, MÉTI, Rennes, France

**Background and Aims:** End-stage kidney disease (ESKD) is a major challenge for health-care systems around the world because of its ever-rising rates and the ensuing rise in health-care costs. The objective of this study was to compare the cost of four dialysis modalities that enable patients to play a substantial role in their own care and have social and professional lives.

**Method:** We identified all patients in the national French ESKD REIN registry aged 18–65 years who received any dialysis treatment in 2015–2019, used stepwise indirect linkage with the national health database to analyse exhaustive hospital stays and outpatient health-care utilisation. Four treatment groups were defined: non-assisted haemodialysis in self-care units (scHD), non-assisted automated peritoneal dialysis (naAPD), daily home HD (dhHD), and non-hospital-based nocturnal extended hours HD (neHD). Total costs by categories and subcategories were aggregated monthly and by patient. Costs are expressed as their medians and interquartile ranges (Q1-Q3).

**Results:** Our study included 1932 patients with 39 966 patient treatment-months. The median monthly cost for one patient was €6154 (IQR €5088–€7566) and varied from €5700 for naAPD to €7903 for dhHD. Analysis by cost subcategories showed that the main cost came from dialysis fee payments —60% of the monthly cost. Hospitalization costs came next (11%). The costs of the different subcategories varied between dialysis modalities. During the study period, the hospitalization rate was 33 per 100 months at risk: 14 for inpatient admissions and 19 for day hospitalization. Day hospitalization was more frequent for patients with home treatment. Various compensatory allowances were paid to 49% of the patients.

**Conclusion:** Most of the cost difference variability related to payment methods for the different dialysis techniques. Our study shows that different care strategies could be offered to French dialysis patients. Underused techniques such as neHD might usefully be promoted as they do not involve any excess costs, at least compared with dhHD. Real cost analyses are however needed because these reimbursements are not adapted and deserve to be revised upwards.
Table 1: Distribution of the monthly cost by cost subcategories in each subgroup.

<table>
<thead>
<tr>
<th>Monthly cost (€)</th>
<th>Nighttime Extended HD (neHD)</th>
<th>HD in self-care unit (scHD)</th>
<th>Non-assisted APD (naAPD)</th>
<th>Daily home HD (dhHD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>q1</td>
<td>q3</td>
<td>Median</td>
<td>q1</td>
</tr>
<tr>
<td>Total</td>
<td>5801</td>
<td>4859</td>
<td>7193</td>
<td>6020</td>
</tr>
<tr>
<td>Dialysis</td>
<td>3024</td>
<td>2804</td>
<td>3231</td>
<td>2933</td>
</tr>
<tr>
<td>Various compensatory allowance</td>
<td>449.8</td>
<td>114.8</td>
<td>954.3</td>
<td>740</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>352.4</td>
<td>99.7</td>
<td>776.2</td>
<td>299.5</td>
</tr>
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<td>Drugs</td>
<td>218</td>
<td>123.4</td>
<td>367.5</td>
<td>301.3</td>
</tr>
<tr>
<td>Technical medical acts</td>
<td>36.7</td>
<td>15</td>
<td>75</td>
<td>28.4</td>
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<tr>
<td>Transport</td>
<td>810.1</td>
<td>202.8</td>
<td>1449</td>
<td>810</td>
</tr>
<tr>
<td>Laboratory</td>
<td>135.9</td>
<td>107.1</td>
<td>179.6</td>
<td>142.5</td>
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<tr>
<td>Imaging</td>
<td>47</td>
<td>26.1</td>
<td>78.9</td>
<td>45.6</td>
</tr>
<tr>
<td>Equipment</td>
<td>23.7</td>
<td>8.1</td>
<td>77</td>
<td>28.3</td>
</tr>
<tr>
<td>Medical remuneration</td>
<td>51.3</td>
<td>26</td>
<td>157</td>
<td>37.5</td>
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<tr>
<td>Paramedical remuneration</td>
<td>4.6</td>
<td>1.1</td>
<td>18.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Other</td>
<td>392.5</td>
<td>8.7</td>
<td>1401</td>
<td>586.6</td>
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</tbody>
</table>

*Including dialysis fees and third-party allowance

#6576
SERUM INTERLEUKIN-6 LEVELS AS A PREDICTOR OF ALL-CAUSE MORTALITY IN MAINTENANCE HEMODIALYSIS PATIENTS WITH COVID-19-OMICRON INFECTION: AN OBSERVATIONAL STUDY
Qirong Song, Yuxin Luo, Sha Fu, Xiaohong Wang, Ying Tang, Junzhe Chen and Aiqun Liu
The Third Affiliated hospital of Southern Medical University, Department of Nephrology, Guangzhou, P.R. China

Background and Aims: Interleukin-6 (IL-6) is a key mediator of inflammation and has been linked to the severity and mortality of COVID-19-Omicron in the general population. With higher mortality rates observed in maintenance hemodialysis (MHD) patients infected with COVID-19-Omicron, the study aimed to examine the correlation between IL-6 levels and mortality in this patient population and to identify the optimal IL-6 level for predicting the risk of death.

Method: The retrospective observational study was conducted in MHD patients diagnosed with COVID-19-Omicron infection between December 01, 2022 and January 31, 2023 at the Third Affiliated Hospital of Southern Medical University during the first wave of infection in COVID-19-Omicron outbreak in China. Clinical and biochemical data were collected during the infection, IL-6 levels of the patients were measured before consecutive dialysis sessions by a commercial kit. The Cox model was used to investigate the risk factors of mortality, meanwhile, ROC curve to determine the cut off value of IL-6 levels on mortality.

Results: A total of 162 MHD patients infected with COVID-19-Omicron were included in this study. During a median follow-up period of 40 days, 10 (6.2%) deaths occurred due to COVID-19 infection. IL-6 levels were significantly higher in patients who died. Univariate Cox regression analyses showed that the risk factors associated with death included IL-6 levels (HR: 1.009; p < 0.001), C-reactive protein (HR: 1.01; p = 0.016), serum potassium (HR: 2.258; p = 0.015, procalcitonin(PCT) (HR: 1.01; p = 0.048), and the Charlson comorbidity index(CCI)(HR: 1.34; p = 0.002). However, in multivariate analysis, only IL-6 levels was independently associated with all-cause mortality(HR: 1.01; p = 0.001).The ROC curve and Kaplan-Meier survival analysis revealed a significantly worse survival risk among MHD patients with higher serum IL-6 levels (≥104.87 pg/mL) (sensitivity:100%; specificity:78.2%; AUC: 0.92; p = 0.001).

Conclusion: Serum IL-6 levels greater than 104.87 pg/mL were associated with an increased risk of all-cause mortality in MHD patients infected with COVID-19-Omicron. Hemoperfusion or hemofiltration to remove IL-6 may provide appropriate treatment options for hemodialysis patients with COVID-19-Omicron.

Figure 1: Receiver operating characteristic curves of Interleukin-6(IL-6) for MHD with COVID-19-Omicron infection for predicting mortality.
Figure 2: Kaplan-Meier curves showing survival of the primary endpoint for MHD with COVID-19-Omicron infection grouped by the cut-off value of 104.87 pg/mL of blood IL-6 for predicting probability of death.

Table 1: Baseline characteristics of MHD patients with COVID-19-Omicron infection in the overall study.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Survivors n=152</th>
<th>Non-survivors n=10</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61(52–73)</td>
<td>74(56.25–81)</td>
<td>0.124</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>60(39.5)</td>
<td>2(20.0)</td>
<td>0.220</td>
</tr>
<tr>
<td>Follow-up time, days</td>
<td>44.5(40-48)</td>
<td>17.5(9.5-30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis period, months</td>
<td>25(7.25–58.5)</td>
<td>29.5(4-86.25)</td>
<td>0.691</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.13 ± 3.62</td>
<td>21.63 ± 2.05</td>
<td>0.116</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>134(88.2)</td>
<td>8(80.0)</td>
<td>0.447</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>65(42.8)</td>
<td>6(60)</td>
<td>0.220</td>
</tr>
<tr>
<td>Coronary heart disease, n (%)</td>
<td>31(21.4)</td>
<td>3(30)</td>
<td>0.470</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>3(2.5)</td>
<td>4.5(3.75,6.75)</td>
<td>0.020</td>
</tr>
<tr>
<td>Vaccination status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated, n (%)</td>
<td>95(62.5)</td>
<td>7(70.0)</td>
<td>0.634</td>
</tr>
<tr>
<td>First/Second dose, n (%)</td>
<td>33(21.7)</td>
<td>1(10.0)</td>
<td>0.378</td>
</tr>
<tr>
<td>Third dose, n (%)</td>
<td>119(12.5)</td>
<td>1(10.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COVID-19 disease severity</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild,n (%)</td>
<td>40(26.3)</td>
<td>0(0)</td>
<td>-</td>
</tr>
<tr>
<td>Moderate,n (%)</td>
<td>75(49.3)</td>
<td>0(0)</td>
<td>-</td>
</tr>
<tr>
<td>Severe,n (%)</td>
<td>33(21.7)</td>
<td>1(10.0)</td>
<td>-</td>
</tr>
<tr>
<td>Critical,n (%)</td>
<td>4(2.6)</td>
<td>9(90.0)</td>
<td>-</td>
</tr>
<tr>
<td>Neutrophils, 10^3/L</td>
<td>4.48(3.19–6.73)</td>
<td>7.05(4.02–9.01)</td>
<td>0.117</td>
</tr>
<tr>
<td>Lymphocytes, 10^3/L</td>
<td>0.82(0.62–1.13)</td>
<td>0.78(0.51–1.00)</td>
<td>0.493</td>
</tr>
<tr>
<td>NLR</td>
<td>5.58(3.73–9.76)</td>
<td>8.35(3.9519.38)</td>
<td>0.218</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>102.5 ± 22.54</td>
<td>106.7 ± 20.6</td>
<td>0.770</td>
</tr>
<tr>
<td>IL-6, mg/dL</td>
<td>32.68(10.33–89.25)</td>
<td>228.85(128.3–162.48)</td>
<td>0.001</td>
</tr>
<tr>
<td>PCT, μg/dL</td>
<td>1.20(0.48–2.27)</td>
<td>9.84(1.16–19.35)</td>
<td>0.011</td>
</tr>
<tr>
<td>CRP, mg/dL</td>
<td>11.48(3.22–26.55)</td>
<td>83.99(23.53–131.8)</td>
<td>0.010</td>
</tr>
<tr>
<td>Iron protein, ng/mL</td>
<td>385.23(181.9–717.53)</td>
<td>363.99(172–2728)</td>
<td>0.776</td>
</tr>
<tr>
<td>Serum calcium, mmol/L</td>
<td>2.10 ± 0.04</td>
<td>2.02 ± 0.25</td>
<td>0.391</td>
</tr>
<tr>
<td>Serum phosphorus, mmol/L</td>
<td>1.93 ± 0.61</td>
<td>2.07 ± 0.65</td>
<td>0.429</td>
</tr>
<tr>
<td>Serum phosphorus, mmol/L</td>
<td>4.71 ± 0.84</td>
<td>5.40 ± 1.13</td>
<td>0.063</td>
</tr>
<tr>
<td>PTH, pg/mL</td>
<td>365.6(197.70–682.60)</td>
<td>462(131.55–707.7)</td>
<td>0.912</td>
</tr>
<tr>
<td>ALB, g/dL</td>
<td>35.63(31.05–38.03)</td>
<td>30.72(24.5–37.32)</td>
<td>0.118</td>
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<tr>
<td>ALP, μkat/L</td>
<td>85(66–119)</td>
<td>92.5(58–176.25)</td>
<td>0.901</td>
</tr>
<tr>
<td>D-Dimer, μg/L</td>
<td>647(338.5–1050)</td>
<td>2188(513.25–7129.5)</td>
<td>0.041</td>
</tr>
<tr>
<td>NT-proBNP, pg/mL</td>
<td>9130.5(3026.5–31513)</td>
<td>33170.5(14799–35000)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Continuous variables are presented as mean ± SD for normally distributed data or as median with IQR range (in square brackets) if non-normally distributed. Categorical variables given as absolute numbers with percentage in brackets. BMI, body mass index; NLR; neutrophil-to-lymphocyte ratio; IL-6, Interleukin 6; PCT, procalcitonin; CRP, C reactive protein, ALP, Alkaline phosphatase.
#2518

EFFECT OF VACCINATION ON OXIDANT/ANTIOXIDANT STATUS IN HEMODIALYSIS PATIENTS WITH POST-COVID CONDITIONS

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Background and Aims: Hemodialysis (HD) patients are at high risk for post-COVID conditions and a high mortality rate over a 1-year period after diagnosis of COVID-19, especially in the first 3 months. Evidence shows that vaccinated individuals who experience breakthrough infection are less likely to report post-COVID conditions compared with unvaccinated individuals. Although oxidative stress has been shown to be an important cause of post-COVID conditions, there is a general lack of data on oxidant/antioxidant status in HD patients with post-COVID conditions. The present study aimed to evaluate the oxidant/antioxidant markers in HD patients with post-COVID conditions according to vaccination status.

Method: A total of 106 HD patients, aged 52.4 ± 10.2 years, and dialysis vintage of 68 (29-134) months, were enrolled in this cross-sectional observational cohort study. Patients were divided into 3 groups according to their vaccination status and the presence of post-COVID conditions. Group 1 consisted of 36 HD patients who had been fully vaccinated against COVID-19 with either Pfizer-BNT-162b2 or Moderna-mRNA-1273 vaccine and had experienced a post-vaccination SARS-CoV-2 infection and had at least 1 post-COVID symptom. Group 2 consisted of 35 fully vaccinated HD patients who had never been infected with COVID-19 (vaccinated control group), and Group 3 included 35 unvaccinated HD patients who had experienced COVID-19 and had post-COVID conditions (unvaccinated control group).

Concentrations of malondialdehyde in serum (MDAs) and erythrocytes (MDAe), sulfhydryl groups (SH-groups), serum catalase activity (CTs), serum transferrin and ceruloplasmin levels were determined 3 months after COVID-19 recovery. Data were expressed as a median and interquartile range [Me (Q25-Q75)] and compared with the Kruskal-Wallis test.

Results: The vaccinated HD patients with post-COVID conditions had the highest concentrations of MDAs and ceruloplasmin, and lower serum levels of CTs and transferrin compared with the vaccinated and unvaccinated control groups (Table 1).

Conclusion: Our findings suggest a significant oxidative imbalance in HD patients with post-COVID syndrome most likely due to the synergistic effects of the virus and the vaccine. The use of antioxidant supplements might be a possible strategy to treat post-COVID conditions in HD patients.
EFFECTS OF DIALYSIS PATIENTS’ HEALTH-RELATED QUALITY OF LIFE AND SYMPTOM BURDEN ON CAREGIVERS

Esmee Dreihuis1,2, Theodör Vogels3, Wanda Konijn3, Anneke Roeterdink2,1, Thomas Sebastiaan van Lieshout2,5, Namiko Goto6,7, Marjolein Broese van Groenou7, Friedo W. Dekker9, Brigit Van Jaarsveld2,10 and Alfesco C. Abrahams3

1University Medical Center Utrecht, Department of Nephrology and Hypertension, Utrecht, Netherlands, 2Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Nephrology, Amsterdam, Netherlands, 3Dialysis Center Maxima, Maxima Medical Center, Eindhoven, Netherlands, 4Dutch Kidney Patients Association (NVN), Bussum, Netherlands, 5Northwest Clinics, Department of Internal Medicine, Alkmaar, Netherlands, 6University Medical Center Utrecht, Department of Geriatric Medicine, Utrecht, Netherlands, 7Jeroen Bosch Hospital, Department of Geriatric Medicine, ’s Hertogenbosch, Netherlands, 8Vrije Universiteit Amsterdam, Department of Sociology, Amsterdam, Netherlands, 9Leiden University Medical Center, Department of Clinical Epidemiology, Leiden, Netherlands and 10Diaipriva Dialysis Center, Amsterdam, Netherlands

Background and Aims: Starting dialysis has a major impact on patients’ lives. Dialysis patients experience impairments in health-related quality of life (HRQoL) and high symptom burden. Informal caregivers are crucial for dialysis patients’ well-being, as patients often rely on their support and care. However, informal caregivers who provide long-lasting, intensive care may also experience a significant burden. This, in turn, may lead to impaired HRQoL of both the informal caregiver and the patient. To date, little research has been done among informal caregivers of dialysis patients, even though they may experience negative effects of the impaired functioning of the patient. Therefore, the aim of this study was to assess the impact of dialysis patients’ HRQoL and symptom burden on HRQoL of their informal caregivers. We hypothesize that impaired HRQoL and high symptom burden of dialysis patients have a significant impact on informal caregivers’ mental HRQoL, but little to no impact on their physical HRQoL.

Method: We conducted a cross-sectional study with 193 dyads of adult dialysis patients and their informal caregivers. Data at dialysis initiation were obtained from the ongoing multicenter, observational cohort study on informal caregivers of dialysis patients, which is an extension of the Dutch nOcturnal hOmeDialysis Study To Improve Clinical Outcomes (DOMESTICO). The 12-item Short Form Health Survey (SF-12), which provides mental component summary (MCS) and physical component summary (PCS) scores (range 0-100), was used to measure HRQoL in both informal caregivers and dialysis patients. To date, little research has been done among informal caregivers of dialysis patients, even though they may experience negative effects of the impaired functioning of the patient. Therefore, the aim of this study was to assess the impact of dialysis patients’ HRQoL and symptom burden on HRQoL of their informal caregivers. We hypothesize that impaired HRQoL and high symptom burden of dialysis patients have a significant impact on informal caregivers’ mental HRQoL, but little to no impact on their physical HRQoL.

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Results: Mean age of informal caregivers was 60 ± 15 years, 72.0% were female, and 77.2% were spouses of the dialysis patient. Mean age of patients was 65 ± 14 years, 32.1% were female, and 62.7% were on in-centre hemodialysis. Mean MCS and PCS scores of informal caregivers were 47.8 ± 9.7 and 48.7 ± 9.8, respectively. Mean MCS and PCS scores of patients were 47.9 ± 9.0 and 35.7 ± 10.3, respectively, and mean symptom number and burden were 11.3 ± 5.9 and 31.5 ± 17.6, respectively. After adjustment for confounders, significant effects of patients’ (1) MCS score (β = 0.305; p = 0.003), (2) symptom number (β = -0.434; p = 0.002), and (3) symptom burden (β = -0.151; p < 0.001) were found on caregivers’ MCS score. No significant effects on caregivers’ PCS score were found.

Conclusion: Lower mental HRQoL, higher symptom number, and higher symptom burden of dialysis patients are associated with lower mental HRQoL of their informal caregivers. These findings underline the importance of maintaining patients’ HRQoL and reducing symptom burden, as these also affect informal caregivers. In addition, given that improving patients’ HRQoL and reducing symptom burden are not always within reach, these findings emphasize the importance of supporting informal caregivers of dialysis patients.

ASSOCIATION BETWEEN AMORPHOUS CALCIUM-PHOSPHATE RATIOS IN CIRCULATING CALCIOPROTEIN PARTICLES AND PROGNOSTIC BIOMARKERS IN HEMODIALYSIS PATIENTS

Kimihiko Nakamura, Naohito Isoyama, Koji Shiraishi and Makoto Kuro-O

Japan

Background and Aims: Calcioprotein particles (CPPs) are circulating colloidal mineral-protein complexes containing crystalline and/or non-crystalline (amorphous) calcium-phosphate (CaPi). Serum CPP levels correlate with vascular stiffness and calcification in patients with chronic kidney disease (CKD). In vitro studies showed that CPPs containing crystalline CaPi were more arteriosclerogenic and inflammagogenic than CPPs without containing crystalline CaPi. Thus, we hypothesized that not only the quantity but also the quality of CPPs (the phase of CaPi) might affect clinical outcomes.

Method: To test this hypothesis, we quantified amorphous CaPi ratio defined as the ratio of the amorphous CaPi amount to the total CaPi amount in serum CPPs from 183 hemodialysis patients and explored its possible correlation with serum parameters associated with prognosis of hemodialysis patients.

Results: Multivariate analysis revealed that the amorphous CaPi ratio correlated positively with hemoglobin and negatively with fibroblast growth factor-21 (FGF21), which remained significant after adjusting for the total CaPi amount. Because, low hemoglobin and high FGF21 were associated with increased mortality. Patients with low amorphous CaPi rate tended to have lower 2-year survival rates (p = 0.07).

Figure 1: Scattered plots between CPP and other serum parameters. Correlation coefficient (R) is indicated. Association of serum phosphate levels with total (A, blue), crystalline (A, red), and amorphous CaPi (B) amounts. Association of serum calcium levels with total (C) and amorphous (D) CaPi amounts. Association of amorphous CaPi ratios with hemoglobin (E) and FGF21 (F).
#3968
DIFFERENCES IN MENTAL HEALTH STATUS DURING COVID-19 PANDEMIC BETWEEN IN-CENTER HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS
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1 Maastricht University, CARIM - School for Cardiovascular Diseases, Maastricht, Netherlands, 2 MUMC+ - Internal Medicine, Division of Nephrology, Maastricht, Netherlands, 3 UMC Utrecht, Nephrology and Hypertension, Utrecht, Netherlands, 4 Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands, 5 Nierpatiënten Vereniging Nederland, Bussum, Netherlands, 6 Bernhoven, Internal Medicine, Uden, Netherlands, 7 Scheper Hospital, Nephrology, Emmen, Netherlands and 8 Amsterdam UMC, locatie VUmc, Nephrology, Amsterdam, Netherlands

Background and Aims: Results from previous studies suggest that mental health of dialysis patients was unaffected during the first wave of the COVID-19 pandemic. However, the location of dialysis treatment might have had a different impact on patients during the ongoing COVID-19 pandemic, especially at time of restrictions. Studies comparing the mental health of ICHD and PD patients during the pandemic are scarce. Therefore, we aimed to assess whether dialysis modality differently affected the mental health of patients during the COVID-19 pandemic.

Method: This study used data of patients participating in the Dutch nocturnal and hoME dialysis Study To Improve Clinical Outcomes (DOMESTICO). We conducted repeated cross-sectional analyses between ICHD and PD patients from the start of the COVID-19 pandemic in March 2020 until August 2021. For this, we divided the study period into six periods of three months. The year before the pandemic was used as reference period. Mental health-related quality of life (HRQOL) was assessed using the mental component summary (MCS) score of the 12-item Short Form (SF-12) health survey. The presence of mental symptoms was determined using the Dialysis Symptom Index (DSI). Both questionnaires were provided at start of dialysis, at 3 months, 6 months and each 6 months thereafter. Patients were included for analysis if a questionnaire was available in at least one period. MCS scores and the prevalence of mental symptoms between ICHD and PD patients were compared with Student’s t-test and Chi-square test, respectively. Moreover, we performed multivariable regression analyses to adjust for possible confounders.

Results: For this analysis, 1274 patients (968 ICHD and 306 PD) were included. Mean age was 65±14 and 64±14 years, respectively. Most patients were male (ICHD: 68%, PD: 61%). Before the pandemic the ICHD patients reported similar MCS scores, yet more often reported feeling nervous (32% vs. 22%, P = .03) and sad (40% vs. 29%, P = .03). During the pandemic, mean MCS scores also did not differ between ICHD and PD patients. In contrast, ICHD patients more often reported feeling nervous during period 3 (32% vs. 15%, P = .04), feeling irritable and anxious during period 3 (31% vs 18%, P = .03, 26% vs. 9%, P = .002, resp.) and period 4 (34% vs 22%, P = .04, 22% vs 11%, P = .03, resp.), and feeling sad in period 4 (38% vs 26%, P = .04) and period 5 (37% vs 22%, P = .009). In a multivariable regression analysis, these differences persisted after correction for several confounders.

Conclusion: ICHD patients experienced more mental symptoms compared to PD patients in the period September 2020 to June 2021, which corresponds with the second lockdown of the COVID-19 pandemic. This higher prevalence of specific mental symptoms in ICHD patients was not reflected by a decrease in mental HRQOL.

#6235
ELEVATED PLASMA ANGIOPOETIN-2 PREDICT THE NEED FOR DIALYSIS INITIATION IN PATIENTS WITH CKD 4 AND 5 WITHIN TWO YEARS
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1 Wrocław Medical University, Nephrology and Transplantation Medicine, Wrocław, Poland, 2 Wrocław Medical University, Cardiology, Wrocław, Poland and 3 University of Opole, Opole, Poland

Background and Aims: Volume status, congestion and endothelial activation/injury were found to play a role in GFR decline and CKD progression. This pilot study aimed to determine whether the plasma markers of endothelial injury and activation as well as markers of fluid overload could serve as independent predictors for dialysis initiation in stable patients with CKD 4 and 5 and preserved EF.

Method: This prospective study was conducted from March 2019 to March 2022 and enrolled consecutive patients with GFR <30ml/min/1.72 m² and preserved LVEF. Plasma levels of angiotensin (Ang)-2, Vascular Endothelial Growth Factor-C (VEGF-C), Vascular Cell Adhesion Molecule-1 (VCAM-1), Copeptin (CPP), beta-trace protein (BTP), brain natriuretic peptide (BNP), cardiac troponin 1 (cTnI) were measured (Quantikine ELISA, R&D Systems Inc, Minneapolis, MN). Clinical markers of congestion were also recorded: lung US (B-lines), bioimpedance (ECV/ICV), echocardiography with global longitudinal strain (GLS), pulse wave velocity (PWV). Study outcome was need to initiate dialysis during 24-months follow-up.

Results: We analyzed a total of 105 patients with mean eGFR 21.3 ml/min/1.73m. The median age at enrollment was 52 (±14.8) years and 65% of the patients were male; 79% were hypertensive and 24% were diabetic. A positive correlation between concentration of Ang-2 and VCAM-1 and BTP was observed. Ang-2 concentration correlated positively with BNP, Trt, sCr, e/e’, ECV/ICV. Over a follow-up period of 24 months, the deterioration of renal function was observed in 47 patients (58%), 31 (38%) presented stable or ameliorated renal function and 24 on maintenance dialysis formed a control group. In Kaplan-Meier analysis significant impact of Ang-2 on renal survival (Figure) was found. Namely, 72% of patients with Ang-2 concentrations below the median (3.15 ng/ml) survived without dialysis for two years, compared to 42% of those with Ang-2 concentrations above the median. Such impact was not observed for GFR, VCAM, CCP, VEGF-C, BTP.

Conclusion: Endothelial activation, quantified by plasma levels of Ang-2 may play an important role in GFR decline and need for dialysis initiation in patients with CKD 4 and 5.

#6864
IMMUNE RESPONSES OF PATIENTS ON MAINTENANCE HEMODIALYSIS AFTER INFECTION BY SARS-COV-2: A PROSPECTIVE OBSERVATIONAL COHORT STUDY
Dimitra Bacharaki1, Minas Karagiannis1, Evangelos Papachristou1, Dimitrios Divanis2, Adamantia Bratsiakou2, Panagiotis Giannakopoulos2, Georgia Damoraki3, Vassilios Liakopoulos3, Dimitrios Goumenos4 and Evangelos Giamarellos2
1 Attikon General University Hospital, 2nd Department of Propedeutic Medicine, Chaidari, Greece, 2 Rion University Hospital, Nephrology, Rio, Greece, 3 AHEPA Hospital, Nephrology, Thessaloniki, Greece and 4 Attikon General University Hospital, 4th Department of Internal Medicine, Chaidari, Greece

Background and Aims: We aimed to study the immune response of maintenance hemodialysis (HD) patients to Corona Virus Disease-19 (COVID-19) since it is not fully elucidated.

Method: In this prospective study, hospitalized HD patients with moderate-to-severe COVID-19 and matched non diseased HD comparators were analyzed.
Figure 1: Circulating cytokines were measured before start of hemodialysis, after the end of hemodialysis and in the dialysate in patients on maintenance hemodialysis with COVID-19 and matched comparators. Line represents the median of the distribution. Comparisons between patients and comparators are shown: ns, non-significant; \*p < 0.05; \***p < 0.0001.

Abbreviations: IFN, interferon; IL, interleukin; MC, matched comparators; n, number of patients; PDGF, platelet-derived growth factor; TNF, tumour necrosis factor.

Results: 59 HD patients with acute COVID-19 HD and 20 comparators were enrolled. Circulating median (range) of interferon-gamma (IFN-\( \gamma \)) at the start of HD was 125 (125-1777) pg/ml in comparators and 810 (125-4000) pg/ml in SARS-CoV-2 (\( p < 0.00001 \)) and 125 (125-1278) pg/ml and 738 (125-4000) pg/ml at the end of HD (\( p < 0.0001 \)). Respective concentrations of platelet derived growth factor-A were 8286 (4600-28150) and 27938 (8285-99256) pg/ml (\( p < 0.0001 \)) and 7779 (5055-28128) and 27410 (6836-87887) pg/ml respectively. Similar increases were found for tumor necrosis factor-alpha (TNF-\( \alpha \)) only at the start of the HD whereas no differences were found for interleukin (IL)-6, IL-10 and IL-38. Respective mean (SD) CD4-counts were 881.3 (407.6) and 461.6 (365.4) per microliter (\( p < 0.0001 \)) and 839.4 (509.7) and 483.6 (329.9) per microliter (\( p < 0.0001 \)). MFI expression of HLA-DR on CD14-monocytes was 97.2 (28.2) and 67.4 (44.7) (\( p < 0.0001 \)) and 87.3 (26.7) and 63.3 (36.3) (\( p < 0.0001 \)). The respective mean (SD) MFI expression of HLA-DR on CD14-monocytes was 97.2 (28.2) and 67.4 (44.7) (\( p < 0.0001 \)) and 87.3 (26.7) and 63.3 (36.3) (\( p < 0.0001 \)). MFI of HLA-DR on CD14-monocytes before the first HD session less than 44 was associated with 100% sensitivity for unfavorable outcome (defined as respiratory failure or death) after 28 days. An absolute CD19-count more than 40 per microliter before the first HD session was associated with 8.70 odds ratio for cure favorable outcome after 28 days.

Conclusion: HD patients develop an inflammatory reaction to Severe Acute Respiratory Syndrome Coronavirus 2 characterized by increase of the inflammatory mediators IFN-\( \gamma \), PDGF-A and TNF-\( \alpha \) and decrease of circulating T helper lymphocytes. Decreased expression of HLA-DR on CD14-monocytes is a hallmark of unfavorable prognosis.

#3430
MORTALITY AND RISK FACTORS IN VERY ELDERLY PATIENTS WHO START HAEMODIALYSIS: KOREAN RENAL DATA SYSTEM (KORDS), 2016-2020
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1National Police Hospital, Department of Internal Medicine, Seoul, Rep. of South Korea, 2Kangnam Sacred Heart Hospital, Department of Internal Medicine, Seoul, Rep. of South Korea and 3Oryeon Samsung Medical Center, Incheon, Rep. of South Korea

Background and Aims: The number of elderly patients with end-stage renal disease (ESRD) is increasing worldwide. However, decision-making about elderly patients with ESRD remains complex because of the lack of studies, especially in very elderly patients (\( \geq 75 \) years). We examined the characteristics of very elderly patients starting haemodialysis (HD) and the associated mortality and prognostic factors.

Method: Data were analysed retrospectively using a nationwide cohort registry, the Korean Renal Data System. Patients who started HD between January 2016 and December 2020 were included and divided into three groups according to age at HD initiation (<65, 65–74, and \( \geq 75 \) years). The primary outcome was all-cause mortality during the study period. Risk factors for mortality were analysed using Cox proportional hazard models.

Results: In total, 22,024 incident patients were included with 10,006, 6,350 and 6,350 in each group (<65, 65–74, and \( \geq 75 \) years, respectively). Among the very elderly group, women had a higher cumulative survival rate than men (91.2% vs. 90.3% at 1 year and 56.4% vs. 51.9% at 3 years, respectively) (Figure 1a). The survival rate was lower in patients with vascular access via a catheter than those with an arteriovenous fistula or graft (72.0% vs. 95.1% at 1 year and 23.8% vs. 60.7% at 3 years, respectively) (Figure 1b). Very elderly patients with more comorbid diseases had a significantly lower survival rate that those with fewer comorbidities (log-rank: \( p < 0.001 \)) (Figure 2).

Conclusion: Preparation of an arteriovenous fistula or graft when starting HD should be considered in very elderly patients with fewer comorbid diseases.
EFFECT OF THE RATE OF ALBUMIN DECREASE ON LONG-TERM PROGNOSIS IN DIALYSIS PATIENTS

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**Background and Aims:** The malnutrition is often prevalent in hemodialysis (HD) patients, and the risk of mortality is strongly correlated with malnutrition. We assume the dynamic change and trend of albumin in HD patients are mortality essential, however there is not enough information on these data. The aim of this study was to investigate the association of long-term prognosis and decrease rate of albumin for one-year.

**Method:** We enrolled HD patients in six centers to a retrospective follow-up study. All patients had received HD from January 2014 to December 2014 and serum albumin data were collected every month in this period. We defined decrease rate in serum albumin as (average of albumin value for the year - decrease value for the year) / average of albumin value for the year. We categorized these patients into two groups according to the median value of the decrease rate. Then these patients were observed for three years. The primary and secondary outcome of this study was all-cause mortality and the combined endpoint of mortality and major cardio-cerebrovascular adverse events (MACCE). To evaluate cut-off value in decrease rate of serum albumin, Receiver Operating Characteristic (ROC) curve analysis was performed. Moreover, restricted cubic splines were used to detect the possible nonlinear dependency of the relationship between decrease rate in serum albumin and mortality.

**Results:** Six-hundred twenty-one HD patients were enrolled into this study. The median rate of decrease in albumin in the enrolled patients was 7.5%. Compared to the low decrease fluctuation group (n = 321), the high decrease fluctuation group (n = 300) was significantly older (67 vs 66 years; p = 0.03), more frequently had diabetes mellitus (51.7 vs 39.3%; p = 0.02), had lower serum creatinine (9.34 vs 10.69 mg/dl; p <0.001) and lower body mass index (20.3 vs 21.3; p = 0.01). The mean follow-up period was 31.0±10.1 months. During the follow-up period, there were 121 cases (19.5%) in all cause death and 191 cases (30.5%) in combined endpoint, respectively. Kaplan-Meier analysis showed that high decrease fluctuation in serum albumin group had a significantly worse prognosis in both all-cause mortality (Log-rank, p = 0.01) and combined endpoint (Log-rank, p = 0.002) than low decrease fluctuation group (Figure 1). Multi-variate Cox proportional hazard model revealed that high decrease fluctuation in serum albumin was significantly associated with a higher risk of all-cause mortality and combined endpoint (hazard ratio 1.47 (95%CI: 1.02-2.13), p = 0.03, hazard ratio 1.49 (95%CI:1.11-1.99), p = 0.007). The cut-off value for all-cause mortality in decrease rate of serum albumin was 8.4% by ROC curve analysis. Moreover, through multivariable restricted cubic spline regression, continuous variation in decrease rate in serum albumin was found to be related to all-cause mortality in a nonlinear manner (Figure 2).

**Conclusion:** In HD patients, high decrease fluctuation in serum albumin was significantly associated with an increased risk of all-cause mortality compared low decrease fluctuation in serum albumin. Our findings suggest that regarding serum albumin, we might need to pay attention not only to its monthly value, but also to its decreasing fluctuation.
Background and Aims: Although the initiation of unplanned dialysis in elderly patients is associated with a higher risk of death, overall this is still poorly understood and measured. The aim of the present study is to evaluate the unplanned population of patients who started planned or unplanned dialysis at the Policlinico “A. Gemelli” and the “SS. Annunziata” University Hospital of Chieti in the period from 1 January 2016 to 31 December 2020. All Patients in the unplanned population started emergency hemodialysis treatment during hospitalization. The primary outcome was all-cause mortality at three and six months. The main demographic, clinical features and the Couchoud Score, a prognostic score that stratifies elderly patients (age > 75 years) with ESRD into groups with variable risk of short-term mortality after initiation of dialysis, of two group are shown in Table 1.

Results: During the whole study period, endend on 30 September 2022, 84 (68.3%) patients died in the unplanned group and 17 (24.6%) in the planned group. The unplanned group showed a higher Couchoud score (4.07 ± 2.63 vs 7.02 ± 3.05 p < 0.001). In the unplanned group, 54.5% of patients died within 3 months and 58.3% within 6 months. In the Planned group, we observed only one death within 6 months. The mean survival of the unplanned group was 366 (± 544) days. In the unplanned group, 51 patients died during the hospital stay in which the hemodialysis treatment was started. The mean survival in these patients was 23 (± 71 SD) days. The difference in survival in the two cohorts of patients is shown in the Kaplan-Mayer analysis and is statistically significant (Logrank p < 0.001) (Figure 1). Interestingly, Couchoud Score (Spearman rho = -0.44; p < .001) and unplanned treatment initiation (Spearman rho = -0.59; p < .001), but not patients’ age (Spearman rho = -0.10; p = .168) presented a strong and inverse correlation with observed lifespan. The logistic regression model confirmed that Couchoud score was significantly and independently associate with mortality at three (p < .001, 95%CI 0.16-0.49, McFadden R2 = 0.126) and six months (p < .001, 95%CI 0.14-0.45, McFadden R2 = 0.105). In the subsequent logistic regression model, evaluating the individual variables contained in the Couchoud Score, only lack of autonomy was significantly associated with mortality both at three and six months (three months: OR 8.230, p < .001, 95%CI 1.073-3.143; six months: OR 5.504, p = <.001, 95%CI 0.726-2.685).

Conclusion: In elderly patients, unplanned dialysis is associated with a significant increase in in-hospital and at six-month mortality. In our study, the Couchoud Score represented an accurate and reliable short-term prognostic evaluation tool and may help nephrologist in the context of a shared decision-making process to select elderly patients more suitable for renal replacement therapy.

Table 1: Demographic and clinical characteristics and Couchoud Score in the two group of our population.

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<td>Couchoud Score (SD)</td>
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</table>

Figure 1: Kaplan-Meier survival curves for hemodialysis patients with median by albumin category. (A) all-cause death (B) composite event-free rate. LD-F: low decrease of fluctuation serum albumin <7.5%; HD-F: serum albumin fluctuation of decrease range ≥7.5%.

Figure 2: Association between the decreased rate of serum albumin and all-cause death in dialysis patients, allowing for nonlinear effects, with 95% CIs. Curves show ORs compared with the chosen reference decrease rate of serum albumin of 8.4%.

#3435

UNPLANNED INITIATION OF HEMODIALYSIS IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE: RISK FACTORS FOR SHORT TERM MORTALITY

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Background and Aims: Although the initiation of unplanned dialysis in elderly patients is associated with a higher risk of death, overall this is still poorly understood and measured. The aim of the present study is to evaluate how “planned” or “unplanned” beginning of renal replacement therapy might influence the main clinical outcomes.

Method: We carried out an observational, retrospective, multicenter study on ESRD patients’ population who started planned or unplanned dialysis at the Policlinico “A. Gemelli” and the “SS. Annunziata” University Hospital of Chieti in the period from 1 January 2016 to 31 December 2020. All Patients in the unplanned population started emergency hemodialysis treatment during hospitalization. The primary outcome was all-cause mortality at three and six months. The main demographic, clinical features and the Couchoud Score, a prognostic score that stratifies elderly patients (age > 75 years) with ESRD into groups with variable risk of short-term mortality after initiation of dialysis, of two group are shown in Table 1.
### #4659

PREVALENCE OF LIVER STEATOSIS MEASURED BY MULTIFREQUENCY BIOIMPEDANCE IN PATIENTS WITH CKD

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**Background and Aims:** The increase in visceral fat is one of the factors that contribute to the increased cardiovascular risk associated with CKD. There are few data on the prevalence of hepatic steatosis in patients with CKD. The Maltron multifrequency BIA offers us the possibility of evaluating it. The purpose of this study was to determine the prevalence of hepatic steatosis by means of multifrequency bioimpedance and to correlate it with ultrasound or CT in patients with CKD on Advanced CKD (ACKD) and HD.

**Methods:** We carried out a study of body composition with BIA in 315 patients, analyzing with the Maltron monitor Bioscan i-touch8 the determination of hepatic steatosis and its classification into 4 stages of involvement (normal, mild, moderate, moderately-severe and severe steatosis). We also correlated with ultrasound studies that had In order to see coincidence, we also obtained data from 9 patients without CKD. We established correlation/coincidence between ultrasound/CT and BIA in 72 patients. We found a healthy liver BIA-ECHO correlation in 43 cases (93.4%), steatosis by BIA coincides with ECHO in 50.0%.

**Results:** 315 patients evaluated for CKD 151 (48%) and HD 163 (52%), 65.9% men aged 70.79 ± 12.87 years (sig difference between CKD and HD (72.4 ± 2.7) vs 69.2 ±14.3) p0.023. Globally we found healthy liver in 37.9% and steatosis in 61.3% appearing mild-13.4%, moderate 11.8%, light-high 11.4% and high 24.5%. We observed healthy liver in 35.1% in ACKD vs 40.5% in HD. We did not find significant differences between liver enzyme values between healthy liver and steatosis at a global level. We established correlation/coincidence between ultrasound/CT and BIA in 72 patients. We found a healthy liver BIA-ECHO correlation in 43 cases (93.4%), steatosis by BIA coincides with ECHO in 41.6%. If we combine healthy liver + mild steatosis by BIA, the BIA-Echo healthy liver coincides in 92.7% and steatosis in 50%. Establishing cut-off points for BMI, % fat mass and waist/height index using COR curves, we obtain areas-under-the-curve 0.828, 0.738 and 0.853 respectively, being Waist-height index (WC/0.6) with better sensitivity 80% and specificity 71.3%. If we determine the area of fat mass with another tool, we see AUC 0.838 with 72.3% specificity and 91.3% sensitivity to detect normal liver.

**Conclusion:** 1) A high prevalence of hepatic steatosis due to IAB appears in patients with CKD greater in CKD than in HD. 2) There is a good correlation with ECO for a healthy liver and there are parameters that correlate well in a healthy liver diagnosis. 3) Specific studies of Ultrasound-BIA are needed to validate the diagnosis of steatosis.

### #2594

ELEVATED SERUM IL-17 LEVEL IS ASSOCIATED WITH THE PERSISTENCE OF POST-COVID SYNDROME AND VACCINATION STATUS IN HEMODIALYSIS PATIENTS

Natalia Stepanova1, Victoria Driianska1, Andriy Rysyev2, Valeriia Kholod1, Viktoria Savchenko1 and Mykola Kolesnyk1

1State Institution "Institute of Nephrology of the National Academy of Medical Science of Ukraine", Nephrology & Dialysis, Kyiv, Ukraine and 2Dialysis Medical Center LLC "Link-Medital", Nephrology, Odesa, Ukraine

**Background and Aims:** Interleukin-17 (IL -17) is thought to play an important role in the immune response and severity of coronavirus disease 2019 (COVID-19). In addition, elevated serum IL-17 levels have been detected in the general population of SARS-CoV-2-infected patients with post-COVID syndrome. Although hemodialysis (HD) patients belong to the high-risk group COVID-19 with an attenuated immune response to mRNA vaccination and a high incidence rate of post-COVID syndrome, IL-17 has never been studied in this cohort.

**Method:** A total of 80 HD patients aged 56 (44-63.2) years with a dialysis vintage of 40 (23-74) months who had experienced COVID-19 at least 5 months before enrollment were included in this cross-sectional cohort study. Aiming to analyze serum IL -17 according to the persistence of post-COVID syndrome, the patients we divided into 2 groups: post-COVID with (n = 36)
Figure 1: Serum IL-17 in HD patients stratified by the persistence of post-COVID syndrome and the interval between acute SARS-CoV-2 infection and blood collection.

and without (n = 44) sequelae. IL-17 was measured at 2-time points: at 5 (n = 30) and 10 months (n = 50) after acute SARS-CoV-2 infection using an ELISA assay. Data were expressed as median (Me) and interquartile ranges (Q25-Q75) and compared with the Mann-Whitney test.

Results: Serum IL-17 ranged from 0.01 to 15.14 pg/mL and was significantly elevated in HD patients with post-COVID sequelae compared to fully recovered patients: 0.45 (0.08-1.6) vs 0.08 (0.025-0.15) pg/mL, p = 0.0002. In the general cohort of HD patients with a 5-month interval between acute SARS-CoV-2 infection and blood collection, IL-17 was statistically greater than in patients with a 10-month interval: 0.24 (0.06-1.2) vs 0.11 (0.03-0.37) pg/mL, p = 0.04. In subgroup analysis, the patients with post-COVID sequelae had higher IL-17 levels than fully recovered patients at both time points (Fig. 1). Notably, mRNA-vaccinated HD patients with post-COVID sequelae had higher IL-17 levels than unvaccinated patients at both time points: 3.83 (0.47-6.47) vs 0.88 (0.04-1.5) pg/mL, p = 0.03 and 0.57 (0.09-5.3) vs 0.08 (0.03-0.13) pg/mL, p = 0.01, respectively.

Conclusion: Serum IL-17 level is associated with the persistence of post-COVID syndrome in HD patients even 10 months after acute COVID-19 and is significantly higher in mRNA-vaccinated HD patients with post-COVID sequelae compared to unvaccinated patients. Further studies are needed to postulate IL-17 as a useful biomarker for post-COVID syndrome in HD patients.

#3161
CLINICAL EFFICACY AND OPTIMAL REGIMEN OF BNT162B2 VACCINE IN CHRONIC DIALYSIS PATIENTS
Keren Cohen Hagai1, Tzipi Hornik-Lurie2, Yael Einbinder1, Naomi Nacasch1, Ayelet Grupper3, Ori Wand4, Moshe Shashar4 and Sydney Benchetrit1
1Nephrology, Kfar Saba, Israel, 2Kfar Saba, Israel, 3Nephrology, Israel and 4Israel

Background and Aims: Highly effective vaccines against severe acute respiratory syndrome virus 2 (SARS-CoV-2) have been developed and administered worldwide. Protection from coronavirus disease 2019 (COVID-19), however, is not absolute, and optimal vaccination regimens need to be established. Concerns regarding breakthrough COVID-19 disease in vaccinated patients are increasing, as vaccine efficacy appears to gradually decline in the months following vaccination. The emergence of highly infective variants, escalates these issues. This study assessed the clinical efficacy of the BNT162B2 vaccine and all-cause mortality among dialysis patients receiving varying numbers of vaccine doses.

Method: This study was conducted using the electronic database of Clalit Health Services in Israel. Patients receiving chronic hemodialysis or peritoneal dialysis during COVID-19 pandemic were included in the analysis. The control group consisted of age- and sex-matched individuals, in a 4:1 ratio to the dialysis group. The study included the pre- and post-vaccination periods.

Results: A total of 14,230 people were included; 2,846 on chronic dialysis and 11,384 controls. Mean age was 66.2 ± 14.3 years (range 18-97). Before the vaccine was available in Israel, 223 dialysis patients were infected with SARS-CoV2. Their mortality rate was 18.4% compared to 10.8% among uninfected, unvaccinated patients in the same period (p = 0.001). On post-vaccination period, we compared the clinical efficacy of a fourth dose to patients who received only 3 doses of BNT162b2 vaccine. SARS-CoV-2 infection rates, hospitalizations due to severe COVID-19, COVID-19–related mortality and all-cause mortality rates were lower among chronic dialysis patients who received a fourth dose of vaccine as compared to those who received only 3 doses (after adjusting for age, sex and comorbidities). Despite lower mortality rates observed with the Omicron variant, an additional booster dose was associated with reduced COVID-19–related mortality (1.7% vs. 3.8%, p = 0.04, HR 0.44 (95% CI 0.2–0.98) in patients who received 4 doses compared to 3 doses.

Conclusion: As seen in the general population, and with previous vaccine boosters, the fourth dose of the BNT162b2 vaccine reduced rates of severe COVID-19 hospitalization and mortality among chronic dialysis patients. This study strengthens the recommendation to administer a fourth booster dose of vaccine to dialysis patients. Further studies are needed to establish the exact dose and schedule of the COVID-19 vaccine in the vulnerable population patients on chronic maintenance dialysis.
SARS-COV-2 OMICRON INFECTIONS AMONG VACCINATED MAINTENANCE HEMODIALYSIS PATIENTS: OUTCOMES AND COMPARISON TO DELTA VARIANT

Keren Cohen Hagai¹, Ori Wand², Idan Drori¹, Yael Einbinder¹, Naomi Nacasch¹ and Sydney Benchetrit¹

¹Meir Medical Center, Kfar Saba, Israel and ²Israel

Background and Aims: Infections with the B.1.1.529 Omicron variant of SARS-CoV-2 became predominant worldwide in late 2021, replacing the previously dominant B.1.617.2 Delta variant. While these variants are highly transmissible and can evade vaccine protection, population studies suggested that outcomes after infection with Omicron variant were better than with Delta. Data regarding prognosis of maintenance hemodialysis (MHD) patients infected with Omicron vs. Delta variants are limited.

Method: This retrospective, cohort study included all patients with end-stage kidney disease treated with MHD at Meir Medical Center, Kfar Saba, Israel, who were diagnosed with SARS-CoV-2 infection between June 2021 and May 2022.

Results: Twenty-six MHD patients were diagnosed with the Delta variant and 71 with Omicron. SARS-CoV-2 infection severity was significantly worse among those infected with the Delta variant: 50% developed severe or critical COVID-19 vs. 5% in the Omicron group (p<0.001). Among MHD infected with Omicron, 57% were asymptomatic during their illness. For the entire cohort, 30-day mortality was 5.2%. It was higher among MHD in the Delta group (5/26, 19.2%) than in the Omicron group (0/71; p<0.001), as was 90-day mortality (5/26, 19.2% vs. 3/71, 4.2%, respectively; p = 0.02). Mean age was comparable between groups. Patients infected with Omicron variant received a higher mean number of vaccine doses before infection, as compared to Delta group (p<0.001).

Conclusion: Infection with the SARS-CoV-2 Delta variant was associated with worse outcomes compared with Omicron, among patients on MHD. However, despite mild disease among vaccinated MHD patients, infection with Omicron variant was still associated with significant 90-day mortality rate.

COVID-19 INFECTION AMONG HAEMODIALYSIS PATIENTS - EXPERIENCE FROM A HONG KONG COHORT

Zi Chan, Ka Lok Chan, Chi Kwan Lam, Way Ping Law, Wai Lun Will Pak, Yick Hei Wong and Sunny Sze-Ho Wong

United Christian Hospital, Renal Unit, Department of Medicine, Hong Kong, P.R. China

Background and Aims: Many haemodialysis patients were infected by COVID-19 during a severe wave of outbreak due to the Omicron variant in Hong Kong in 2022, which had a great impact on the hospital haemodialysis service. To better prepare for future outbreaks, the patient characteristics and outcomes were examined in this study.

Method: This was a retrospective cohort study of all haemodialysis patients infected with COVID-19 from February to April 2022 in our hospital. The infection rates of in-centre and home haemodialysis were analysed. The mortality rate and the rate of moderate to severe disease (as defined by requiring 2L of oxygen or above) were recorded. Factors affecting mortality and disease severity were analysed using Fisher’s exact test and independent t test.

Abstracts

Figure 1: Cox regression analysis survival curves of MHD patients infected with Delta vs. Omicron variants. Mortality over time was higher in the Delta group in a model that incorporated age and sex in addition to SARS-CoV-2 variant (p = 0.04).
Results: There were ninety-nine haemodialysis patients infected with COVID-19 during the study period (Table 1). The infection rate of in-centre haemodialysis patients was 98/232 (42.2%) compared with 1/19 (5.3%) of home haemodialysis patients. The mortality rate was 7.1%, and the rate of moderate to severe disease was 10.1%. A higher Charlson Comorbidity Index was identified as the only significant factor associated with mortality (6.7±3.4 vs. 4.9±2.0) and disease severity (6.5±3.0 vs. 4.9±2.0). Age, gender, presence of diabetes mellitus and vaccination status did not correlate with the outcome in this cohort.

Conclusion: Home haemodialysis had the benefit of a lower infection rate during the COVID-19 outbreak. A higher burden of comorbidities increased the risk of mortality and the severity of COVID-19. Close monitoring is warranted in these groups of haemodialysis patients.

Table 1: Baseline characteristics of the cohort.

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</table>

At least 2 doses of vaccine* 36.4%

*Either 2 doses of Biotech or 2 doses of Sinovac

Results: Physical frailty and depressive symptoms were prevalent in 268 (65.5%) and 143 (35.0%) of the population, respectively. Physical frailty and depressive symptoms were present in 103 people (25.2%). 129 (31.5%) people died during the follow-up period (median 49 months). In all patients, Cox regression analysis revealed that physical frailty and no depressive symptoms (hazard ratio [HR], 1.86; 95% confidence interval [CI], 1.01–3.44) and coexistence of physical frailty and depressive symptoms (HR, 2.30; 95% CI, 1.23–4.28) were significantly associated with an increased risk of death. In the ≤75-year-old group, a combination of physical frailty and depressive symptoms was significantly associated with an increased risk of death (HR, 2.45; 95% CI, 1.23–4.88). In the ≥75-year-old group, however, combined physical frailty and depressive symptoms were not significantly associated with mortality (HR, 2.06; 95% CI, 0.34–12.55), whereas C-reactive protein was (HR, 1.59; 95% CI, 1.10–2.28).

Conclusion: Physical frailty and depressive symptoms were common in HD patients. In terms of prognosis, the coexistence of physical frailty and depressive symptoms were linked to mortality in the ≤75-year-old group, whereas in the ≥75-year-old group, the coexistence of physical frailty and depressive symptoms was not associated with death, but higher inflammation was associated.

#4818

IMPACT OF COMBINED PHYSICAL FRAILTY AND DEPRESSIVE SYMPTOMS ON MORTALITY IN PATIENTS ON HEMODIALYSIS

Asumi Tobita1, Keigo Imamura1,2, Shun Yoshikoshi1,3, Juri Uchida1, Takuya Nakajima1, Narumi Fukuzaki1, Sayaka Nikkawa1, Manae Harada3 and Atsuhiko Matsumaka1

1Kitasato University Graduate School of Medical Sciences, Department of Rehabilitation Sciences, Sagamihara, Japan, 2Tokyo Metropolitan Institute of Gerontology, Japan and 3Sagami Circulatory Organ Clinic, Department of Rehabilitation, Japan

Background and Aims: Patients receiving hemodialysis (HD) are getting older, with 38.8% of patients in Japan being 75 years or older. HD patients also have multiple comorbidities, which are known to be associated with poor clinical outcomes, especially in the older patients. Moreover, physical frailty and depressive symptoms in HD patients and these are known to be risk factors for poor prognosis. However, it is unclear whether the coexistence of physical frailty and depressive symptoms contributes to an increased risk of mortality in older patients with multiple comorbidities. As a result, the goal of this study was to look at the relationship between physical frailty and depressive symptoms and mortality in HD patients of different ages.

Method: This study included 409 Japanese outpatients with HD (mean age 65.9 years, 62.6% male, and 2.0 years of hemodialysis history). Slow walking speed and/or weak hand grip strength were used to define physical frailty. The Center for Epidemiological Studies-Depression scale was used to assess depressive symptoms. Patients were divided into four groups: (1) no depressive symptoms, no physical frailty; (2) depressive symptoms, no physical frailty; (3) no depressive symptoms, physical frailty; and (4) depressive symptoms, physical frailty. All-cause mortality was the outcome; Cox regression analysis was performed, with analysis stratified by age group (<75 years, ≥75 years) to examine differences by age.

Results: Physical frailty and depressive symptoms were prevalent in 268 (65.5%) and 143 (35.0%) of the population, respectively. Physical frailty and depressive symptoms were present in 103 people (25.2%). 129 (31.5%) people died during the follow-up period (median 49 months). In all patients, Cox regression analysis revealed that physical frailty and no depressive symptoms (hazard ratio [HR], 1.86; 95% confidence interval [CI], 1.01–3.44) and coexistence of physical frailty and depressive symptoms (HR, 2.30; 95% CI, 1.23–4.28) were significantly associated with an increased risk of death. In the ≤75-year-old group, a combination of physical frailty and depressive symptoms was significantly associated with an increased risk of death (HR, 2.45; 95% CI, 1.23–4.88). In the ≥75-year-old group, however, combined physical frailty and depressive symptoms were not significantly associated with mortality (HR, 2.06; 95% CI, 0.34–12.55), whereas C-reactive protein was (HR, 1.59; 95% CI, 1.10–2.28).

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Table 1: Association between combined of physical frailty and depressive symptoms and All-cause mortality.

<table>
<thead>
<tr>
<th>Combined of depressive symptoms and physical frailty</th>
<th>All</th>
<th>≤75 years group</th>
<th>≥75 years group</th>
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<tr>
<td>(1) No depressive symptoms, no physical frailty</td>
<td>Reference</td>
<td>0.52 (0.15–1.75)</td>
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<tr>
<td>(2) Depressive symptoms, no physical frailty</td>
<td>1.00 (0.44–2.27)</td>
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<td>(3) No depressive symptoms, physical frailty</td>
<td>1.86 (1.01–3.44)</td>
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<td>(4) Depressive symptoms, physical frailty</td>
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<td>CRP</td>
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HR: hazard ratio, CI: confidence interval, CRP: C-reactive protein

Adjust for age, sex, body mass index, hemodialysis vintage, comorbidity score, serum albumin and C-reactive protein.

#6691

COMPREHENSIVE TWO-DAY IN-HOSPITAL ASSESSMENT MODE IS ASSOCIATED WITH THREE-YEAR AND FIVE-YEAR MORTALITY IN PERITONEAL DIALYSIS PATIENTS

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West China Hospital of Sichuan University, P.R. China

Background and Aims: The study aims to explore the relationship between a "comprehensive 2-day in-hospital assessment management mode" (C2IAMM) and survival and technical survival rates of patients undergoing peritoneal dialysis (PD).

Method: Eight hundred and thirty PD patients were retrospectively analyzed from January 1, 2011, to October 31, 2017. The "C2IAMM" includes admitting patients undergoing PD to the hospital for 2 days for various assessments. Based on these results, comprehensive interventions were provided. The 1-year, 3-year and 5-year survival and technical survival rates of patients following the C2IAMM were analyzed, and subgroup analysis were further performed.

Results: The 830 PD patients following C2IAMM achieved 1-year, 3-year and 5-year survival rates of 98.0%, 91.4% and 84.3%, respectively; the corresponding technical survival rates were 97.1%, 87.1% and 80.5%. The subgroup analysis showed that age ≥60 years, diabetes mellitus, cardiovascular and cerebrovascular diseases, and respiratory diseases (all P < 0.001) were associated with survival.

Conclusion: This article implies that the C2IAMM may be associated with higher survival and technical survival.

Table 1: Association between combined of physical frailty and depressive symptoms and All-cause mortality.

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HR: hazard ratio, CI: confidence interval, CRP: C-reactive protein

Adjust for age, sex, body mass index, hemodialysis vintage, comorbidity score, serum albumin and C-reactive protein.
Figure 1: Flow chart of C2IAMM.

Figure 2: Kaplan–Meier curves were used to observe patient survival and peritoneal dialysis (PD) technical failure rates. On the patient survival curve, the event is death. On technical survival 1 curve, the event is transfer to hemodialysis. On technical survival 2 curve, the events are transfer to hemodialysis and death. On technical survival 3 curve, the events are transfer to hemodialysis, death and kidney transplantation.
ASSOCIATION OF CONSTIPATION, MICROBIAL TRANSLOCATION, AND INFLAMMATION IN HD PATIENTS
Yu-Kang Chang1 and Paik Seong Lim2

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Background and Aims: Increased gut permeability and intestinal dysbiosis may contribute to chronic inflammation, leading to accelerated atherosclerosis and cardiovascular complications in patients on haemodialysis (HD). Constipation is highly prevalent in HD patients and growing evidence suggested constipation can aggravate gut microbiota dysbiosis and gut inflammation. The aim of this study was to evaluate the association between markers of microbial translocation, intestinal permeability and inflammation in HD patients with and without constipation.

Method: A cross-sectional, observational study was conducted and 200 stable prevalent HD were enrolled. Serum zonulin, eotaxin-1, amyloid A, intestinal fatty acid-binding protein (iFABP), IL-6, endotoxin core antibodies (EndoCAb) and lipopolysaccharide binding protein (LBP) levels were measured. Functional constipation was defined according to the Rome IV criteria.

Results: Serum levels of zonulin and eotaxin-1 but not LPS, endo-Cab IgG, amyloid A and IL-6 were significantly higher in HD patients with constipation than in non-constipated HD controls. The multiple logistic regression analysis in constipated HD patients after adjustment for age, and BMI demonstrated that serum zonulin and eotaxin-1 were independently associated with constipation with an odds ratio (OR) of 1.24 (95% CI = 1.09-1.42, p = 0.0016) and 1.02 (95% CI = 1.01-1.03, p = 0.0001), respectively.

Conclusion: We demonstrate that there was association between serum eotaxin-1 and zonulin levels in constipated HD patients. This may indicates that increased intestinal inflammation or intestinal permeability in these patients but the significance of these findings need further investigation.

#3182
IT FOLLOWS: THE EFFECTS OF COVID ON THE INCIDENCE OF OPTIMAL RENAL REPLACEMENT THERAPY YEARS AFTER ITS ONSET
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La Fe University and Politechnic Hospital, Valencia, Spain

Background and Aims: Patients with advanced chronic kidney disease and those on dialysis have had increased morbidity and mortality in relation to COVID infection. However, patients who did not contract the infection also suffered its effects; since the lack of face-to-face consultations and the impossibility of going to the Emergency Department during the pandemic had negative results on the care of these patients’ kidney condition.

Method: We present a single-center retrospective observational study of a cohort of 423 patients that were discharged from the ACKD clinic from the start of 2018 to the end of 2022 to initiate renal replacement therapy. We recorded whether the initiation had been optimal or not, defining non-optimal renal replacement therapy as patients who had:
• Initiated RRT due to an acute decompensation of their underlying disease that required hospitalization.
• Initiated hemodialysis through a central venous catheter instead of an arteriovenous fistula, because the access was not mature yet or otherwise unavailable.
• Had to change their preferred form of renal replacement therapy because of rapid decompensation.
• Chose conservative management, but died without benefiting from home medical and nursing care.
We also collected their age, cardiovascular risk factors (hypertension, diabetes mellitus, dyslipidemia, obesity and smoking), initial preferred therapy, actual

Table 1: The content of the 2-day in-hospital evaluation management mode.

<table>
<thead>
<tr>
<th>Day of admission</th>
<th>Project</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission assessment</td>
<td>Symptoms and complications: nausea, vomiting, constipation, sleep, etc. Vital signs: body temperature, heart rate, respiratory rate, blood pressure records, weight changes. Dialysis status: dialysis mode, exchange capacity/frequency, dialysate type, ultrafiltration rate, infusion and drainage speed, exudate properties, and catheter outlet status.</td>
<td></td>
</tr>
<tr>
<td>Sample collection and auxiliary examination</td>
<td>Sample collection training: explain the collection method for blood, dialysate and urine samples to the patients. Laboratory test Results: pay attention to routine test indicators according to the patients’ conditions. According to the patient’s condition, chest X-ray and cardiac color Doppler ultrasound should be performed as appropriate.</td>
<td></td>
</tr>
<tr>
<td>Dialysis adequacy test</td>
<td>Blood, urine and peritoneal dialysis fluid samples collected for balance test and adequacy test (Kt/V)</td>
<td></td>
</tr>
<tr>
<td>Communication</td>
<td>Address the existing doubts and questions of the patients and their families and teach patients how to implement the methods and monitor for complications. For patients of ethnic minorities who live far away from home, nurses will coordinate relevant language experts in advance to assist with communication.</td>
<td></td>
</tr>
<tr>
<td>The day after admission</td>
<td>Evaluate solute removal and capacity balance According to the PD evaluation test results, evaluate the solute clearance and volume balance of the patients, consult with doctors to formulate dialysis prescriptions for the patients, and track and determine the reasons for insufficient solute clearance or overload of volume.</td>
<td></td>
</tr>
<tr>
<td>Nutritional assessment and guidance</td>
<td>The nutritional assessment includes diet record assessment, skinfold thickness, grip strength, body composition analysis, hemoglobin, albumin, and SGA. Dietitians will guide and plan diets for patients according to their nutritional assessment results.</td>
<td></td>
</tr>
<tr>
<td>Replacement of the external catheter</td>
<td>According to the operational recommendations for PD, patients who have had the same external catheter for 6 months and patients with external catheter dysfunction should undergo catheter replacement and assessed.</td>
<td></td>
</tr>
<tr>
<td>PD knowledge and operation training</td>
<td>PD patients who cannot perform standard PD operations will receive health education on capacity balance, water and salt control, prevention and treatment of complications, and medication guidance based on the problems identified.</td>
<td></td>
</tr>
</tbody>
</table>
RRT, reason of non-optimal therapy and whether there had been an intercurrent COVID infection at the time of initiation.

Results: We analyzed 423 patients that had chosen a preferred RRT (16.8% chose conservative therapy and were treated by home care services, 34% initiated hemodialysis through an AVE, 27.4% initiated dialysis through a permanent central venous catheter, 5.2% through a temporal CVC, 13.5% initiated peritoneal dialysis, 1.7% died before initiating their preferred technique and 1.4% underwent a preemptive kidney transplant). The patients that initiated hemodialysis before the pandemic started had a significantly lower risk (p<0.001) of starting RRT in a non-optimal manner (HR 0.514 [95% CI 0.341-0.775] compared to those after the pandemic. Of the cardiovascular risk factors, only diabetes mellitus was significantly associated with non-optimal RRT (p<0.005). Patients without diabetes had significantly less risk of substandard RRT initiation (HR 0.561 [95% CI 0.373-0.849]). Patients with COVID at the time of starting renal replacement therapy had a significantly higher risk of beginning it in a non-optimal way (p<0.013). Age had no statistically significant relation to optimal RRT. The most frequent reason for non-optimal RRT was an acute decompensation that required hospitalization, which accounted for 62% of the patients. 9.6% had a catheter inserted even though they were arteriovenous fistula carriers, and 9% had to change techniques. As for the rest, they chose conservative management but died without home care or two or more reasons were named.

Conclusion: The incidence of COVID has decreased since the early years of the pandemic, and the effects of the virus are less lethal thanks to vaccines. However, the harmful effects of the pandemic on the care of renal patients and the evolution of their disease are still present, as it is shown by the result of our study. We should be especially mindful of patients with diabetic disease and undergoing a covid infection, because these factors may precipitate non-optimal renal replacement therapy initiation.

#2974

SERUM CHEMOKINE CC-MOTIF LIGAND 17 IS A PREDICTIVE MARKER OF SEVERE COVID-19 IN HAEMODIALYSIS PATIENTS

Hiroko Beppu1,2, Tatsuya Fukuda3,4, Naoya Otsubo1, Tomoko Kawanishi3, Toshiie Ogawa1, Yasutomo Abe1, Mariko Endo1, Tomohide Hanawa1, Chise Sugita3, Shuji Hatakeyama5,6, Tetsuya Yamada5 and Sachiko Wakai1

1Tokyo Metropolitan Okubo Hospital, Nephrology, Shinjuku, Japan, 2Niigata University, Cooperative Graduate School, Graduate School of Medical and Dental Sciences, Niigata, Japan, 3Tokyo Medical and Dental University, Molecular Endocrinology and Metabolism, Graduate School of Medical and Dental Sciences, Bunkyo, Japan, 4Tokyo Metropolitan Okubo Hospital, Endocrinology and Metabolism, Shinjuku, Japan, 5Tokyo Metropolitan Okubo Hospital, Pulmonary Medicine, Shinjuku, Japan and 6Jichi Medical University Hospital, General Internal Medicine/Infectious Diseases, Shimotsuke, Japan

Background and Aims: Maintenance haemodialysis (HD) patients are at higher risk for severe coronavirus disease 2019 (COVID-19). Because of a limited number of facilities that can provide inpatient treatment for COVID-19 and HD, it is important to identify HD patients who are at high risk for severe COVID-19. For mild to moderate COVID-19 patients, chemokine CC-motif ligand 17 (CCL17) was reported to be a predictive marker for severe COVID-19; however, the validity of CCL17 among HD patients is unknown.

Method: This retrospective observational study enrolled 107 HD patients with mild or moderate COVID-19 at hospitalisation (mean age 70.1±15.1 years; 71.0% male). Receiver operating characteristic and logistic regression analyses were used to examine the predictive validity of indices for severe COVID-19 which is defined as partial pressure of oxygen/fraction of inspired oxygen (P/F) ratio <300 or SpO2 <94%. Multi-variate logistic regression models were used to investigate the association of CCL17 level with the development of severe COVID-19. Furthermore, to evaluate the degree of improvement in predicting performance in the pre-existing model with the addition of CCL17 compared to the pre-existing model, we calculated net reclassification improvement (NRI) and the integrated discrimination improvement (IDI).

Results: During hospitalisation, 32 patients developed severe COVID-19. Serum CCL17 collected at admission exhibited a higher area under the curve value (0.818) compared with that of other indicators including LDH and C-reactive protein for the prediction of severe COVID-19. The optimal cut-off value for CCL17 was 150.5 pg/ml. A multi-variate logistic analysis revealed that CCL17 (above 150.5 pg/ml) was significantly associated with severe COVID-19 (Odds ratio, 0.063; 95% Confidence interval [CI], 0.017–0.227; P<0.001) even after adjustment for covariates. The addition of the CCL17 to a model consisting of vaccination status, albumin, blood urea nitrogen, C-reacting protein and lactate dehydrogenase, that are variables incorporated in multivariate logistic model, significantly improved classification performance for severe COVID-19 using the NRI (1.16, 95% CI: 0.82–1.50, P<0.001) and IDI (0.18, 95% CI: 0.09–0.26, P<0.001).

Conclusion: CCL17 levels in HD patients with mild or moderate COVID-19 predict risk of developing severe COVID-19.
#4261

**RELATIONSHIP BETWEEN FLUID OVERLOAD AND AVERAGE PLASMA REFILL RATE IN HEMODIALYSIS PATIENTS**

Lin-Chun Wang1, Ariella Mermelstein1,2, Jochen Raimann1,2, Ulrich Moissl3, Hanjie Zhang4, Stephan Thijssen1 and Peter Kotanko1,4

1Renal Research Institute, New York, United States of America, 2Katz School of Science and Health at Yeshiva University, New York, United States of America, 3Fresenius Medical Care, Bad Homburg vor der Höhe, Germany and 4Icahn School of Medicine at Mount Sinai, New York, United States of America

**Background and Aims:** Attaining the optimal balance between achieving adequate volume removal while preserving organ perfusion remains challenging in patients on maintenance hemodialysis (HD). Quantification of fluid status using bioimpedance spectroscopy (BIS) has become routine in many countries. Inadequate vascular space refill from the interstitial tissue (plasma refill rate, PRR) is the main contributing factor of hemodynamic instability during HD. We aimed to explore the association between fluid overload (FO) and plasma refill rate (PRR) in chronic HD patients.

**Method:** Pre-HD FO [l] was assessed once per subject by BIS (Body Composition Monitor; Fresenius Medical Care) in four urban HD dialysis clinics in the U.S. For each treatment within 30 days before and after the BIS measurement, we calculated the respective pre-HD FO by assuming that differences in pre-HD body weight were equivalent to differences in FO. We then used intradialytic hematocrit (measured with the Crit-Line® Monitor, Fresenius Medical Care) and ultrafiltration data to quantify the average PRR, normalized by body weight (Wang et al. Kidney360, 2023): To calculate the starting blood volume (BV), we first calculated the ending BV using the Nadler equation, followed by back-calculating the starting BV based on the cumulative change in relative BV. Plasma refill volume was calculated as the sum of the changes in blood volume and ultrafiltration volume; plasma refill volume was then divided by treatment time and estimated clinical dry weight to calculate the PRR [ml/kg/hr].

**Results:** We analyzed 746 HD sessions from 79 patients (age 61±15 years; 52 (66%) males; 41 (52%) black and 33 (42%) white). Across all HD sessions, PRR was positively associated with FO (slope estimate 0.92 (95% confidence interval 0.83 to 1.02) ml/kg/hr per 1 l of FO, P value < 0.0001) (Figure 1). This was also the case in subgroup analyses of fluid depleted (r = 0.94, P<0.001), normohydrated (r = 1.03, P<0.0001), and fluid overloaded subjects (r = 0.83, P<0.0001).

**Conclusion:** Across the entire fluid status spectrum, from fluid depletion to fluid overload, higher FO was associated with higher PRR on average (overall, an increase of 0.92 ml/kg/hr in PRR for each additional liter of FO). While patients with greater FO would be expected to better tolerate higher ultrafiltration rates, there is large inter-individual variability in PRR. Further investigation of the utility of PRR throughout HD may offer novel insights into fluid management and intradialytic symptom mitigation.

#4597

**REDUCED VO2PEAK IN PATIENTS WITH END-STAGE RENAL DISEASE: UNVEILING THE HIDDEN IMPLICATION OF CEREBRAL AND MUSCULAR HEMODYNAMICS**

Amal Machfer1, Semah Tagougui2, Hayfa Hadd Hassen1, Nadia Fekih3, Hassen Ibn Hadj Amor1, Mohamed Amine Bouzid4 and Hamdi Chtourou1

1University of Sfax, High Institute of Sport and Physical Education, Sfax, Tunisia, 2University of Lille, France and 3Faculté de Medicine, Université de Monastir, Monastir, Tunisia

**Background and Aims:** Aerobic fitness, as reflected by maximal oxygen (O2) uptake (VO2peak), is impaired in chronic kidney disease (CKD) patients. The mechanisms underlying this impairment remain to be explored. This study aimed to investigate whether CKD influence O2 supply including O2 delivery and release to the brain and active muscles during maximal physical exercise.

**Method:** Twenty three male undergoing dialysis therapy (HD group) and twenty three healthy males (CTR group) performed exhaustive incremental exercise to determine VO2peak. Throughout the exercise, near-infrared spectroscopy allowed investigation of changes oxyhemoglobin (O2Hb), deoxyhemoglobin (HHb), and total hemoglobin (THb) in the prefrontal cortex and in the vastus lateralis muscle.

**Results:** VO2peak was significantly lower in HD group compared to CTR. Muscular ΔHHb changes was impaired in HD patients (Figure 1). Increase in ΔTHb (i.e., muscle blood volume) was significantly blunted in HD in both muscular and cerebral side (Figure 1 and 2). A positive correlation has been observed between VO2peak and muscular blood volume (ΔTHb) for both groups.

**Conclusion:** HD patients displayed lower VO2peak that could be linked, in part, to impaired muscular hemodynamics responses during the exercise. Furthermore, reduced exercise muscle and brain blood volume may warm clinicians of brain endothelial or microcirculation dysfunction in HD population occurring even before overt microangiopathy.
Figure 1: Recordings made by NIRS from the vastus lateralis change in $\Delta O_2$Hb (A), $\Delta$HHb (B) and $\Delta$THb (C). Values are means ±SD. HD, black triangles; CTRL, white triangles. *p < 0.05 vs baseline † p < 0.05 vs. HD.
TUMOR NECROSIS FACTOR RECEPTOR 2 POLYMORPHISM (RS1061622) AND INFLAMMATORY RESPONSE IN END-STAGE RENAL DISEASE PATIENTS UNDER DIALYSIS

Susana Coimbra1,2,3, Susana Rocha1,3, Cristina Catarino1,3, Maria João Valente4, Petronila Rocha-Pereira1,3,4, Maria Do Sameiro Faria1,3,6, José Gerardo Oliveira7,8, José Madureira1, João Fernandes9,10, Vasco M.P. Miranda11, Elsa Bronze-Da-Rocha1,3, Luís Belo1,3 and Alice Santos-Silva1,3

1UCIBIO – Applied Molecular Biosciences Unit, Department of Biological Sciences, Faculdade de Farmácia da Universidade do Porto, Porto, Portugal, 2TOXRUN – Toxicology Research Unit, University Institute of Health Sciences, CESPU, Portugal, 3Associate Laboratory i4HB - Institute for Health and Bioeconomy, Faculdade de Farmácia da Universidade do Porto, Porto, Portugal, 4National Food Institute - Technical University of Denmark, Kgs Lyngby, Denmark, 5Health Science Research Centre, University of Beira Interior, Portugal, 6Hemodialysis Clinic Hospital Agostinho Ribeiro, Portugal, 7Hemodialysis Clinic of Porto (CHP), Portugal, 8Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Portugal, 9NefroServe, Hemodialysis Clinic of Barcelos, Portugal, 10NefroServe Hemodialysis Clinic of Viana do Castelo, Portugal and 11Hemodialysis Clinic of Gondomar, Porto, Portugal

Background and Aims: Enhanced levels of soluble tumor necrosis factor receptor 2 (sTNFR2) are known to associate with progressive chronic kidney disease (CKD), and is pointed as a potential biomarker for early detection of CKD; moreover, it has been reported as an independent predictor of all-cause mortality in end-stage renal disease (ESRD) patients under dialysis. Despite the increase in TNFR2 and in other inflammatory markers, recognized as risk factors for mortality in dialysis patients, the hypothesis that genetic polymorphisms of those biomarkers might modulate the inflammatory response and, thereby, the patients’ survival predisposition, has been poorly studied.
Concerning TNFR2 genetic variants, a single nucleotide polymorphism in TNFR2 (rs1061622), that results in amino acid change at position 196 (Met/Arg), was associated with higher levels of sTNFR2 in inflammatory conditions. The aim of this study was to determine the allelic frequencies of TNFR2 in ESRD patients and controls, and to evaluate its relationship with the circulating levels of inflammatory biomarkers.

**Method:** We studied 277 ESRD patients on dialysis and 32 controls, matched for gender, body mass index, and, as far as possible, for age. Real time PCR TaqMan SNP genotyping assay was used to assess allelic frequencies of TNFR2 (rs1061622). We also evaluated the circulating levels of TNF-alpha, sTNFR2, ferritin, hepcidin, elastase and cell-free DNA (cfDNA). Deaths occurring along 1-year follow-up period were recorded and mortality rates were assessed.

**Results:** ESRD patients presented higher levels of all studied biomarkers, as compared to controls; their overall mortality rate was 10.5%. Allelic frequencies in ESRD patients and controls were similar for sTNFR2, considering the homozygous and heterozygous individuals ($\chi^2$, $p = 0.518$). Concerning sTNFR2 values, no significant differences were observed between patients with genotypes TT, GG or TG. The GG genotype patients, compared to TT genotype carriers, presented significantly lower ferritin ($p = 0.048$), hepcidin ($p = 0.038$), elastase ($p = 0.006$) and cfDNA levels ($p = 0.016$); and compared to TG genotype patients, showed significantly lower ferritin ($p = 0.039$) and a trend towards lower values of hepcidin ($p = 0.097$), elastase ($p = 0.079$) and cfDNA ($p = 0.0164$). TG genotype patients showed higher TNF-alpha ($p = 0.049$) and a trend towards lower elastase ($p = 0.081$) than TT genotype subjects. The GG genotype patients presented a trend towards lower mortality rate (6.3%, 7.5%, and 12.4% for GG, TG and TT, respectively).

**Conclusion:** No differences were found in the allelic frequencies between controls and ESRD patients. The GG genotype patients for TNFR2 rs1061622 polymorphism decreased levels of inflammation, suggesting a more favorable inflammatory response, which is usually associated to a lower mortality risk in these patients. In accordance with the scientific community, recommending studies on genetic survival predisposition in dialysis patients, the polymorphisms of TNFR2 and of other inflammatory biomarkers deserve further studies. Acknowledgement: This work was financed by CESPU, through the project SNPsCKD-GI2-CESPU-2022; FCT, through the project UIDP/04378/2020 and UIDB/04378/2020 of the Research Unit on Applied Molecular Biosciences—UCIBIO and the project LA/P/0140/2020 of the Associate Laboratory Institute for Health and Bioeconomy—i4HB.

#5019
**MORTALITY FOR COVID-19 IN UNDERGOING MAINTENANCE DIALYSIS PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background and Aims:** Since December 2019, patients undergoing maintenance dialysis have been significantly affected by COVID-19, facing higher risk of death than general population. However, current evidences assess the mortality of patients with COVID-19 remains incomplete. We performed meta-analyses of overall mortality in dialysis patients after SARS-CoV-2 infection. In addition, this study investigated the differences among different races, viral variants, hemodialysis and peritoneal dialysis with COVID-19. At the same time, the mortality rate of dialysis patients with the COVID-19 after vaccination was also observed.

**Method:** We performed a meta-analysis with literature searching in PubMed, EMBASE, Web of Science and Cochrane databases, published between December 1, 2019 and January 10, 2023. Two authors separately screened the titles and abstracts of the documents and ruled out irrelevant articles. Fixed effects model and random effects model were used for calculating heterogeneity.

**Results:** A total of 83 studies included 7278 died from confirmed COVID-19 cases in a pool of 42925 dialysis patients. Overall mortality of COVID-19 in dialysis patients was 22% (95% Confidence Interval [CI]: 19%-25%, $p < 0.01$; $I^2 = 96.74$%) from 2020 to 2022. In subgroup analysis, compared with ancestral COVID-19 (23%, 95% CI: 20%-25%, $p < 0.01$; $I^2 = 93.93$%) and alpha variant (30%, 95% CI: 21%-54%, $p < 0.01$; $I^2 = 95.35$%), omicron variant (4%, 95% CI: 0-14%, $p = 0.09$; $I^2 = 0$) had a lower mortality significantly ($p < 0.01$; $I^2 < 0.01$). The mortality for Asian and non-Asian were 20% (95% CI: 16%-25%, $p < 0.01$; $I^2 = 96.6$%) and 24% (95% CI: 20%-27%, $p < 0.01$; $I^2 = 96.32$%) respectively. The odds of death for maintenance hemodialysis and peritoneal dialysis were similar (odd ratio [OR] 1.30, 95% CI: 0.88-1.93, $p = 0.191$; $I^2 = 0$). Furthermore, we also compared vaccination with unvaccination, and found out that vaccination was associated with lower mortality (OR = 0.18, 95% CI: 0.11-0.28, $p < 0.01$; $I^2 = 71.4$%) (Figure 2).

**Conclusion:** Patients undergoing maintenance dialysis with COVID-19 have a higher mortality. These findings suggest that the mortality of omicron variant may be lower than other variants. In our study, there’s no significant difference in mortality between hemodialysis and peritoneal dialysis patients with COVID-19. Moreover, vaccines have a good protective effect on dialysis patients.
ASSOCIATION BETWEEN MODIFIED CREATININE INDEX AND MORTALITY IN PATIENTS UNDERGOING HEMODIALYSIS: A STRATIFIED ANALYSIS IN DIABETES MELLITUS

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Background and Aims: Protein-energy wasting, including muscle atrophy, is one of the most frequently reported problems in patients undergoing hemodialysis. A decline in muscle mass leads to limitation and worsening of physical function and is associated with frailty, disability, and decreased survival. Modified creatinine index was used as a marker of lean body mass. Additionally, a longitudinal study revealed that a decrease in the modified creatinine index over time was independently associated with an increased risk of death in patients undergoing hemodialysis. Moreover, the prevalence of diabetes is high among patients undergoing hemodialysis. Diabetes not only leads to reduced skeletal muscle mass but is also a risk factor for cardiovascular events and death among patients undergoing hemodialysis. The relationship between modified creatinine index and mortality can be altered by

Figure 1: Cubic spline of associations between modified creatinine index and hazard ratio in patients undergoing hemodialysis. The red and blue lines indicate the non-diabetic and diabetic groups, respectively. This model was adjusted for age, sex, BMI, vintage, albumin level, and comorbidity scores. The solid line represents the fitted data, and the shaded areas represent 95% confidence intervals. CrI, modified creatinine index.

Table 1: Association between Cr and all-cause mortality by DM status.

<table>
<thead>
<tr>
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<th>HR (95%CI)</th>
<th>P for interaction</th>
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<td>DM group</td>
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<td>Continuous variable</td>
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<td>Non-DM group</td>
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<td>Continuous variable</td>
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<tr>
<td>CrI (per 1 mg/kg/d decrease)</td>
<td>1.33 (1.09, 1.63)</td>
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95%CI, 95% confidence interval; HR, hazard ratio; CrI, modified creatinine index.
the presence of diabetes; however, the effect of diabetes on this relationship among patients undergoing hemodialysis is unclear. This study aimed to examine the association between muscle mass and all-cause mortality in the presence or absence of diabetes, which is highly prevalent in hemodialysis patients.

**Method:** We included 361 outpatients undergoing maintenance hemodialysis treatment in 2013–2021 (mean age, 66.3±12.0 years; 61.0% males). Baseline was defined as the date of the first laboratory data and the modified creatinine index measurements, and participants were followed up from baseline to the date of the event (all-cause death, transfer, or end date of study follow-up [May 2021]). Modified creatinine index was calculated using age, sex, predialysis serum creatinine level, and single-pool Kt/V for urea. The primary outcome was death due to any cause. A Cox proportional hazards regression model was used to examine the association between the modified creatinine index and all-cause mortality. The dose–response association between the modified creatinine index and all-cause death was modeled using a restricted cubic spline model.

**Results:** A significant interaction was found between the presence of diabetes and modified creatinine index (p = 0.04). In the non-diabetic group, a lower modified creatinine index was associated with a higher risk of all-cause death (hazard ratio [HR], 1.33; 95% confidence interval [95% CI], 1.09–1.63), whereas no significant association between modified creatinine index and all-cause death was observed in the diabetic group (HR, 1.00; 95% CI, 0.83–1.20).

**Conclusion:** The modified creatinine index was more strongly associated with all-cause mortality in the nondiabetic group than in the diabetic group. The modified creatinine index is a useful tool for the nondiabetic group, and these results may provide useful information for examining the relationship between skeletal muscle mass and prognosis in patients undergoing hemodialysis.

#3356 COVID-19 PANDEMIC EFFECT ON HOSPITALIZATION OF HEMODIALYSIS PATIENTS

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**Background and Aims:** During the COVID-19 pandemic many facets of our lives were affected, including the healthcare systems worldwide. We aimed to assess the hospitalization rates of hemodialysis (HD) patients with confirmed COVID-19 infection (COVID-19+) versus other patients (i.e., patients with no documented COVID-19 infection in the European Clinical Database (EuCliD®)) in 2020 and their relation to HD patients from the pre-pandemic era in 2019.

**Method:** We included 63,216 HD patients treated in 2019–2020 in NephroCare centers from 23 countries from EuCliD® in the Europe, Middle East, and Africa (EMEA) region. Monthly hospitalization rates (hospital admission per 10,000 patients) were estimated separately for COVID-19+ and other HD patients in 2020, and HD patients treated in 2019, with COVID-19+ status as a time-varying variable. The number of COVID-19 cases and deaths were extracted from data released by the European Commission Joint Research Centre (ECJRC).[1]. The correlation between the monthly hospitalization rates and numbers of COVID-19 cases and deaths in general population (GP) were evaluated.

**Results:** Characteristics of the approximately 42,000-43,000 monthly treated HD patients were comparable between 2019 and 2020 (Table 1). The hospitalization rates were much higher for COVID-19+ HD patients throughout 2020 compared to other HD patients in 2020 and HD patients in 2019. The hospitalization rates were highest in the spring of 2020 for COVID-19+ HD patients. However, in 2020 other HD patients' hospitalization rates were lower than the 2019 HD patients' hospitalization rates. Interestingly the hospitalization rates of other HD patients in 2020 dipped even more below hospitalizations for HD patients in 2019 following the GP pandemic waves (Figure 1). Hospital admission for both COVID-19+ and other HD patients were inversely correlation with the pandemic conditions in GP (Figure 2; spearman correlation coefficients [p] with COVID-19 cases/deaths in GP, -0.77/-0.22 and -0.29/-0.64, respectively, for COVID-19+ and other HD patients).

**Conclusion:** Our study indicated the COVID-19 pandemic had an impact on hospitalization rates of both HD patients with a COVID-19 diagnosis and those patients without a documented COVID-19 infection. Potential reasons of decreased hospitalization rates in patients without a documented COVID-19 diagnosis could be healthcare resource constraints or regarding patient concerns about exposure to COVID-19 in hospital settings [2].

![Figure 1: Monthly hospital admission per 10,000 HD patients in 2019-2020 and incident COVID-19 cases/deaths in general population (GP) in 2020.](image-url)
#4219
NON-INVASIVE ASSESSMENT OF LIVER STIFFNESS, HEPATIC FIBROSIS RISK MARKERS AND OUTCOMES IN A DIALYSIS POPULATION

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**Background and Aims:** People with end stage kidney disease (ESKD) commonly co-exhibit multiple risk factors (type 2 diabetes mellitus, obesity and hypertension) for non-alcoholic fatty liver disease (NAFLD) and its progressive, fibroinflammatory form non-alcoholic steatohepatitis (NASH). NAFLD and NASH both associate with increased risk of fatal cardiovascular events. NASH will additionally soon become the leading cause of cirrhosis both in the UK and worldwide. The cause of systemic inflammation driving early mortality in patients with ESKD is unclear. It is thought that liver disease can contribute to inflammation due to reduced reticuloendothelial function and subsequent penetration of gut-derived toxins into the systemic circulation. Very little is currently known about prevalence of NAFLD and NASH in ESKD, or how these conditions affect patients. By identifying the scale of the risk, this study will help better understand the extent of NAFLD and NASH and their links to clinical outcomes in advanced kidney disease. We report interim results from this study looking non-invasively for liver disease in patients with ESKD.

**Method:** This prospective study involves prevalent patients with ESKD treated with dialysis (for >3 months) at five participating UK kidney centres. Results from this study are derived from analysis of the first 238 patients (final recruitment target 450). A FibroScan® (Echosens) device was used to measure both hepatic steatosis using controlled attenuation parameterography (CAP) and fibrosis using transient elastography. A fibrosis-4 index score was calculated to assess fibrosis risk. These results were supplemented by baseline clinical and radiological data, serum beta-D-glucan levels taken pre- and post-dialysis, clinical assessment of fluid status, and bioimpedance spectroscopy (Fresenius Medical Care). Survival analyses were performed using Kaplan-Meier estimates.

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Hypertension Associates, Bluefield, United States of America, 13 Istanbul, Slovenia, 16 University of Ljubljana, Medical Faculty, Ljubljana, Slovenia, Department of Nephrology, Division of Internal Medicine, Ljubljana, Slovenia, Brigham and Women’s Hospital, Boston, United States of America, Ewa Pawlowicz-Szlarska1, Z. Serhan Tuglular2, Kai-Uwe Eckardt3, Daniel Gallego Zurro4,5, Dmytro Ivanov6, Valerie A. Luyckx7,8, Ionut Nistor9,10, Edita Noruisiene11, Mohamed Sekkarie12, Mehmet Sukru Sever13, Rukshana Shroff14, Andrej Skoberne15,16, Stefano Stuard17, Raymond Vanholder4,18 and Andrzej Jan Wiecek19

Body mass index was 27.8 kg/m². 97% of participants had hypertension, 53% diabetes mellitus and 65% hyperlipidaemia. 231 participant FibroScan scores (97%) were valid (interquartile range <30% over 10 consecutive readings) and available for analysis. 74 participants (31%) had suspected hepatic steatosis of grade S1-S3 and 72 participants (30%) had suspected hepatic fibrosis of grade F2-F4, 53 participants (22%) had suspected F2-F3 fibrosis (moderate fibrosis) and 19 (8%) had suspected F4 fibrosis (advanced fibrosis/cirrhosis). There was increased mortality associated with suspected hepatic fibrosis/steatosis (9.1% absolute risk of mortality with an abnormal CAP or fibrosis score compared to 1.6% in those with normal FibroScan imaging). The majority of mortality in people with suspected hepatic fibrosis was from cardiovascular disease. Overall mortality in participants with suspected hepatic fibrosis remained significant even after adjustment for univariate predictors of survival (median CRP baseline >10 mg/L, age and gender (Figure 1)). Multivariate predictors of survival were Charlson Comorbidity Score and diabetes status.

Conclusion: These results demonstrate a significant burden of suspected hepatic steatosis and hepatic fibrosis in people with ESKD. Suspected hepatic fibrosis assessed by FibroScan imaging is an independent risk factor for mortality based on this interim analysis and strategies to improve liver health in the setting of advanced kidney disease may be of benefit to this group of patients.

#5866

CLINICAL CHARACTERISTICS AND TREATMENT OF ADULT DIALYSIS PATIENTS FROM UKRAINE DISPLACED TO OTHER EUROPEAN COUNTRIES AFTER THE RUSSIAN INVASION

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Background and Aims: The Russian invasion on Ukraine, which started on 24th February 2022 led to migration of millions of people, including some of the about 10,000 adult dialysis patients. A Renal Disaster Relief Task Force (RDRFT) established by the European Renal Association, is dedicated to support the people living with kidney disease and to the nephrology community in Ukraine, working together with WHO, NGOs and industry. Besides these activities, the RDRFT conducted a survey to understand distribution and management of Ukrainian refugees requiring dialysis displaced to other European countries. The study aim was to characterize these patients and evaluate treatment modality and care they received after displacement.

Method: A cross-sectional online survey on status of displaced dialysis patients, clinical data and care they received after migration was sent to all national nephrology societies across Europe with a request to disseminate it to all dialysis centers in their countries. Data were collected between May and August 2022. Fresenius Medical Care (FMC) shared a set of aggregated data without direct center participation.

Results: The mean age of participants was 63 years (67% male). Mean body mass index was 27.8 kg/m². 97% of participants had hypertension, 53% diabetes mellitus and 65% hyperlipidaemia. 231 participant FibroScan scores (97%) were valid (interquartile range <30% over 10 consecutive readings) and available for analysis. 74 participants (31%) had suspected hepatic steatosis of grade S1-S3 and 72 participants (30%) had suspected hepatic fibrosis of grade F2-F4, 53 participants (22%) had suspected F2-F3 fibrosis (moderate fibrosis) and 19 (8%) had suspected F4 fibrosis (advanced fibrosis/cirrhosis). There was increased mortality associated with suspected hepatic fibrosis/steatosis (9.1% absolute risk of mortality with an abnormal CAP or fibrosis score compared to 1.6% in those with normal FibroScan imaging). The majority of mortality in people with suspected hepatic fibrosis was from cardiovascular disease. Overall mortality in participants with suspected hepatic fibrosis remained significant even after adjustment for univariate predictors of survival (median CRP baseline >10 mg/L, age and gender (Figure 1)). Multivariate predictors of survival were Charlson Comorbidity Score and diabetes status.

Conclusion: These results demonstrate a significant burden of suspected hepatic steatosis and hepatic fibrosis in people with ESKD. Suspected hepatic fibrosis assessed by FibroScan imaging is an independent risk factor for mortality based on this interim analysis and strategies to improve liver health in the setting of advanced kidney disease may be of benefit to this group of patients.

#5867

Abstracts i789

SEROREVOLUTION OF COVID-19 INFECTION BASED ON IGG ANTIBODY AGAINST NUCLEOCAPSID PROTEIN (NP) AND SPIKE PROTEIN (S) IN HEMODIALYSIS PATIENTS

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Background and Aims: Maintenance hemodialysis (MHD) patients have been identified as a high-risk group for COVID-19 infection. Serological testing can be used to monitor disease prevalence & evaluate screening measures & protocols aiming at limiting transmission within dialysis units. This study was conducted to observe the sero prevalence of COVID-19 infection among maintenance hemodialysis patients.

Method: The study was conducted during the 3rd wave of covid-19 infection. Total 194 in-center MHD patients were included from three dialysis centers. Relevant history regarding covid-19 symptom, testing, managements and vaccination were collected. During our study a serum sample was collected to test IgG antibody against nucleocapsid protein (NP) (cut-off positive when > 1.5) and spike protein (S) (cut-off positive when > 50 AIU/L) of COVID-19 infection and tested by Chemiluminescent microparticle immunoassay (CMIA) method developed by Abbott (FDA-EUA approved).

Results: Mean age of the MHD subjects was 48±12 years where male was 60%, Duration of MHD was 31±22 (6-120) months. Renal pathology was DN in 31%, possible GN 31%, HTN 19% and rest from others. From records past covid infection was clinically diagnosed in 39% of which 10% based on RT-PCR and another 29% fell into suspected category (i.e. symptom with/or suggestive serology). Presentation pattern was mild in 75%, moderate 15% (requiring oxygen), severe in 5% (requiring hospitalization) and asymptomatic rest 5%. Vaccine against covid-19 was avalied by 38%. In vaccinated vs. non-vaccinated patients the IgG for NP was positive in 63% vs. 561% (P = 0.65) and IgG for S was 99% vs. 98% (P = 0.56). These indicate naturally acquired immunity in most before any vaccination. The IgG titer against spike (S) protein between vaccinated and non-vaccinated groups was 7743±8920 and 5386±6839 AIU/L (p = 0.06). The correlation study showed that IgG titer against S has no correlation with dialysis duration, age, BMI, Hb%, serum albumin or Kt/V. Similarly IgG titer against NP shows mostly no significant correlation with laboratory parameters.
Conclusion: These data demonstrate that seroprevalence in hemodialysis population based on antibody against nucleocapsid protein only half infected by SARS-CoV-2 where as antibody against spike protein indicates larger number of patients are naturally infected even before vaccinated. Therefore for seroprevalence studies both antibody testing should be used to identify greater population infected until more sensitive tools are established.

Background and Aims: Chronic kidney disease (CKD) is a leading cause of morbidity and mortality worldwide, with African descendants being at increased risk of occurrence and progression to end-stage renal disease (ESRD). However, the burden of CKD and ESRD in African continent is still largely conjectural and access to treatment of CKD complications, VA for HD, and vascular access (VA) dysfunction in 6.3% (n=8); these 8 patients with VA dysfunction were already on hemodialysis program before their evacuation to Portugal and they were mainly from Cape Verde (n=4), Angola (n=3), and one patient from Guinea-Bissau. At arrival, patients who initiated HD in our unit had mean serum creatinine 9.4 ± 4.4 mg/dL, urea 182.5 ± 109.1 mg/dL, Hb 9.6 ± 1.7 g/dL, serum albumin 3.6 ± 0.6 g/dL, PTH 491.7 ± 392.6 pg/mL. Patients referred due to VA dysfunction had mean Hb 10.1 ± 1.8 g/dL, serum albumin 3.7 ± 1.0 g/dL, PTH 918.9 ± 541.6 pg/mL. There were no statistically significant differences in both groups concerning country of origin, although hypalbuminemia was more frequent in patients from Saint Thomas and Prince (50%) and Angola (42.9%). All patients started HD with a central venous catheter (CVC). During follow-up, CVC remained the vascular access in 51.6% (n = 65), arteriovenous fistula in 42.9% (n = 54), and arteriovenous graft in 3.6% patients (n = 7). Nine patients had exhaustion of VA for HD. Mean follow-up time was 70.5 ± 41.3 months, 1.6% of the patients transitioned to peritoneal dialysis (n = 2) and 15.1% were submitted to renal transplantation (n = 18). The mortality rate during follow-up was 14.3% (n = 18).

Conclusion: There are few studies about African patients undergoing HD and this is the first study presenting the clinical characteristics and outcomes of hemodialysis patients from ACPOL. These are young patients, almost all with hypertension, with a high prevalence of anemia, malnutrition, and secondary hyperparathyroidism. All patients started HD with CVC and several presented multiple access dysfunction. These data reinforce the urgent need of improvement and investment in African countries' healthcare, especially on what concerns the ESRD, as it contributes to serious consequences in these patients’ survival and quality of life. With the cooperation protocol, Portugal provides these patients with RRT, treatment of the CKD complications, VA care, possibility of peritoneal dialysis and renal transplantation, ultimately improving their chance of survival and quality of life.

#6242

CLINICAL CHARACTERISTICS OF HEMODIALYSIS PATIENTS FROM AFRICAN COUNTRIES OF PORTUGUESE OFFICIAL LANGUAGE: A PORTUGUESE COHORT

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Background and Aims: Chronic kidney disease (CKD) is a leading cause of morbidity and mortality worldwide, with African descendants being at increased risk of occurrence and progression to end-stage renal disease (ESRD). However, the burden of CKD and ESRD in African continent is still largely conjectural and access to treatment of CKD complications, VA for HD, and vascular access (VA) dysfunction in 6.3% (n=8); these 8 patients with VA dysfunction were already on hemodialysis program before their evacuation to Portugal and they were mainly from Cape Verde (n=4), Angola (n=3), and one patient from Guinea-Bissau. At arrival, patients who initiated HD in our unit had mean serum creatinine 9.4 ± 4.4 mg/dL, urea 182.5 ± 109.1 mg/dL, Hb 9.6 ± 1.7 g/dL, serum albumin 3.6 ± 0.6 g/dL, PTH 491.7 ± 392.6 pg/mL. Patients referred due to VA dysfunction had mean Hb 10.1 ± 1.8 g/dL, serum albumin 3.7 ± 1.0 g/dL, PTH 918.9 ± 541.6 pg/mL. There were no statistically significant differences in both groups concerning country of origin, although hypalbuminemia was more frequent in patients from Saint Thomas and Prince (50%) and Angola (42.9%). All patients started HD with a central venous catheter (CVC). During follow-up, CVC remained the vascular access in 51.6% (n = 65), arteriovenous fistula in 42.9% (n = 54), and arteriovenous graft in 3.6% patients (n = 7). Nine patients had exhaustion of VA for HD. Mean follow-up time was 70.5 ± 41.3 months, 1.6% of the patients transitioned to peritoneal dialysis (n = 2) and 15.1% were submitted to renal transplantation (n = 18). The mortality rate during follow-up was 14.3% (n = 18).

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#5794

WHERE DOES THE PATIENT ON CHRONIC RENAL REPLACEMENT TREATMENT DIE?

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Background and Aims: In the last years, the age of patients on maintenance renal replacement treatment (RRT) became higher and higher. In addition, they have an increasing number of serious comorbidities, such as cardiovascular diseases, diabetes, chronic obstructive pulmonary diseases and peripheral vascular disease. Consequently, there was a rise in hospitalization rate for these patients, nearly achieving 1.48 per person-year, in 2020. One out of 11 hospital discharges among End Stage Renal Disease (ESRD) patients in 2020 was followed by death without re-hospitalization within 30 days. The 5-years survival rate for patients in hemodialysis is 40%, with a median lifespan of 47 months [1]. In the clinical practice, nephrologists use to focus on the complex clinical picture of these patients, but rarely they consider them for palliative care [2]. Nephrology community awareness is growing up concerning palliative care and end-of-life issue, taking into account a simultaneous palliative care, for these patients and their families as well [3]. The aim of the study was to investigate the end-of-life treatment of patients on chronic dialysis.

Method: We analyzed data of patients dead on maintenance renal replacement therapy (RRT) in Policlinico A. Gemelli (Rome), in a five years period from January 2018 to January 2023. We collected relevant data from clinical and administrative records. In particular, we focused on demographic data, comorbidities (Figure 1), causes and places of deaths (home, hospital, hospice). We considered place of death as a surrogate indicator of the use of palliative care.

Results: Ninety four out of 623 patients on maintenance dialysis (15%) died in the 5 years of observation, with a mean age of 73.8 ± 8.9 years (median 76 years) and an average dialytic vintage of 5.9 ± 4.5 years (median 4.4 years). Seventy-three patients died on chronic hemodialysis (68.6%) and 24 patients on peritoneal dialysis (22.6%). None of them died from dialysis withdrawal, and we did not stop RRT close to death in any patient. The main cause of
death were cardiovascular diseases (35.6%), followed by sepsis (20.2%) and malignancies (12.5%) (Figure 2). Sudden cardiac death occurred in 7 patients (7.4%), while cachexia in 4 (4.2%). Only 5 patients (4.7%) were considered for palliative care: 4 of them died before the start of palliative treatment and 1 died one month later. Sixty-seven (67.3%) patients died during hospitalization. Only 26 (27.6%) patients died at home and 1% in hospice (n = 1).

**Conclusion:** The high percentage of in-hospital mortality, the low in-hospice mortality and the absence of mortality due to treatment withdrawal, indicate a lacking of end-of-life recognition in RRT patients. Hence, our experience demonstrates that the use of palliative care in patients on chronic dialysis is still poor and underestimated. Therefore, we need an urgent educational program about end-of-life issue for nephrologists, aiming at an earlier multidisciplinary approach, in order to improve patients' quality of life and of their end-life.

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PATIENT ACUTY AND CARDIOVASCULAR OUTCOME IN HEMODIALYSIS PATIENTS: A KOREAN NATIONWIDE COHORT STUDY

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Background and Aims: Patients acuity has been reported to be associated with poor outcome in hospitals. However, the effect of the patient acuity of hemodialysis center on the prognosis of individual patients is not well known. In this study, the association between the severity of illness in hemodialysis facility and major adverse cardiac and cerebrovascular event (MACCE) in patients undergoing hemodialysis was investigated.

Method: 15,633 participants receiving hemodialysis in the primary health care center who participated in the Periodic Hemodialysis Quality Assessment by Health Insurance Review & Assessment Service (HIRA) were examined. The main predictor was severity-to-nurse ratio, defined as a sum of Charlson comorbidity index of all patients divided by the number of nurses in each hemodialysis facility. The primary and secondary outcome were MACCE, and all-cause mortality, respectively.

Results: During a median follow-up of 5.5 years, MACCE and all-cause mortality occurred in 7,966 (51.0%) and 6,536 (41.8%) participants. Participants with higher severity-to-nurse ratio tended to have higher incidence rate of MACCE. The hazard ratios (HRs) of MACCE for the second, third, and highest quartiles compared with the lowest quartile of severity-to-nurse ratio were 1.05 (95% confidence intervals [CI], 0.98-1.11; P = 0.053), 1.07 (95% CI, 1.00-1.14; P = 0.010), and 1.08 (95% CI, 1.00-1.16; P = 0.040). When treating severity-to-nurse ratio as a continuous variable, MACCE risk increased by 1% per 1 increase in severity-to-nurse ratio (HR, 1.01; 95% CI, 1.00 - 1.02; P = 0.003). Compared to the lowest quartile group, the HRs of all-cause mortality for second, third and fourth quartile were 1.12 (95% CI, 1.04-1.19; P = 0.002), 1.11 (95% CI, 1.03-1.19; P = 0.005), and 1.16 (95% CI, 1.07-1.25; P<0.001), respectively.

Conclusion: As the part of the Joint Project on Quality Assessment Research by HIRA, the present study showed that the patient acuity was strongly associated with an increased risk of poor outcomes in hemodialysis patients.

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#4843

EFFECT OF MORNING VACCINATION COMPARED WITH AFTERNOON/EVENING VACCINATION ON HUMORAL RESPONSE TO COVID-19 VACCINE IN HEMODIALYSIS PATIENTS

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Background and Aims: Patients with ESKD who are undergoing hemodialysis have impaired immunogenicity to SARS-CoV-2 vaccination. Age, dialysis vintage, use of immunosuppressive drugs, serum albumin, lymphocyte count, vaccine type, and COVID-19 experience have been identified to be associated with humoral and cellular responses. A recent review highlights that vaccination responses also exhibit circadian rhythmicity. However, the benefits of vaccination in the morning compared with later times in the day among hemodialysis patients remain unclear. Therefore, we aimed to determine if morning vaccination with a COVID-19 vaccine was able to induce a higher antibody response than afternoon/evening vaccination among hemodialysis patients.

Method: We conducted a prospective observational study in the hemodialysis unit of Taipei Tzu Chi Hospital, Taiwan. Prevalent hemodialysis patients were stratified into two groups based on time of vaccination and were followed up for 5 weeks. Data were analyzed using repeated measure ANOVA and chi-square tests.

Results: A total of 171 patients were included (median age, 69 years; 55% men). The median time from the first dose of COVID-19 vaccine was 8 weeks (IQR, 5-12 weeks). The antibody response was significantly higher in the morning group than in the evening group (p = 0.007). The percentage of patients with undetectable antibody response was lower in the morning group than in the evening group (p = 0.017). The percentage of patients with seroconversion was higher in the morning group than in the evening group (p = 0.029). The percentage of patients with high antibody response was higher in the morning group than in the evening group (p = 0.010).

Conclusion: Morning vaccination was associated with higher antibody response and seroconversion compared with evening vaccination in hemodialysis patients.
aged 20 years or over with no history of SARS-CoV-2 infection were eligible for enrollment. Patients were excluded if they had been vaccinated, refused vaccination, had inadequate dialysis, or declined to participate. Patients with current use of immunosuppressants were also excluded. All participants received a priming dose of ChAdOx1 nCoV-19, an adenovirus-vectorized vaccine, on June 16 or 17, 2021 during the hemodialysis session. IgG antibodies to the receptor binding domain (RBD) of the S1 subunit of the spike protein of SARS-CoV-2 were measured using the AdviseDx SARS-CoV-2 IgG II assay (Abbott Laboratories, Abbott Park, IL, USA) at Day 28 and Day 56 after vaccination. The cutoff value for positivity was set at ≥50 arbitrary units per mL (AU/mL) based on manufacturer’s recommendations. Multivariable logistic regression analyses were used to evaluate the relationship between time of day of vaccination and antibody response. Covariates identified by prior studies as significant predictors of vaccine response or with a P value <0.1 between responders and nonresponders were fitted.

**Results:** A total of 201 participants were included, with a male to female distribution of 52% to 48%, a mean age of 67 years, and a median dialysis vintage of 7.7 years. Among the participants, 70 were diazylized in the morning (between 7:00 AM and 12:00 PM), 69 in the afternoon (between 12:00 and 5:00 PM), and 62 in the evening (between 5:00 and 10:00 PM). Overall, 137 (68.2%) participants developed antibodies against the SARS-CoV-2 spike protein after a single dose of ChAdOx1 nCoV-19. The median antibody level was 184.6 AU/mL. In the multivariable model, morning vaccination, age, coronary artery disease, and lymphocyte count independently predicted a humoral response at Day 28. Participants who received morning vaccination were more likely to develop seroconversion compared with those who received afternoon/evening doses (odds ratio 3.81, 95% confidence interval 1.59–9.15; P = 0.003). Anti-spire antibody titers were measured in 198 participants at Day 56. The median antibody level was 153.7 AU/mL. A significantly higher proportion of morning-vaccinated hemodialysis patients remained seropositive (odds ratio 2.54, 95% confidence interval 1.15–5.61; P = 0.021).

**Conclusion:** Our preliminary results showed that circadian rhythms might be harnessed to optimize vaccination strategies for hemodialysis patients. Future studies with larger sample size are required to validate our findings.

**#3882**

**THE PREVALENCE AND EVOLUTIONARY EFFECTS OF FRAILTY IN PERITONEAL DIALYSIS PATIENTS**

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**Background and Aims:** Frailty is an age-related condition that predicts adverse outcomes. The clinical effect of frailty in peritoneal dialysis (PD) patients is unmet. The study was aimed to investigate the clinical implications of frailty in PD patients.

**Method:** In this prospective study, PD patients completed frailty assessment at entry and 6 months by a semiautomated frailty index of 80 risk factors (FI80) which also contained the 5 components of Fried frailty phenotype. A score ≥13/80 (FI80 ≥0.16) or ≥3/5 (frailty phenotype) was designated to define frailty.

**Results:** A total of 337 PD patients were recruited (new-onset 23.4%, prevalent 76.6%). Two hundred (59.3%) and 163 (48.4%) patients were frail by FI80 and frailty phenotype, respectively. Predictors for frailty were old age, dialysis, diabetes mellitus, gout and sleep disorder. New-onset patients aged <55 years displayed the best evolution of frailty over 6 months (stable or improved, n = 29/47, 61.7% by FI80, p = 0.0293), compared with other groups. Survival analysis found that frail patients exhibited the worse outcomes (overall death and hospitalization) than their robust and prefrail counterparts. Poisson regression showed frailty was associated with increased utilisations of outpatient and ER visit; however multivariate Cox models identified only diabetes, gout history and low body mass index (<19kg/m²), but not frailty, predicted overall death and hospitalizations.

**Conclusion:** Our data indicate that frailty is a common medical condition in PD patients, and the status of which can be stabilized or improved in new-onset, young patients at least over the short term. Compared with frailty, certain comorbidities (diabetes and gout history) and undernutrition appeared to be more robust in the prediction of adverse outcomes.
Figure 1: Kaplan-Meier curve mortality analysis according to QOL items. (A) short form-36 (B) ESRD-targeted item score (C) Physical component scale (PCS) score (D) Mental component scale (MCS) score.

Table 1: Associations of QOL items and mortality in Cox regression analysis.

<table>
<thead>
<tr>
<th></th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
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<tbody>
<tr>
<td></td>
<td>HR (95% CI) P value</td>
<td>Model 1 HR (95% CI) P value</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥51.3 (reference)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&lt;51.3</td>
<td>0.74 (0.57-0.95) 0.018</td>
<td>0.81 (0.63-1.05) 0.105</td>
</tr>
<tr>
<td>ESRD</td>
<td></td>
<td></td>
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<tr>
<td>≥66.2 (reference)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&lt;66.2</td>
<td>0.83 (0.62-1.10) 0.195</td>
<td>0.88 (0.66-1.18) 0.390</td>
</tr>
<tr>
<td>PCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥51.5 (reference)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&lt;51.5</td>
<td>0.56 (0.43-0.72) &lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.63 (0.48-0.82) &lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥51.0 (reference)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&lt;51.0</td>
<td>0.92 (0.72-1.18) 0.516</td>
<td>1.01 (0.78-1.30) 0.946</td>
</tr>
</tbody>
</table>

Model 1. adjusted age and sex.
Model 2. Model1 + mCCI.
Model 3. Model2 + Albumin, Creatinine, hs-CRP, Uric acid, and Intact PTH.
Abbreviations: HR, hazard ratio; CI, confidence interval; SF-36, short form-36; ESRD, end stage renal disease targeted items; PCS, physical composite scale; MCS, mental composite scale.
<sup>a</sup>P for trend.

#5268
PREGNANCY OUTCOMES IN DIALYSIS PATIENTS: A TEN-YEAR SERIES FROM A TERTIARY CENTER
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<sup>2</sup>Centro Hospitalar Universitário Lisboa Norte, Gynecology and Obstetrics, Lisboa, Portugal

Background and Aims: Pregnancy in dialysis patients was almost prohibited a decade ago, as fetal and maternal outcomes were very poor. In the last years,
there has been a paradigm shift, as the introduction of intensive hemodialysis (HD) schedules has been associated with an impressive improvement on fetal outcomes, making motherhood a possibility in these women. Nevertheless, pregnancy in women on dialysis remains associated with a high incidence of complications and is extremely demanding for both patients and clinicians.

We describe the maternal, obstetric, and perinatal outcomes of pregnancies in women on dialysis followed at the Nephro-Obstetric Clinic at Centro Hospitalar Universitario Lisboa Norte (CHULN).

**Method:** Retrospective analysis of pregnancies in women on dialysis and surveilled at the Nephro-Obstetric Clinic at CHULN from 2011 to 2022.

**Results:** We considered 17 pregnancies from 16 women. One of the women accounted was submitted to voluntary termination of pregnancy. Mean age was 31.5 ± 6.1 years; 76.6% were Black (n = 11) and 29.4% (n = 5) Caucasian; 58.8% were nulliparous (n = 10). All patients had chronic hypertension (HTN), although only 75.0% were under therapy (12/16). Additionally, 3/16 patients had diabetes and 2/16 hyperthyroidism. The mean of overall renal replacement therapy (RRT) duration was 9.1 ± 8.2 years (dialysis and renal transplantation time), being on dialysis program 43.7 ± 37.5 months before gestation. One patient was on peritoneal dialysis (PD) and two patients started HD during pregnancy. Five patients (31.2%) were exposed to teratogenic drugs during gestation. Pregnancy diagnosis occurred at 13.4 ± 5.6 weeks; 76.6% of the patients were on low dose acetylsalicylic acid (n = 12). HD mean time per week according to each trimester was 13.7 ± 2.8 hours/week, 24.5 ± 7.3 hours/week and 28.0 ± 8.0 hours/week during the 1st/2nd/3rd respectively. Mean pre-dialysis urea was 62.1 ± 28.0 mg/dL during gestation. Regarding maternal outcomes, worsening HTN occurred in 62.5% (n = 10) of patients during the 1st (4/10) and 2nd trimester (7/10) and pre-eclampsia (PE) occurred in 6/16 patients (1 with HELLP syndrome). One patient developed polyhydramnios and another one cholestasis of pregnancy. Premature rupture of membranes (PRM) occurred in 3 patients (at 17, 25 and 36 weeks); One patient asked for medical termination of pregnancy due to severe growth restriction and oligohydramnios at 20 weeks. Stillbirth occurred in 4 gestations (cervical insufficiency in a twin pregnancy, severe congenital fetal cardiopathy in a patient with PE, severe growth restriction and premature rupture of membranes (PRM). In the 2 patients with early PRM, the neonates died in the following week due to severe prematurity complications. Labor was induced in 9 patients, mainly due to PE (7/9). Cesarean was performed in 10/17 patients and mean gestation age at delivery was 29.8 ± 6.6 weeks. Extreme prematurity (<28 weeks) occurred in 3 pregnancies and there were three term babies. Mean birth weight was 1554.0 ±613.6 grams with 4 newborns having extremely low birth weight (<1000g) and 6 requiring neonatal care.

**Conclusion:** Our study reveals that pregnancy in women on dialysis is challenging and still associated with significant maternal, obstetric and perinatal complications. This population was highly heterogeneous, with a significant number of patients living under unfavorable social conditions, and with significant comorbidities. The diagnosis of pregnancy took place mainly during the 2nd trimester, preventing early initiation of intensive dialysis schedules which could have significantly improved outcomes. Pregnancy planning, early diagnosis and management by a multidisciplinary experienced team are of paramount importance to improve outcomes and reduce complications.

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**Background and Aims:** Chronic kidney disease (CKD) is considered a high-stress disease because of its chronicity, co-morbidity, and lifelong treatment. Family members are often the main caregivers of end stage kidney disease (ESKD) patients and they are involved in various roles. Caregivers of ESKD patients experience emotional stress, anxiety and depression as they support their family members throughout the disease and treatment. This cross-sectional study aimed to assess depression and anxiety in caregivers of ESKD patients and to compare these disorders between caregivers of hemodialysis (HD) patients’ and kidney transplant recipients (KTR), as well as to investigate potential social-demographic parameters associated with caregivers’ depression and anxiety.

**Method:** A total of 342 participants (171 couples of patients and caregivers) were recruited. Structured interviews and self-completed questionnaires were obtained from HD patients, KTR (138 HD patients and 33 KTR) and their caregivers. The Beck Depression Inventory and the Generalized Anxiety Disorder-2 scales were used as screening tools. Depression scores were classified into four levels based on the level of severity (low, mild, moderate, severe). The collected data were encoded and analyzed using IBM SPSS version 25 and R Statistical Software.

**Results:** Mean age of caregivers was 58 years and the majority were females (67.2%). Total anxiety score was high (Mdn = 3) with a mildly increased score of depression (Mdn = 9.5). Caregivers’ anxiety and depressive symptoms were significantly associated with gender, duration of caregiving, educational level, financial status, and caregivers’ age (p<0.01 for all). Caregivers’ depression and anxiety were also, related to the type of patients’ treatment (Table 1). HD caregivers reported significantly higher anxiety scores (Mdn = 3(2–5)) in comparison to KTR caregivers (Mdn = 2(2–4)) (p = 0.048) (Table 2). Moreover, HD caregivers revealed higher (Mdn = 11(0–46)) levels of depression than the KTR group (Mdn = 6 (0-25)) (p = 0.049) (Table 3).

**Conclusion:** Based on the findings of this study, the type of ESKD treatment displayed an important role in caregivers’ anxiety and depression symptoms, with KTR caregivers having the best scores. In particular, KTR caregivers appeared to have lower levels of depression and anxiety than caregivers of HD patients.

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**Table 1: Caregivers’ BDI levels and patients method.**

<table>
<thead>
<tr>
<th>BDI level</th>
<th>HD caregivers</th>
<th>KTR caregivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>76, 55.1%</td>
<td>26, 78.8%</td>
</tr>
<tr>
<td>Mild</td>
<td>31, 22.5%</td>
<td>2, 6.1%</td>
</tr>
<tr>
<td>Moderate</td>
<td>22, 15.9%</td>
<td>5, 15.2%</td>
</tr>
<tr>
<td>Severe</td>
<td>9, 6.5%</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>138, 100%</td>
<td>33, 100%</td>
</tr>
</tbody>
</table>

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**#5602 DEPRESSION AND ANXIETY IN FAMILY CAREGIVERS OF END STAGE KIDNEY DISEASE PATIENTS IN GREECE: A COMPARISON BETWEEN DIALYSIS AND KIDNEY TRANSPLANTATION**

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HEALTH-RELATED QUALITY OF LIFE AND SYMPTOM BURDEN IN YOUNGER AND OLDER HAEMODIALYSIS PATIENTS: A PROSPECTIVE COHORT STUDY

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1Leiden University Medical Center, Department of Internal Medicine, Leiden, Netherlands, 2Jeroen Bosch Hospital, Department of Internal Medicine, ’s-Hertogenbosch, Netherlands, 3Amsterdam Cardiovascular Sciences, Amsterdam University Medical Center, Department of Nephrology, Amsterdam, Netherlands, 4University Medical Center Utrecht, Department of Nephrology and Hypertension, Utrecht, Netherlands, 5Deventer Hospital, Department of Internal Medicine, Deventer, Netherlands, 6St. Antonius Hospital, Department of Internal Medicine, Nieuwegein, Netherlands, 7Sparna Hospital, Department of Internal Medicine, Hoofddorp, Netherlands, 8Haga Hospital, Department of Nephrology, Den Haag, Netherlands and 9Leiden University Medical Center, Department of Internal Medicine, Leiden, Netherlands

Background and Aims: Patients on haemodialysis generally report poor health-related quality of life (HRQoL) and a broad range of physical and emotional symptoms, but it is unknown if this differs between younger and older patients. We aimed to describe the trajectories of HRQoL and symptom burden of patients <70 and ≥ 70 years old after dialysis initiation and to assess the impact of symptom burden on HRQoL.

Method: Incident Dutch haemodialysis patients were included between December 1st, 2017, and January 19th, 2019. HRQoL and symptom were measured with the 12-item Short Form Health Survey (range 0-100, higher scores indicate better HRQoL) and the Dialysis Symptom Index (range 0-150, higher scores indicate more symptoms and/or higher severity). Questionnaires were taken at the start of dialysis and after 3, 6 and 12 months. We used (multilevel) linear regression to examine the trajectories of HRQoL and symptom burden, and the impact of symptom burden on HRQoL.

Results: In 774 patients, the trajectories of physical HRQoL, mental HRQoL and symptom burden were stable. Compared with patients aged < 70 years, patients ≥ 70 years reported similar physical HRQoL (crude mean difference -0.61, 95% CI -1.86; 0.63, p = .33) but slightly better mental HRQoL (1.77, 95% CI 0.54; 3.01, p = .005) and lower symptom burden (-2.38, 95% CI -5.08; 0.32, p = .08) during the first year of dialysis. With increasing symptom burden, physical HRQoL declined more in older than in younger patients (β = -2.87 versus β = -1.89, respectively, p-value for interaction = .007). For mental HRQoL, this decrease was similar (β = -2.92 versus -2.88, p-value for interaction = .847).

Conclusion: Older haemodialysis patients generally experience better mental HRQoL and a (non-statistically significant) lower symptom burden in the first year after dialysis initiation, compared to younger patients. However, their physical HRQoL declines more rapidly with increasing symptom burden, compared to younger patients.

SURVIVAL OF HEMODIALYSIS PATIENTS: A LARGE RETROSPECTIVE STUDY

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1University of Modena and Reggio Emilia, Surgical, Medical and Dental Department of Morphological Sciences, Section of Nephrology, Italy and 2Policlinico di Modena, Nephrology, Dialysis and Renal Transplant Unit, Italy

Background and Aims: Despite the evolution of haemodialysis (HD) technique, long-term prognosis for HD patients remains poor. The major causes of mortality for HD patients are cardiovascular diseases, followed by infections and tumors. Survival difference between HD and general population is related to chronic exposition to uremic toxin and continuous cardiovascular stress. Currently there is no consensus about the weight of different mortality factors. Our aim is to delve into some risk factors using a large sample of HD patients.

Method: We performed a longitudinal retrospective analysis with data collected from patients that started HD from 1969 to 2021 in the dialysis center of Modena, Italy. Patients with < 18 years old or < 3 months of HD were excluded. The included characteristics were sex, age of starting HD and duration of treatment, any previous substitutive treatment (e.g., peritoneal dialysis (PD), transplant (TX)) and inscription on waiting list for TX. Statistical tests were performed using Shapiro-Wilk, t-test and ANOVA. Survival analysis was employed using the Kaplan–Meier estimate and Cox regression models with 95% confidence interval (CI).

Results: A total of 2290 patients were submitted to study, 63% of them were male (n = 1451), 10% were placed on waiting list for Tx (n = 224) and 9% came from any substitutive treatment (n = 45 from Tx, n = 154 from PD). At time of HD started, average age was 67.7 (Standard Deviation: 14.8 years). In this group, 22% (n = 504) were older than or equal to 80 years, 40% (n = 911) were between 60 and 85 years, 23% (n = 534) were between 65 and 50 years, 15% (n = 341) were younger than 50 years. The average survival in HD was 1894.2 days, 80% of patients died (n = 1829) and 9% received kidney transplant (n = 190). One-year mortality rate was 13% (n = 297), with the highest mortality rate in the eldest people (n = 115, Log-Rank p<0.0001). At fifteen years of follow-up 76% died (n = 1740) and 8% (n = 183) were submitted to transplant. Age remained an important risk factor of mortality (Log-Rank p<0.0001) (Figure 1). Conversely, inscription on waiting list for TX (Log-Rank p<0.0001) and previous DP (Log-Rank p = 0.0002) were protective factors. An important mortality predictor at 15 years was the age of beginning HD (p<0.0001). Indeed, using patients with <50 years as dummy variable, patients with age between 50 and 65 years had hazard ratio (HR) of 2.7 (CI 2.2-3.4); HR for age between 65 and 80 years was 5 (CI 4.1-6.1); patients aged >80 years had HR of 11 (CI 8.9-13.7). Other mortality predictors were the inscription on waiting list (HR 0.4, CI 0.2-0.5, p<0.0001) and previous PD treatment (HR 0.76, CI 0.61-0.95, p = 0.01). Sex and previous transplantation were not statistically significant.

Conclusion: The medical progress reached nowadays allows us to keep patients longer out of HD. This leads to an increasing average age of patients
starting hemodialysis. Our results show that age is an important factor to determine the survival in HD and this becomes dramatically true for octogenarian patients. On the other side, patients on the waiting list for transplant have a better survival, probably due to a better health status. In conclusion, the challenge of the future will be to act on modifiable risk factors with adequate prevention and treatment of comorbidities. This will allow us to reduce the weight of age as a mortality predictor.

#3957
SUSTAINED RECOVERY OF KIDNEY FUNCTION IN PATIENTS WITH ESKD UNDER CHRONIC DIALYSIS TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS
Carlo Garofalo, Luca De Nicola, Roberto Minutolo, Giuseppe Conte, Simona Andriella, Federica Marzano, Tino Paolo Ambrosino and Silvio Borrelli
University of Campania “Luigi Vanvitelli”, Nephrology, Italy

Background and Aims: The prevalence of recovery of kidney function (RKF) in patients under maintenance dialysis is poorly defined mainly because of different definitions of RKF. The accurate assessment of sustained RKF is critical because the survival and quality of life of patients treated by maintenance dialysis are dramatically poor as compared to patients under conservative treatment. The sustained withdrawal of chronic dialysis has moreover a significant social and economic impact, considering the high burden of dialysis on health resources.

Method: Therefore, to gain more insights into the epidemiology of RKF, we performed a systematic review and meta-analysis of studies addressing the prevalence of sustained (at least for 30 days) RKF in patients under maintenance dialysis. Acute kidney injury (AKI) and RKF in the first 90 days of dialysis were the main exclusion criteria.

Results: Overall, 7 studies (10 cohorts) including 2,444,943 chronic dialysis patients (range: 430-1,900,595 patients) were meta-analyzed. The period of observation ranged from 4 to 43 years. The prevalence of RKF was 1.49% (95% C.I.:1.05-2.11; \( p<0.001 \)) with high heterogeneity I²: 99.8%, \( P<0.001 \) (Figure 1). The weighted mean dialysis vintage before RKF was 294±165 days; RKF persisted for a weighted mean of 27.5 months. The percentage of RKF was higher in studies from the U.S. (1.96% [95% C.I.: 1.24-3.07]) as compared to other countries (1.04% [95% C.I.: 0.66-1.62]; \( P = 0.049 \)).

Conclusion: In conclusion, sustained RKF unrelated to AKI occurs in about 1.5% of patients under maintenance dialysis. On average, RKF patients discontinue chronic dialysis about ten months after starting treatment and live free of dialysis for more than two years. The higher prevalence of RKF reported in the U.S. versus other countries suggests a major role of country-specific policies for dialysis start.
IDENTIFICATION OF FACTORS ASSOCIATED WITH DEATH IN DIALYSIS PATIENTS USING A MACHINE LEARNING-BASED PREDICTIVE MODEL
Carolina Aparecida de Almeida Vicentini, Luis Gustavo Modelli de Andrade and Daniela Ponce

Unesp Campus de Botucatu, Brazil

Background and Aims: Few studies including unplanned dialysis starts have used machine learning for the prediction of death in dialysis patients. The objective of the study was to use R software algorithms to develop machine learning predictive models for the identification of death-related factors in patients undergoing hemodialysis (HD) and peritoneal dialysis (PD).

Method: This study included adult patients undergoing HD and PD started in a planned or urgent manner in a dialysis center between January 2014 and January 2019. Epidemiological, clinical and laboratory data were collected. Univariate analysis was followed by ML-based analyses. Then, multivariate regressions were obtained using stepwise and Cox regression analyses. Finally, a Random Forest predictive model was generated after variables with missing values > 30% were removed.

Results: Of 581 patients included, 170 died (29.2%). On univariate analysis death was associated with age, number of comorbidities, dialysis modality switching, creatinine, PTH and albumin values at dialysis initiation, presence of diabetes (DM), hospitalization, function recovery and central venous catheter (CVC) for dialysis access. Patients who started dialysis with a CVC had a worse survival (p = 0.0034) than those who did not use CVC, started HD with AVF, or received PD (Figure 1). Data were split into 20% for testing the regression model, and 80% for training the model. Data preprocessing for Cox regression included imputing some values using bag impute (decision trees), creating dummy variables, and removing collinear variables. Death was associated with older age (p < 0.001), fewer ESI-free months (p < 0.001) and lower initial creatinine (p = 0.008) (Table 1). The model C-index was 0.8099. Random forest ranked the following variables predictive of death in descending order of importance: ESI-free months; age; initial levels of creatinine, PTH and albumin; number of comorbidities; dialysis-related infection; initial phosphorus and hemoglobin; hospitalizations; male gender; modality switching (Figure 2). The agreement of the model obtained was 0.8110.

Conclusion: ESI-free months, age and initial levels of creatinine were associated with death on both multivariate and ML-based analyses.

Figure 1: Survival Analysis of patients who started dialysis with a CVC vs patients who did not use CVC.

Figure 2: Variables importance ranked by Random Forest.
Background and Aims: Dry weight (DW) estimation is important for patients undergoing hemodialysis. Although bioimpedance spectroscopy (BIS) is often employed to evaluate DW, BIS-based DW frequently differs from clinical DW. In this study, the characteristics of elderly patients were evaluated by separating them into groups based on the degree of disparity between the BIS-based DW and the clinically appropriate (DWGAP), and the mortality of each group was compared.

Method: This retrospective study included patients who underwent hemodialysis at Chungnam National University Hospital from January 1, 2016, to June 2020. All patients were aged ≥60 years. Patients with cancer, recipients of kidney transplant, and patients who dropped out of the study within 3 years were excluded. Body composition was assessed using a portable BIS device (Fresenius Medical Care, Bad Homburg, Germany). The BIS dataset includes extracellular water (ECW), intracellular water (ICW), and total body water (TBW) as well as the lean tissue index (LTI), fat mass index (FTI), and body cell mass (BCM). The absolute value of the gap between the BIS-based DW and the actual clinically appropriate dry weight was determined (DWGAP). To assess differences in blood chemistry and survival rate, four groups were classified based on the absolute value of DWGAP: Group 1: DWGAP ≤ 0.5 kg, Group 2: 0.5 kg < DWGAP ≤ 1 kg, Group 3: 1 kg < DWGAP ≤ 2 kg, and Group 4: 2 kg < DWGAP. The mortality data of patients up to 3 years after BIS measurement were collected.

Results: There were 1024 patients in all. The study excluded 29 individuals with cancer, recipients of KT, and 249 participants with a loss of follow-up before 36 months. A total of 715 patients were analyzed: Group 1 (n = 236), Group 2 (n = 171), Group 3 (n = 137), and Group 4 (n = 171). The mean age for each group was 71.97, 70.73, 71.58, and 70.4 years, respectively. Groups 1 and 2 had the same survival rates (78%); however, Group 3 had a lower rate (73%) and Group 4 showed a significant decline (59%). In the laboratory test, Group 4 had lower hemoglobin, total protein, albumin, creatinine, and chloride levels than Groups 1, 2, and 3. In the BIS data, ECM and E/I were higher in Group 4 than in Groups 1, 2, and 3.

Conclusion: In the elderly patient group, mortality increased in the group where the DWGAP was ≥ 2 kg. Lower blood albumin levels, total protein levels, and E/I ratios of ≥1 were detected in the group with a gap of ≥ 2 kg, and these parameters are likely to adversely affect the survival of elderly patients requiring dialysis.

### Table 1: Clinical characteristics as a subdivision of DWGAP.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard Ratio1</th>
<th>95% CI1</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.02</td>
<td>1.01–1.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.14</td>
<td>0.80–1.63</td>
<td>0.5</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>1.10</td>
<td>0.97–1.23</td>
<td>0.14</td>
</tr>
<tr>
<td>(ESI-free days)/(30)*</td>
<td>0.97</td>
<td>0.95–0.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PTH</td>
<td>1.00</td>
<td>1.00–1.00</td>
<td>0.2</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.94</td>
<td>0.85–1.04</td>
<td>0.2</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.86</td>
<td>0.62–1.18</td>
<td>0.3</td>
</tr>
<tr>
<td>P</td>
<td>0.99</td>
<td>0.96–1.02</td>
<td>0.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.85</td>
<td>0.58–1.25</td>
<td>0.4</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.89</td>
<td>0.82–0.97</td>
<td>0.008</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>1.45</td>
<td>0.92–2.29</td>
<td>0.11</td>
</tr>
<tr>
<td>CVC for initial access (HD)</td>
<td>2.14</td>
<td>0.51–8.97</td>
<td>0.3</td>
</tr>
<tr>
<td>APD as the initial modality (PD)</td>
<td>2.48</td>
<td>0.58–10.5</td>
<td>0.2</td>
</tr>
<tr>
<td>AVF for initial dialysis access</td>
<td>1.09</td>
<td>0.23–5.04</td>
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</tr>
<tr>
<td>Dialysis modality switching</td>
<td>0.90</td>
<td>0.52–1.56</td>
<td>0.7</td>
</tr>
</tbody>
</table>

1 HR = Hazard Ratio, CI = Confidence Interval
2 ESI-Free months

#4979

MORTALITY AND BIOIMPEDANCE SPECTROSCOPY–BASED DRY WEIGHT MEASUREMENT ERROR IN ELDERLY PATIENTS UNDERGOING HEMODIALYSIS

Hae Ri Kim1, Moo Jun Kim1, Jae Wan Jeon1, Dae Eun Choi2, Ki Ryang Na2 and Kang Wook Lee2

1Chungnam National University Sejong Hospital, Nephrology, Sejong, Rep. of South Korea and 2Chungnam National University Hospital, Nephrology, Daejeon, Rep. of South Korea

Background and Aims: Dry weight (DW) estimation is important for patients undergoing hemodialysis. Although bioimpedance spectroscopy (BIS) is often employed to evaluate DW, BIS-based DW frequently differs from clinical DW. In this study, the characteristics of elderly patients were evaluated by separating them into groups based on the degree of disparity between the BIS-based DW and the clinically appropriate (DWGAP), and the mortality of each group was compared.

Method: This retrospective study included patients who underwent hemodialysis at Chungnam National University Hospital from January 1, 2016, to June 2020. All patients were aged ≥60 years. Patients with cancer, recipients of kidney transplant, and patients who dropped out of the study within 3 years were excluded. Body composition was assessed using a portable BIS device (Fresenius Medical Care, Bad Homburg, Germany). The BIS dataset includes extracellular water (ECW), intracellular water (ICW), and total body water (TBW) as well as the lean tissue index (LTI), fat mass index (FTI), ECW/ICW ratio (E/I), lean tissue mass, fat mass (FAT), adipose tissue mass (ATM), and body cell mass (BCM). The absolute value of the gap between the BIS-based DW and the actual clinically appropriate dry weight was determined (DWGAP). To assess differences in blood chemistry and survival rate, four groups were classified based on the absolute value of DWGAP: Group 1: DWGAP ≤ 0.5 kg, Group 2: 0.5 kg < DWGAP ≤ 1 kg, Group 3: 1 kg < DWGAP ≤ 2 kg, and Group 4: 2 kg < DWGAP. The mortality data of patients up to 3 years after BIS measurement were collected.

Results: There were 1024 patients in all. The study excluded 29 individuals with cancer, recipients of KT, and 249 participants with a loss of follow-up before 36 months. A total of 715 patients were analyzed: Group 1 (n = 236), Group 2 (n = 171), Group 3 (n = 137), and Group 4 (n = 171). The mean age for each group was 71.97, 70.73, 71.58, and 70.4 years, respectively. Groups 1 and 2 had the same survival rates (78%); however, Group 3 had a lower rate (73%) and Group 4 showed a significant decline (59%). In the laboratory test, Group 4 had lower hemoglobin, total protein, albumin, creatinine, and chloride levels than Groups 1, 2, and 3. In the BIS data, ECM and E/I were higher in Group 4 than in Groups 1, 2, and 3.

Conclusion: In the elderly patient group, mortality increased in the group where the DWGAP was ≥ 2 kg. Lower blood albumin levels, total protein levels, and E/I ratios of ≥1 were detected in the group with a gap of ≥ 2 kg, and these parameters are likely to adversely affect the survival of elderly patients requiring dialysis.

### Table 1: Cox Regression based on Machine Learning.

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<th>P</th>
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<td>Dialysis modality switching</td>
<td>0.90</td>
<td>0.52–1.56</td>
<td>0.7</td>
</tr>
</tbody>
</table>

1 HR = Hazard Ratio, CI = Confidence Interval
2 ESI-Free months
mortality risk factors was performed. Causes of mortality were obtained by hospital discharge forms. COVID-19 related cause of death was defined through intra-hospital codes as COVID-19 pneumonia, COVID-19 ARDS and COVID-19 respiratory failure.

Results: One hundred and fifty-two chronic HD patients were hospitalized for COVID-19 infection. Table 1 shows the general characteristics of the patients. The 28-day all-cause mortality was 21.9%, which 11.9% was COVID-19 related cause of death. Table 2 shows the causes of mortality. Multivariate Cox regression demonstrated that an increased risk of death from COVID-19 at 28 days was significantly and independently associated with age (73 years (HR 1.05, 95% CI 1.01-1.09; p = 0.01), Charlson Comorbidity Index (CCI) > 5 at entry (HR 1.28, 95% CI 1.02-1.60; p = 0.01), Continuous Renal Replacement Therapies (CRRT) (HR 2.89, 95% CI 1.03-8.11; p = 0.04) and the presence of peripheral vasculopathy (HR 3.48, 95% CI 1.31-9.27; p = 0.01). Plasma albumin >25 g/L at entry (HR 0.87, 95% CI 0.80-0.96; p <0.01) and pre-admission SARS-CoV-2 vaccination (HR 0.25, 95% CI 0.09-0.72; p = 0.01) significantly reduced the risk of mortality.

Conclusion: Our study shows that on the total of deaths with a positive COVID-19 test, 59% were caused by the infection while the remaining 41% occurred from other causes. Age, CCI, the presence of peripheral vascular disease and the need for CRRT are independent risk factors for mortality. Vaccination was confirmed as a protective factor.

Table 1: Characteristics of the study population.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>100/52</td>
</tr>
<tr>
<td>Middle age (mean ± DS)</td>
<td>69 ± 14.14</td>
</tr>
<tr>
<td>N° HD</td>
<td>1007</td>
</tr>
<tr>
<td>N° HD average/patients (mean ± DS)</td>
<td>7.66 ± 6.54</td>
</tr>
<tr>
<td>N° Hospitalized Intensive Care Unite</td>
<td>18</td>
</tr>
<tr>
<td>Average days of hospitalization (mean ± DS)</td>
<td>23.57 ± 24.55</td>
</tr>
<tr>
<td>Charlson Comorbidity Index (mean ± DS)</td>
<td>6.44 ± 2.64</td>
</tr>
<tr>
<td>COMORBIDITY</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>52 (34.2%)</td>
</tr>
<tr>
<td>Vasculopathy</td>
<td>53 (34.9%)</td>
</tr>
<tr>
<td>Cardiopathy</td>
<td>64 (42.1%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>30 (19.7%)</td>
</tr>
<tr>
<td>ADMISSION DIAGNOSIS</td>
<td></td>
</tr>
<tr>
<td>COVID-19 pneumonia</td>
<td>59 (38.8%)</td>
</tr>
<tr>
<td>Symptomatic SARS-CoV-2 infection</td>
<td>53 (34.9%)</td>
</tr>
<tr>
<td>Asymptomatic SARS-CoV-2 infection</td>
<td>8 (5.3%)</td>
</tr>
<tr>
<td>SARS-CoV-2 respiratory failure</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Radiological diagnosis of pneumonia</td>
<td>74 (48.7%)</td>
</tr>
</tbody>
</table>

Results: Vaccination was confirmed as a protective factor.

Background and Aims: Fatigue and the need for recovery time after a hemodialysis session are frequent complaints in patients with chronic kidney disease treated with maintenance hemodialysis (MHD). In the present study, we investigated whether there is an association between self-reported fatigue and the need for recovery time after HDM sessions.

Method: This is a cross-sectional study with data from 239 adult patients participating in the prospective cohort study “Prognostic Study of Patients on Chronic Hemodialysis” (PROHEMO), developed in Salvador, BA, Brazil. We used “The Chalder Fatigue” questionnaire (CFQ-11) to calculate fatigue scores. CFQ-11 scores can range from 0 to 33; Higher scores mean more intense fatigue. Fatigue was categorized as: absent or mild if the score was <4 and moderate to severe if the score was ≥4. To assess the need for recovery time from hemodialysis, participants answered a question: After finishing dialysis, do you usually need some time to recover? with two answer options (yes or no). We used logistic regression to estimate the odds ratio (OR) of the association between fatigue and need for recovery after hemodialysis, with adjustments for age, sex, diabetes, and heart failure.

Results: The mean age was 52.5 ± 12.5 years, 57.7% were men, 94.5% were non-white. Self-reported fatigue as absent or mild was 28.4% (68/233) and moderate to severe fatigue was 71.5% (171/233). The prevalence of need for recovery time after hemodialysis was 2.5 times higher in patients with moderate to severe fatigue than in patients with no or mild fatigue (prevalence: 20.6%; prevalence ratio: 2.50 (95% confidence interval: 1.53; 4.08)). In logistic regression, an association between moderate to severe fatigue and need for recovery was observed even after adjusting for the effects of age, sex, diabetes, and heart failure (OR = 4.36; 95% CI: 2.21; 8.59).

Conclusion: The results suggest that patients who report a more intense degree of fatigue, more often have a greater need for time to recover after the end of the hemodialysis session. It is interesting to investigate whether interventions that reduce fatigue in patients undergoing MHD treatment result in a reduction in the need for recovery time after the hemodialysis session.

#4200

INTERACTIONS BETWEEN INTRADIALYTIC CENTRAL VENOUS OXYGEN SATURATION, RELATIVE BLOOD VOLUME, AND ALL-CAUSE MORTALITY IN HEMODIALYSIS PATIENTS

Hanjie Zhang1, Priscila Preciado Rojas1, Laura Rosales Merlo1, Jeroen Kooman2, Frank Van Der Sande2 and Peter Kotanko1,3

1 Renal Research Institute, New York, United States of America, 2 Maastricht University Medical Center, Maastricht, Netherlands and 3 Icahn School of Medicine at Mount Sinai, New York, United States of America

Background and Aims: In maintenance hemodialysis patients, low central venous oxygen saturation (ScvO2) and small decline in relative blood volume

Table 2: Causes of death for the study population.

<table>
<thead>
<tr>
<th>CAUSE OF DEATH</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 Related</td>
<td>N (%)</td>
</tr>
<tr>
<td>COVID-19 pneumonia</td>
<td>16 (41%)</td>
</tr>
<tr>
<td>COVID-19 ARDS</td>
<td>2 (5.1%)</td>
</tr>
<tr>
<td>Other respiratory failure, not elsewhere</td>
<td>2 (5.1%)</td>
</tr>
<tr>
<td>COVID-19 respiratory failure</td>
<td>3 (7.7%)</td>
</tr>
<tr>
<td>Total deaths</td>
<td>23 (59%)</td>
</tr>
<tr>
<td>Not COVID-19 Related</td>
<td>N (%)</td>
</tr>
<tr>
<td>Heart attack</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>DM type II decompensated</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>Embolism and thrombosis of unspecified artery</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Vasculopathy</td>
<td>1 (6.3%)</td>
</tr>
<tr>
<td>Pneumonia in other infectious diseases classified elsewhere</td>
<td>3 (18.8%)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>5 (31.3%)</td>
</tr>
<tr>
<td>Total deaths</td>
<td>16 (41%)</td>
</tr>
</tbody>
</table>

#6837

ASSOCIATION BETWEEN SELF-REPORTED FATIGUE AND THE NEED FOR RECOVERY TIME AFTER THE MAINTENANCE HEMODIALYSIS SESSION: PROHEMO

Gabriel Bryan Gutierrez Peredo1, Márcia Tereza Silva Martins1, Fernanda Albuquerque Da Silva1, Marcelo Lopes1,2, Gildete Barreto Lopes1 and Antonio Alberto Lopes1

1 Federal University of Bahia, Núcleo de Epidemiologia Clínica e Medicina Baseada em Evidências, Salvador, Brazil and 2 São Rafael Hospital, Nephrology, Salvador, Brazil.

Figure 1: Association of fatigue and need for recovery time after hemodialysis.
up, 44 patients (20.4%) died. Kaplan-Meier analysis is shown in Figure 1. In the median RBV change was –5.5% and median ScvO2 was 58.8%. During follow-up, patients with ScvO2 above median and RBV change below median were defined as reference. The follow up period was 3 years. We constructed a Cox proportional hazards model with adjustment for age, diabetes, and dialysis vintage to assess the association between ScvO2 and RBV and all-cause mortality during follow-up.

**Results:** Baseline comprised 5,231 dialysis sessions in 216 patients. The mortality during follow-up.

**Method:** We conducted a retrospective study in maintenance hemodialysis patients with central venous catheters as vascular access. During a 6-month baseline period, Crit-Line (Fresenius Medical Care, Waltham, MA) was used to measure continuously intradialytic ScvO2 and hematocrit-based RBV. We defined four groups per median change of RBV and median ScvO2. Patients with RBV above median and RBV change below median were defined as reference. The follow up period was 3 years. We constructed a Cox proportional hazards model with adjustment for age, diabetes, and dialysis vintage to assess the association between ScvO2 and RBV and all-cause mortality during follow-up.

**Results:** Baseline comprised 5,231 dialysis sessions in 216 patients. The median RBV change was –5.5% and median ScvO2 was 58.8%. During follow-up, 44 patients (20.4%) died. Kaplan-Meier analysis is shown in Figure 1. In the adjusted model, all-cause mortality was highest in patients with ScvO2 below median and RBV change above median (HR 6.32; 95% confidence interval [CI] 1.37 to 29.06), followed by patients with ScvO2 below median and RBV change below median (HR 5.04; 95% CI 1.14 to 22.35) and ScvO2 above median and RBV change above median (HR 4.52; 95% CI 0.95 to 21.36).

**Conclusion:** Concurrent combined monitoring of intradialytic ScvO2 and RBV change may provide additional insights into a patient’s circulatory status. Patients with low ScvO2 and small changes in RBV may represent a specifically vulnerable group of patients at particularly high risk for adverse outcomes, possibly related to poor cardiac reserve and fluid overload.

**REFERENCES**


**IMPLEMENTING THE SERIOUS ILLNESS CARE PROGRAMME (SICP) WITHIN AN OUTPATIENT HAEMODIALYSIS UNITS: A FEASIBILITY STUDY**

Hannah Sammut1, Anirudh Rao1,2, Asheesh Sharma1, Tamsin Mcglincheys and Stephen Mason1

1Liverpool University Hospital Foundation Trust, Nephrology, Liverpool, United Kingdom, 2University of Liverpool, Liverpool, United Kingdom and 3University of Liverpool, Palliative Care Unit, Liverpool, United Kingdom

**Background and Aims:** End-stage renal failure affects a frail, elderly, and multimorbid population with high physical and psychological symptoms. The care should integrate core palliative care principles to thoroughly address and support patients’ needs. The Serious Illness Care programme (SICP) is a multi-component intervention that promotes meaningful conversations between clinician and patient. The intervention identifies what matters most to the patient, their goals and priorities, and how this aligns with their treatment and care. The SICP was implemented in two dialysis units in the North of England, and we report on the outcomes and learning from this process.

**Method:** Using a modified cohort design, we applied the principles and tools of the programme within a renal unit in the North of England. We selected two outpatient dialysis units, Unit A (with a population of 43 patients) and Unit B (with 150 patients). An MDT approach was employed to develop a process specific to each unit (Figure 1). Clinician training was complemented with mentoring support and informative education of nursing and administration teams. Outcome data were collected from August 2019 to February 2022. Outcomes recorded (reach metrics and process outcomes) were the number of patients offered a conversation, accepted or declined, the timing of the conversation and follow-up. We applied structured reflection on elements that facilitated participation in the SICP.

**Results:** Of the conversations that happened, 10 patients preferred to have the conversation on their own, and 7 patients chose to have a family or carer present. In 17 (100%) patients, the conversation naturally led to a ‘statement of wishes’ about their health. In 5 (29%) patients, there was a detailed conversation regarding resuscitation decisions in the event of a cardiopulmonary arrest (DNACPR). Three (17%) patients accepted a ‘Planning your Future Care Guide’, to help them think about more specific advance care planning conversations in the future. Three (17%) accepted a ‘Talking to your Family and Friend’s leaflet to help guide conversations with family’. Structured reflection identified two elements that facilitated participation in the SICP were:

- Regular focused review of the holistic needs of patients as an MDT, which included the consultant and nursing team
- Creating flexibility in appointment time for conversations to happen

Over this period, 18 (53%) of the 34 patients offered the conversation died.

**Conclusion:** This study demonstrates that the SICP can be successfully implemented within a dialysis unit. It is essential to recognise that some patients want to talk about the future of their illness, whilst some prefer not to. Understanding the person-centred illness and environmental factors that enable patients to engage in these ‘future care planning’ conversations is important for this intervention’s progression. For example, we were surprised that the majority within our small sample wanted to have this conversation.

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**Figure 1:** Kaplan-Meier analysis of survival probabilities in the four subgroups of patients based on the level of central venous oxygen saturation (ScvO2) and relative blood volume (RBV) above and below the median of 58.8% and —5.5%, respectively.
in the absence of large epidemiological studies, whether the use of CIEDs in hemodialysis patients is associated with a lower mortality benefit than in pre-dialysis patients remains controversial. In this cross-sectional study, we evaluate the prevalence of CIEDs in a cohort of patients with CKD.

**Method:** The study includes patients with CIEDs with estimated GFR <45 ml/min/1.73 m² from two hospitals in Milan, divided into two groups based on treatment with conservative therapy (IRC stage IIIb-V) or hemodialysis.

**Results:** Of the 499 patients enrolled, 268 had CKD stage IIIb-V, and 231 were in hemodialysis (Table 1).

Among CRT carriers, the prevalence in the CKD IIIb-V group is significantly higher than in the hemodialysis group (4.09% vs 0.86%; p = 0.025) (Figure 1), even if among the hemodialysis patients the prevalence of patients with previous stroke and hypertension was significantly higher (Table 1).

Furthermore, in multiple logistic regressions, hemodialysis was a variable independently correlated with reduced use of CRTs (OR 0.27; 95% CI = 0.01-0.96; p = 0.04), while the other devices (individually and cumulatively) correlated positively only with age and previous myocardial infarction (MI) (Table 2).

**Conclusion:** The reduced prevalence of CRT in hemodialysis patients is probably related to the shorter life expectancy and the higher rate of related complications, such as the increased risk of infectious complications and/or stenosis of the central venous vessels. Further studies are needed to evaluate the impact of these devices on the cardiac mortality of hemodialysis patients and the associated complication rate.
Table 1: Baseline characteristics of the patients.

<table>
<thead>
<tr>
<th></th>
<th>CKD IIIb-V (n = 268)</th>
<th>Hemodialysis (n = 231)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - years – median (IQR)</td>
<td>81 (72-85)</td>
<td>73 (61-81)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male – n (%)</td>
<td>181 (67.5)</td>
<td>144 (62.3)</td>
<td>0.25</td>
</tr>
<tr>
<td>Dialysis vintage – median (IQR)</td>
<td>—</td>
<td>4.3 (2.1-7.6)</td>
<td>—</td>
</tr>
<tr>
<td>Comorbidities- n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>250 (93,3)</td>
<td>226 (97,8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Heart failure</td>
<td>58 (21,6)</td>
<td>47 (20,4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Previous MI</td>
<td>52 (20,1)</td>
<td>52 (22,6)</td>
<td>0.58</td>
</tr>
<tr>
<td>Previous stroke / TIA</td>
<td>24 (8,9)</td>
<td>42 (18,2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>67 (25)</td>
<td>69 (30)</td>
<td>0.23</td>
</tr>
<tr>
<td>Other arrhythmias</td>
<td>28 (10,1)</td>
<td>26 (11,3)</td>
<td>0.77</td>
</tr>
<tr>
<td>COPD</td>
<td>38 (14,2)</td>
<td>33 (14,3)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Diabetes</td>
<td>125 (46,6)</td>
<td>93 (40,3)</td>
<td>0.18</td>
</tr>
<tr>
<td>Therapy – n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE-I / ARB</td>
<td>138 (51,5)</td>
<td>68 (29,4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>162 (64)</td>
<td>124 (60,2)</td>
<td>0.43</td>
</tr>
<tr>
<td>Low-dose aspirin</td>
<td>145 (57,3)</td>
<td>92 (44,7)</td>
<td>0.0085</td>
</tr>
<tr>
<td>Oral anticoagulant</td>
<td>51 (20,4)</td>
<td>26 (13,8)</td>
<td>0.08</td>
</tr>
<tr>
<td>Antiarrhythmic drugs</td>
<td>28 (11)</td>
<td>31 (15)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

ACE-I: Angiotensin Converting Enzyme Inhibitor; ARB: Angiotensin II Receptor Blocker; COPD: Chronic Obstructive Pulmonary Disease; MI: Myocardial Infarction; IQR: Interquartile Range; TIA: Transient Ischemic Attack

Figure 1: Comparison of the prevalence of implantable cardiac devices between patients with CRF stage IIIb-V and on hemodialysis.

Table 2: Multiple logistic regression: correlation between the use of implantable cardiovascular devices and hemodialysis, previous acute myocardial infarction, age and type of vascular access.

<table>
<thead>
<tr>
<th></th>
<th>CIED OR (95% CI)</th>
<th>PM OR (95% CI)</th>
<th>ICD OR (95% CI)</th>
<th>CRT OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis</td>
<td>0.75 (0.40-1.36)</td>
<td>0.84 (0.38-1.74)</td>
<td>0.89 (0.22-3.23)</td>
<td>0.27 (0.01-0.96)</td>
<td>0.35; 0.65; 0.87; 0.04</td>
</tr>
<tr>
<td>Previous MI</td>
<td>2.33 (1.37-3.90)</td>
<td>1.11 (0.53-2.17)</td>
<td>5.67 (2.09-16.19)</td>
<td>4.29 (1.37-13.87)</td>
<td>&lt;0.001; 0.76; &lt;0.001; 0.01</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>2.26 (1.32-3.96)</td>
<td>2.82 (1.42-6.02)</td>
<td>1.72 (0.60-4.96)</td>
<td>6.32 (1.17-117.3)</td>
<td>&lt;0.003; &lt;0.005; 0.31; 0.08</td>
</tr>
<tr>
<td>Vascular Access (CVC)</td>
<td>0.84 (0.39-1.83)</td>
<td>0.98 (0.37-2.68)</td>
<td>2.44 (0.65-10.14)</td>
<td>—</td>
<td>0.66; 0.97; 0.18</td>
</tr>
</tbody>
</table>

CVC: Central Venous Catheter.

#5277

THE EVALUATION OF FLUID VOLUME AND PROGNOSIS IN HEMODIALYSIS PATIENTS UTILIZING PLASMA HUMAN ATRIAL NATRIURETIC PEPTIDE

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¹Niigata University, Division of Clinical Nephrology and Rheumatology, Kidney Research Center, Japan, ²The Jikei University Daisan Hospital, Division of Nephrology and Hypertension, Department of Internal Medicine, Japan and ³Tachikawa General Hospital, Department of Nephrology, Japan

Background and Aims: Volume overload leads to the development of heart failure, which contributes to the high mortality in patients on hemodialysis. The post-dialysis plasma level of human atrial natriuretic peptide (hANP) reflects the fluid volume in patients on hemodialysis. The threshold hANP level is reportedly 100 pg/mL; however, the clinical usefulness of the threshold hANP level for volume control has not been sufficiently studied.

Method: We conducted a single-center, retrospective, observational study that included 156 hemodialysis patients without atrial fibrillation. First, we examined the usefulness of the threshold hANP level (100 pg/mL) for predicting hypoxemia due to congestion in a short-term observational study from December 30, 2015 to January 5, 2016. Subsequently, we conducted a 5-year follow-up study wherein the outcomes were hospitalization due to acute heart failure (AHF), development of cardiovascular diseases (CVD), and all-cause death. Finally, we collected echocardiography data to investigate the relationship between cardiac function and hANP.

Results: Our short-term observational study showed that patients with an hANP level ≥ 100 pg/mL developed hypoxemia due to congestion (odds ratio, 3.52; 95% confidence interval, 1.06–11.71; P = 0.040). At the 5-year follow-up, patients with an hANP level ≥ 100 pg/mL had significantly higher
rates of hospitalization due to AHF, CVD, and all-cause death based on the log-rank test (P = 0.003, P < 0.019, P < 0.001, respectively). Analysis of echocardiography data showed that the presence of reduced left ventricular ejection fraction and left ventricular diastolic dysfunction were significantly associated with high plasma hANP levels. However, the threshold hANP level (100 pg/mL) remained independently associated with hospitalization due to AHF after adjusting for cardiac dysfunctions in the multivariable model.

Conclusion: The hANP level is indicative of both fluid volume and cardiac dysfunction. In clinical practice, we suggest utilizing hANP as an easily accessible measure to identify high-risk patients for developing AHF initially. If the hANP level exceeds 100 mg/dL, we propose to perform echocardiography and consider reducing the DW. In clinical practice, the plasma hANP level could serve as a valuable indicator for assessing the risk of developing AHF and managing fluid volume.

#6075
GENDER DISPARITIES IN HEMODIALYSIS PATIENTS: WORKING LIFE, MENTAL STATUS AND PHYSICAL CAPACITY

Saliha Yildirim1, Haluk Cihad Albayrak 1, Özantı Helvacı 1, Yasemin Ertenc 1, Ulver Derici 1, Deniz Ayli 1, Murat Duranay 1 and Galip Güz 1

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Background and Aims: Globally, there are more women with chronic kidney disease (CKD) than men, but there are disparities in even receiving dialysis treatment. Gender disparity is a common problem in many fields. In this study, we aimed to determine the gender disparities in a sample of Turkish hemodialysis patients in the terms of working life, symptoms, depression, dementia and physical activity.

Methods: 219 patients (ages 18–65 years) were included in this study. Demographic characteristics, laboratory parameters and social status were recorded. All participants completed the Beck depression scale, standardized mini-mental test, physical activity score and a questionnaire consisting of symptoms related to hemodialysis.

Results: 132 male and 87 female patients were included in this study. Male patients and female patients were statistically similar in the terms of age (p = 0.604), CKD vintage (p = 0.226), RRT vintage (0.559) and laboratory parameters (p = 0.05). Weakness (p = 0.001), palpitation (p < 0.001), chest pain (p = 0.015), hypotension (p < 0.001), myalgia (p < 0.001) and forgetfulness (p = 0.002) were more common in female patients. Serious depression was similar in the two groups (p = 0.525) while physical inactivity (p = 0.022) and dementia (p = 0.024) were more often in female patients. Unemployment was more in the female group (p < 0.001) although willingness to work is similar in both groups and female patients had a low salary than male patients (p = 0.033).

Conclusion: Women with CKD face many challenges in daily life but the major disparities are in the social and economic fields. Not only laboratory parameters but also gender disparities in the social field must be improved to achieve equal care for all people with CKD.

#5819
HAEMODIALYSIS EFFECT ON METABOLIC THERAPY WITH [131INa]: A COMPARATIVE STUDY

Paloma Livianos Arias-Camión1, Alessandra Repetto2, Juan Rey Valeriano1, Sandra Chamizo1, Antonio Cherino Talens2, María Cristina Peña Villoria1 and Isabel Garcia Mendez1

1 Hospital Universitari Son Espases, Nephrology Department, Spain, 2 Hospital Universitari Son Espases, Nuclear Medicine Department, Spain and 3 Hospital Universitari Son Espases, Radiotherapy Department, Spain

Method: Two patients on HD were treated with [131INa] in June 2021. A 74 years old women with hyperthyroidism due to a multinodular goitre, resistant to antithyroid drugs (PT1). A 49 years old man candidate to ablation treatment with low activity of [131INa] after a total thyroidectomy due to differentiated thyroidic cancer (PT2). The recommended activity was administered according to clinical indication. PT1 received 555 MBq and PT2 received 1110 MBq of [131INa] in Metabolic Therapy Unit (MTU). The previous HD sessions were in the nephrology ward. The following HD sessions were in MTU (Wed–Fri.). High-flux dialysis was performed using a Reverse Osmosis portable system. The hospital stay was 5 days (Mo at Fri) for each patient. EDRM at 1 meter was measured three times a day. Liquid samples from HD machine (dialysis fluid, water wash) were obtained every day at the same time before and after each session and radioactivity was analysed.

Results: EDRM after second HD at discharge was 12 and 7,4mcSv/h in PT1 and PT2 respectively. After first HD both patients reached EDR <40mcSv/h (22 and 18 mcSv/h). Red bone marrow dose was 130,76mGy and 110,42mGy respectively. Radioactivity in dialysis fluid was: 0,0099MBq PT1- 0,00259MBq PT2 after first HD; 0,0022MBq PT1- 0,00074MBq PT2 after second HD. No radioactivity was detected in washing water of dialysis equipment in both patients during each HD session. There was no secondary complications due to overhydration or dyslektrolythiasms.

Conclusion: External dose rate measurement is key to decide if patients undergoing HD are ready to be discharge. Once EDRM <40mcSv/h at 1 meter has been reached, patients could immediately return to their dialysis centre following the protection radiology rules and so we must always respect the...
distance between the patients, if that cannot be performed the session will be in the hospital. There is no need to modify radioiodine activities neither timing of HD sessions as red bone marrow dose do not exceed recommended value (2Gy). There is no contamination of HD machine, it could be used after usual decontamination for other patients.

#5960
MORBIDITY AND MORTALITY OF SARS-COV-2 POSITIVE HOSPITALISED HEMODIALYSIS PATIENTS IN CASE OF CENTRALIZED ORGANIZATIONAL STRUCTURE IN HEALTHCARE

Armenuhi Hazoyan1,2

1 Saint Gregory the Illuminator Medical Center, Department of Nephrology and Hemodialysis, Yerevan, Armenia and 2 Yerevan State Medical University, Department of Internal Medicine, Yerevan, Armenia

Background and Aims: During the COVID epidemic, hemodialysis patients were a very serious vulnerable group due to the underlying kidney disease, many other comorbid health problems commonly present, the need for regular hospital visits even during the lockdown, and the high risk of staying with other patients in hemodialysis rooms, getting infected and subsequently high mortality. There are about 1000 patients with chronic hemodialysis in Armenia. All SARS-CoV-2 positive hemodialysis patients, regardless of the severity of the infection, were hospitalized in the largest multidisciplinary hospital center in the country, as it was the only dedicated hemodialysis service for SARS-CoV-2 positive cases in the country during the pandemic.

Method: Our prospective, observational study included about 1040 patients (Included re-infection) infected with the new coronavirus and hospitalized in one center between 01/04/2020 and 01/05/2022.

Results: The number of SARS-CoV-2 positive deaths was 183, which was 17.5% of those hospitalized. The number of re-infections was around 15%. A low level of vaccination of hemodialysis patients was recorded in the country, around 13.4%. During the first 6 months post-hospitalization, another 39 deaths were registered, which is 3.75% of those hospitalized. About 25,000 SARS-CoV-2 positive non-hemodialysis patients were hospitalized in the above period, and mortality in this population did not exceed 9% during peak epidemic and periods of maximum mortality.

Conclusion: Even with a centralized health care system, early hospitalization, close monitoring, and urgent access to multidisciplinary care, SARS-CoV-2 positive hemodialysis patients have a high mortality rate, the risk of which persists in the first 6 months of the post-hospital period and perhaps even longer, and this risk correlates also with low vaccination rates in this patients’ population.

#4938
PATIENTS RECEIVING HEMODIALYSIS MAINTAIN STRONGER SARS-COV-2 IMMUNITY AFTER DISEASE RATHER THAN VACCINATION

Ekaterina Parshina1, Aleksei Zulkarnaev2, Alexey Tolkach1, Andrey Ivanov3 and Pavel Kislyy3

1 Saint Petersburg State University Hospital, Department of Nephrology and Dialysis, Saint-Petersburg, Russia, 2 Moscow Regional Research and Clinical Institute (“MONIKI”), Surgical Department of Transplantology and Dialysis, Moscow, Russia and 3 Saint Petersburg State University Hospital, Department of Human Genetics, Saint-Petersburg, Russia

Background and Aims: We aimed to compare the dynamics of humoral and cellular immunity caused by natural COVID-19 or vaccination against of SARS-CoV-2 with Gam-COVID-Vac (Sputnik V) vaccine in patients, receiving maintenance hemodialysis (HD).

Method: Data were extracted from two prospective cohort studies which had investigated the long-term immune responses after SARS-CoV-2 infection (NCT 04633915) or vaccination (NCT 04805632) in patients receiving HD compared with those in healthy individuals. The group of patients after natural COVID-19 (n = 24) had confirmed history of disease, nobody of them received vaccination before and during the study period. Levels of specific IgG and T-cells were quantified in them at 2.5 and 6 months from disease onset. The group of vaccinated patients (n = 23) had been vaccinated twice with Gam-COVID-Vac vaccine and had no prior history of confirmed COVID-19. Levels of anti-SARS-CoV-2-specific IgG and T-cells were quantified at 1 month and 6 months from the second vaccine shot. IgG levels were determined using a semi-quantitative ELISA (Euroimmun, Germany) and converted to Binding Antibody Units (BAU/ml) according to the WHO International Standard.

Specific T-cell responses (CD4+ and CD8+ cytotoxic T-lymphocytes) were evaluated using the TIGRA-test⃝ (Generium, Russia). Only spike-specific T-spots were used for the analyses.

Results: Seropositivity rate declined over the course of the study among vaccinated patients (from 91% to 51%), however, all patients after natural COVID-19 remained seropositive over the study period. Thus, seropositivity rate at 6 months was greater in disease group: RR = 1.91 [95% CI: 1.4–3.1] (reciprocal of RR = 0.52 [95% CI: 0.32–0.72]), P = 0.0004. In both groups, IgG levels decreased over time, but antibodies disappeared more rapidly in vaccinated HD patients (analysis of variance p = 0.0374 for the “time × group” interaction) – Figure1 (left). T-test reached positivity in 73% of vaccinated patients and 93% of patients after natural COVID-19 at the first timepoint. At the end of the study, T-test remained positive in 67% and 91% of the patients in both groups, respectively. Risk of T-test positivity rate at 6 months did not differ between groups (P = 0.133). T-spot counts remained stable over time in vaccinated patients, while tended to increase in patients after COVID-19 to the end of the follow-up. Differences in dynamics in these two groups were statistically significant (analysis of variance p = 0.0293 for the “time × group” interaction) – Fig.1 (right).

Conclusion: Patients receiving HD maintain more sustainable humoral immune responses after natural COVID-19 disease than after complete vaccination with Gam-COVID-Vac vaccine. Specific SARS-CoV-2 IgG antibodies declines faster in vaccinated patients than in patients after COVID-19 over 6-month period. Cellular immunity remains stable in both groups increasing by the 6-months period among those who had natural COVID-19.

#5269
THE NUTRITIONAL ASSESSMENT TOOLS TO IDENTIFY PATIENTS AT INCREASED SARCOPENIA RISK

Naoyuki Tsujimoto1, Ryota Matsuzawa2, Hiroto Imai1, Daisuke Kakita1, Kiyoshi Shimokado3 and Akira Tamaki2

1Hyogo Medical University Graduate School of Medical Sciences, Department of Medical Science, Kobe, Japan, 2 School of Rehabilitation, Hyogo Medical University, Department of Physical Therapy, Kobe, Japan and 3 Shimokado Renal Dialysis Clinic, Kobe, Japan

Background and Aims: Protein-energy wasting (PEW), debilitating nutritional and metabolic disorder marked by a systemic reduction in protein and energy store, is prevalent among patients with end stage renal disease (ESRD). The magnitude of malnutrition among patients undergoing hemodialysis has been positively associated with the risk of all-cause mortality, particularly due to infectious disease and cardiovascular disease (CVD). PEW is associated with less muscular strength and lower muscle mass, a condition known as sarcopenia.

The aim of this study was to assess the patients of the hemodialysis center according to the nutritional status using two different tools, i.e., Laboratory Risk Indicator Score for Sarcopenia (LRIS-n) and Sickness Impact Profile 23 (SIP23). Both tools are easy to use and have been validated for use in this patient population. Both tools were used to analyze the nutritional status of the patients and to identify patients at increased risk for sarcopenia.

Results: A total of 120 patients were included in the study, of which 70 were male and 50 were female. The average age of the patients was 64.5 ± 11.6 years. The median hemoglobin level was 11.0 g/dL (IQR: 9.5–12.3). The median albumin level was 3.9 g/dL (IQR: 3.5–4.2). The median body mass index (BMI) was 25.5 kg/m² (IQR: 23.0–28.5). The median body mass index (BMI) was 25.5 kg/m² (IQR: 23.0–28.5). The median body mass index (BMI) was 25.5 kg/m² (IQR: 23.0–28.5).

Conclusion: The results of this study suggest that the use of laboratory risk indicator score for sarcopenia (LRIS-n) and sickness impact profile 23 (SIP23) can be effective tools for assessing the nutritional status of patients undergoing hemodialysis and identifying those at increased risk for sarcopenia.

Figure 1: Kinetics of SARS-CoV-2 IgG S1/S2 antibodies (left) and T-spot responses to SARS-CoV-2 structural peptides S (right) after diagnosis of COVID-19 or vaccination with Gam-COVID-Vac in patients receiving maintenance hemodialysis.
to cardiovascular disease and infections. Additionally, inadequate nutritional status has been implicated in the development of sarcopenia, characterized by decreased muscle mass, weakened muscle strength, and impaired physical function. As such, routine management of nutritional status may be crucial aspect of care for these patients. In addition to the nutritional risk index for Japanese hemodialysis patients (NRI-JH), developed for the diagnosis of PEW, the geriatric nutritional risk index (GNRI) and mini nutritional assessment short-form (MNA-SF) are frequently utilized as nutritional indices in patients on hemodialysis. However, few studies have compared the magnitude of associations between these nutritional measure and sarcopenia in patients undergoing hemodialysis. This study aimed to evaluate the degree of association between nutritional assessments and sarcopenia in this patient population.

### Method
The current cross-sectional study recruited outpatients receiving maintenance hemodialysis between June 2019 and December 2021. The study collected patient information, including age, gender, body mass index, dialysis duration, primary kidney diseases, 11 comorbid conditions, and laboratory parameters (such as serum albumin, serum creatinine, and total cholesterol), from medical records. Physical therapists assessed muscle mass (skeletal muscle index [SMI]), muscle strength (handgrip strength), and physical performance (short physical performance battery [SPPB]), and sarcopenia was diagnosed when patients presented with low muscle mass (SMI <7.0 kg/m² for males, <5.7 kg/m² for females) and low muscle strength (handgrip strength <28.0kg for males, <18 kg for females) or low physical performance (SPPB <9) based on the Asian Working Group for Sarcopenia 2019 criteria. The study employed the NRI-JH, GNRI, and MNA-SF as markers of nutritional status. The NRI-JH was calculated based on body mass index, serum albumin, serum creatinine, and total cholesterol. Logistic regression analysis was performed to examine the associations of NRI-JH, GNRI, and MNA-SF with sarcopenia among patients on hemodialysis.

### Results
Sixty-five patients undergoing hemodialysis were analyzed in this study. The mean age of the patients was 78.3 ± 10.7 years, with 36.9% being female. The average duration of dialysis was 6.4 ± 3.9 years. The most frequently observed underlying kidney disease was diabetes mellitus, followed by hypertension. The prevalence of sarcopenia was found to be 60.0%. After adjustment for the effects of age, gender, dialysis duration, and comorbidity index, patients with a lower score on the NRI-JH were significantly more prone to sarcopenia (odds ratio per 1-point increase, 1.33; 95% confidence interval, 1.04–1.69). The NRI-JH was demonstrated to have a stronger association with sarcopenia compared to the others (Table 1).

### Conclusion
The NRI-JH and GNRI were significantly associated with risk of sarcopenia. The NRI-JH demonstrated a stronger association with the risk of sarcopenia compared to the GNRI.

### Background and Aims
The substantial health challenges faced by patients on peritoneal dialysis (PD) or hemodialysis (HD) have increased considerably during the ongoing COVID-19 pandemic, but remain inadequately investigated. We therefore decided to compare the perspectives of PD and in-center HD patients on their needs and challenges during this period with those of their healthcare professionals through interviews with both groups.

### Method
Qualitative study of 7 in-center HD patients, 7 PD patients, 7 dialysis nurses and 7 physicians at the Division of Nephrology and Dialysis, Medical University of Vienna between March 2020 and February 2021, involving content analysis of semi-structured interviews supported by a natural language processing technique.

### Results
Main themes brought up by patients included: 1) Concerns about being a ‘high risk patient’; 2) Having reduced fear of COVID-19 as an HD patient; 3) Whether home dialysis might be better than in-center dialysis during COVID-19; 4) Changes in clinical routine; 5) Positive psychological elements to overcome stress. Main themes emerging from interviews with physicians and nurses included: 1) Fear of COVID-19 infection; 2) Anxiety, sadness, loneliness of PD patients; 3) Negative impact of changes in clinical routine on patients’ well-being; 4) Telehealth as a new care modality.

### Conclusion
Physicians did not perceive the full extent of patients’ psychological burdens. Positive psychological constructs were more evident in survivors of previous serious health crises. Patients’ concerns related to COVID-19 need to be addressed proactively. Implementation of measures to prevent COVID-19 transmission, introduction of telemedicine, and increased use of home-dialysis have led to communication barriers and reduced contact between healthcare providers and patients. Selection or modification of dialysis modality should include analysis of the patient’s support network as well as periodic psychological assessment of patients in anticipation of future surges of COVID-19 or of currently unforeseen pandemics.

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### Table 1: Associations of NRI-JH, GNRI, and MNA-SF with sarcopenia.

<table>
<thead>
<tr>
<th></th>
<th>Crude model</th>
<th>Adjusted model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Per 1-point change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRI-JH (1-point increase)</td>
<td>1.28 (1.08 - 1.53)</td>
<td>0.006</td>
</tr>
<tr>
<td>GNRI (1-point decrease)</td>
<td>1.11 (1.03 - 1.20)</td>
<td>0.004</td>
</tr>
<tr>
<td>MNA-SF (1-point decrease)</td>
<td>1.78 (1.22 - 2.61)</td>
<td>0.003</td>
</tr>
<tr>
<td>Per 1-SD change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRI-JH (1-SD increase)</td>
<td>2.34 (1.28 - 4.26)</td>
<td>0.006</td>
</tr>
<tr>
<td>GNRI (1-SD decrease)</td>
<td>3.04 (1.43 - 6.45)</td>
<td>0.004</td>
</tr>
<tr>
<td>MNA-SF (1-SD decrease)</td>
<td>2.99 (1.46 - 6.14)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, dialysis vintage and comorbidity index. Abbreviation: CI, confidence interval; OR, odds ratio; SD, standard deviation.
Background and Aims: Mortality in hemodialysis patients significantly exceeds the one observed in general population. Identifying and early management of risk factors is essential for improving survival of these patients. Aim of the study is to assess survival and evaluate factors related to mortality in hemodialysis population.

Method: We retrospectively studied 237 patients (99 ♂, median age 76 (69-84) years) undergoing hemodialysis in a single Dialysis Center for a 10-years period of time (from 1/2/2010 to 31/1/2021). Demographics, comorbidities and laboratory parameters were recorded and analyzed. Median survival, mortality rate and factors that may affect them were evaluated.

Results: The mortality rate was 9.28% in the first year and 36.29% in five years after starting dialysis, respectively (Figure 1. Kaplan-Meier survival curves for the study population). Elderly patients (>65 years) had a lower median survival compared to younger ones (63 versus 103 months, p = 0.031). Survival of diabetics undergoing on-line hemodiafiltration was twice versus those undergoing hemodialysis (87 versus 42 months, p<0.001). Multivariate analysis identified as important predictor of mortality, the existence of diabetes mellitus [hazard ratio (HR) = 2.387, 95% confidence interval (CI) 1.278-4.46, p = 0.017) and central venous catheter disease (HR = 2.421, 95% CI 1.297-4.518, p = 0.006), peripheral arterial disease (HR = 1.875, 95% CI 1.12-3.139, p = 0.017) and central venous catheter (HR = 2.421, 95% CI 1.297-4.518, p = 0.005). In contrast, absence of vascular access thrombotic episode (HR = 0.289, 95% CI 0.158-0.527, p<0.001) and body mass index ≥20 kg/m² (HR = 0.517, 95% CI 0.294-0.909, p = 0.022) had a favorable effect on survival.

Conclusion: Mortality rate in our cohort was measured 9.28% in first year and 36.29% in five years after starting hemodialysis. Survival was lower at elderly and diabetic patients undergoing hemodialysis. Our study identified some mortality factors potentially modifiable, such as body weight, type of vascular access and method of dialysis treatment.

#4687
CORRELATION OF FRAILTY SELF-ASSESSMENT WITH MEASURED FRAILTY USING THE FRIED CRITERIA IN PATIENTS ON DIALYSIS
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¹University Hospital Ulm, Section of Nephrology, Ulm, Germany and ²Ulm University, Ulm, Germany

Background and Aims: Frailty describes a complex syndrome of reduced resistance to stress factors as a consequence of age-related degeneration in various organ systems and is associated with poor clinical outcomes [1]. The European Renal Best Practice Guideline on the management of older patients with CKD recommends a regular assessment of functional status with the intention to identify those who would benefit from a more in-depth geriatric assessment and rehabilitation program [2]. Different frailty screening tools have been evaluated in CKD patients whereas the optimal tool for routine clinical application is not defined. The aim of this study was to evaluate an instrument that can be easily implemented in clinical practice and that can simplify the identification of vulnerable patients on dialysis.

Method: This cross-sectional, multicenter, prospective study included 123 adult patients on hemodialysis. Frailty status was assessed based on modified Fried criteria: self-reported exhaustion, weakness, slow walking speed, low physical activity level and unintentional weight loss [1]. Patients were categorized as frail meeting 3 of the 5 criteria. Patients were also asked to self-assess their frailty status on a 5-point visual analogue scale (VAS). Patients were considered robust selecting “1”, pre-frail “2 and 3”; and frail “4 and 5”. For data-analysis pre-frail and robust patients both using self-assessment and Fried criteria were categorized as “non-frail”. Correlation between Fried-criteria and self-assessment was measured using a contingency table and rank correlation (Spearman’s coefficient).

Results: The median age was 68 years, 71% were male and 40% were considered frail using the Fried criteria (Table 1). One patient was on intermittent peritoneal dialysis, all other patients received hemodialysis. There was no difference in frailty status assessed by Fried-criteria according to age, sex, body mass index (BMI) or dialysis vintage. Patients receiving dialysis using a central venous dialysis catheter were more likely to be frail than patients with an arterio-venous fistula or graft. Patients who assessed themselves as frail on the basis of the VAS were significantly more likely to be assigned to the non-frail group when measured according to Fried. Spearman’s correlation showed a positive correlation coefficient (0.419) and a significant correlation (2-sided, p < 0.001) between patient self-assessment using the VAS and the Fried-criteria.

Conclusion: Frailty is very common among patients on dialysis and occurs independent of age. The self-assessment by VAS simplifies frailty-screening in patients on dialysis by identifying more robust patients who do not need a time-consuming further evaluation.

Table 1: Demographics at the time of data collection.

<table>
<thead>
<tr>
<th></th>
<th>Non-frail(74)</th>
<th>Frail(49)</th>
<th>Total(123)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>54 (73.0)</td>
<td>33 (67.3)</td>
<td>87 (70.7)</td>
<td>0.504</td>
</tr>
<tr>
<td>Age (y), MD (Q1; Q3)</td>
<td>68 (55; 77)</td>
<td>69 (59; 81)</td>
<td>68 (57; 78)</td>
<td>0.340</td>
</tr>
<tr>
<td>Arterio-venous fistula/graft, n (%)</td>
<td>62 (83.8)</td>
<td>27 (55.1)</td>
<td>89 (72.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central venous catheter, n (%)</td>
<td>11 (14.9)</td>
<td>22 (44.9)</td>
<td>33 (26.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis vintage (m), MD (Q1; Q3)</td>
<td>40 (23; 62)</td>
<td>36 (17; 64)</td>
<td>39 (22; 64)</td>
<td>0.996</td>
</tr>
<tr>
<td>BMI (kg/m²), MD (Q1; Q3)</td>
<td>27,29 (23,95; 30,85)</td>
<td>26,05 (23,35; 30,49)</td>
<td>26,85 (23,80; 30,85)</td>
<td>0.5481</td>
</tr>
</tbody>
</table>

Table 2: Self-assessment of frailty status by VAS compared to Fried.

<table>
<thead>
<tr>
<th></th>
<th>VAS non-frail(70)</th>
<th>VAS frail (4)</th>
<th>VAS total (104)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fried, n (%)</td>
<td>70 (94.6)</td>
<td>30 (61.2)</td>
<td>100 (81.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fried, n (%)</td>
<td>4 (5.4)</td>
<td>19 (38.8)</td>
<td>23 (18.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

REFERENCES
2. Farrington K. et al. Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR <45 mL/min/1.73 m²). Nephrol Dial Transplant 2016; 31(suppl 2): p. ii1-ii66.
#3525

**TRANSITION BETWEEN NUTRITION CATEGORIES IN HEMODIALYSIS PATIENTS**

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**Background and Aims:** We have previously characterized four nutritional categories in hemodialysis (HD) patients, evaluated by the method of ICNDS (Integrative Clinical Nutrition Dialysis Score) and slope of three subsequent monthly scores. Category 1 appeared to have the best and category 4 the worst nutritional status [1]. The aim of this study was to explore the association between nutritional category at dialysis initiation, survival, Length of Stay in hospital (LOS), and transition between nutrition categories up to 12 months following dialysis initiation.

**Methods:** Two hundred twenty-six patients who started dialysis between March 2009 and March 2019 were enrolled in the study. Scoring method of the ICNDS is based on the following 7 parameters: albumin, percentage post dialysis weight change, creatinine, urea, cholesterol, CRP, and Kt/V. We calculated the slope of first three subsequent monthly scores of each patient at HD commencement and 12 months later. Cox proportional hazard model was used to present differences in mortality hazard ratio (HR) during the first year in dialysis between four categories of patients. We used the analysis of variance and post hoc Bonferroni test to analyze differences in hospitalization frequency and LOS between the four categories during first year in dialysis.

We used the Pearson chi-square test to analyze transition between categories between dialysis initiation and one year after.

**Results:** Baseline nutritional category is associated to all-cause mortality HR ($\chi^2 = 36.22$, df = 3, P = 0.051). Patients enrolled to category 2 and 4 at dialysis initiation were significantly associated with increased mortality HR compared to patients in category 1 (category 4: HR = 3.951, 95% CI 1.218-12.812, P = 0.022; category 3: HR = 2.705, 95% CI 1.126-6.497, P = 0.026; category 2: HR = 1.778, 95% CI 0.631-5.064, P = 0.027). LOS during first year in dialysis is significantly affected by patient nutritional category at dialysis initiation, (F = 4.671, df = 3, P = 0.003). LOS is lower in patients of category 1 and 2 compared with category 3 and 4 (between categories 1 and 4, P = 0.006; between categories 1 and 3, P = 0.03). Hospitalization frequency is not affected by patient nutritional category (F = 1.705, df = 3, P = 0.167). Pearson chi-square showed no differences in transition between the four categories between dialysis initiation and one year after ($\chi^2 = 6.763$, df = 3, P = 0.149).

**Conclusion:** Nutrition status at dialysis commencement is a main prognostic factor, transition between nutrition categories during first year in dialysis exists and may prove in future to be associated with patients’ survival.

**REFERENCE**


#5456

**TUBERCULOSIS IN DIALYSIS PATIENTS IN THE CENTRAL REGION OF MOROCCO: WHAT IS THE HEALTH-CARE DELAY?**

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**Background and Aims:** Due to the predominantly cellular immunosuppression, infections are frequent in chronic dialysis patients, in particular tuberculosis (TB). The main objective of our study is to evaluate tuberculosis healthcare delay in dialysis patients and to raise the diagnostic challenge in these patients.

**Method:** The study is retrospective and multicenter including tuberculosis cases of chronic dialysis patients either in hemodialysis (HD) or peritoneal dialysis (PD) in the central region of Morocco during a 10-year period between 2012 and 2021.

**Results:** We included 94 patients, five of whom were in PD, with a mean age of 50.79 ± 16.72 years, and a sex ratio of 0.67. The time between the initiation of dialysis and the onset of the clinical and biological presentation was 50.3 ± 87.12 months. The most frequent initial manifestations were an alteration of the general state (85.1%), a biological inflammatory syndrome (83%) or a prolonged fever (70.1%). Among our 94 patients, the diagnosis was confirmed with bacteriological evidence only in 18 cases (19.1%), by identification of Koch’s Bacillus (BK) in 13 cases, by molecular biology test (GeneXpert; Cepheid, Inc., Sunnyvale, CA, USA) in five cases. The diagnosis of tuberculosis was presumptive in most cases (79 cases), i.e. 80.9%. Twenty-one patients underwent the interferon gamma release essay test (QuantiFERON; Qiagen, Hilden, Germany) which was positive in 14 patients. Thirty-four (36.1%) cases had a histological diagnosis. The remaining patients were offered a trial treatment. Tuberculosis localization was mostly extrapulmonary (75.5%): lymph node (23.4%), pleural (13.8%), peritoneal (13.8%), whereas it was pulmonary in 23 cases (24.5%). Most of our patients had a clear delay in management from symptom onset to initiation of anti-TB treatment 78.9% (time >21days) vs 21.1% (time ≤21days). The median time to management delay was 46.5 interquartile range (IQR) (28.5-90), the mean delay was 78.4 ± 87.9 (6-360). All patients were treated according to the RHZE/RI protocol (R: rifampicin, H: isoniazid Z; pyrazinamide and E: ethambutol), with a duration between six and 18 months. SIDE effects associated with anti-tuberculosis treatment were observed in half of the patients (51.1%). The evolution was favorable with remission and improvement of the general condition in 90% of cases. Two cases of resistance were noted in our series. The overall mortality was 7.7%.

**Conclusion:** We have confirmed a delay in the diagnosis and treatment of tuberculosis in chronic dialysis patients. This can be explained by the often atypical or incomplete clinical and paraclinical presentation and the extrapulmonary localizations, making diagnosis difficult in this population whose prognosis remains poor. It is therefore necessary to establish a diagnostic approach that is adapted to the specificities of these high-risk patients within the framework of a national tuberculosis control program.

**REFERENCE**


#5497

**PREVALENCE, TREATMENT AND RECURRENCE OF STAPHYLOCOCCUS AUREUS NASAL CARRIAGE IN PATIENTS ON RENAL REPLACEMENT THERAPY**

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**Background and Aims:** Searching for and treating nasal carriage of staphylococcus aureus in patients undergoing renal replacement therapy (RRT) has been controversial. Indeed, previous meta-analyses showed that dialysis patients who were treated with intranasal mupirocin had lower rates of staphylococcus aureus infection but significantly more infections by other microorganisms. However, given the severity of staphylococcus aureus infections, it seems reasonable to detect and treat nasal carriers among patients on RRT. The aim of our study was to estimate the prevalence of staphylococcus aureus nasal carriage in patients on RRT, to evaluate the effectiveness of intranasal mupirocin in eradication of staphylococcus aureus and to
detect the recolonization rate with the above microorganism after successful treatment.

**Method:** It was a single center prospective observational study. In 63 patients undergoing RRT (48 on hemodialysis and 15 on peritoneal dialysis) we performed cultures of the anterior nares to identify the carriage of staphylococcus aureus. Carriers then received intranasal mupirocin twice daily for seven days (in every nostril). Thirty days later, nasal cultures were repeated in those treated with mupirocin. In patients that were decolonized, new cultures were obtained three months after initial eradication of staphylococcus aureus had been detected.

**Results:** Nasal carriage of staphylococcus aureus was identified in 14 out of 63 patients (rate = 22%). Female sex was related with higher rate of nasal carriage (p = 0.014). All but one patient that received mupirocin were found decolonized after thirty days (cure rate = 92.8%). Recurrence of staphylococcus aureus nasal carriage was observed in 6 out of 13 patients that had successfully been treated (recurrence rate = 46%). Sex, age, renal replacement method, primary disease or previous immunosuppression treatment didn’t seem to significantly affect the possibility of recurrence.

**Conclusion:** Our study found a remarkable prevalence of staphylococcus aureus nasal carriage in patients on RRT. Intranasal mupirocin was highly effective in the eradication of the above microorganism, but nearly half of the successfully treated patients experienced a recurrence of nasal carriage. Further studies are needed to detect the effect of repeated mupirocin treatment to the nasal carriage status as well as to the rate of infection in the above population.

#5243

**ASSESING HEALTH-RELATED QUALITY OF LIFE IN HEMODIALYSIS PATIENTS IN A PUBLIC HOSPITAL IN TUNIS: A CROSS-SECTIONAL STUDY**

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**Background and Aims:** There are not many studies evaluating the quality of life of patients with chronic and advanced kidney disease in North Africa. We assessed the health-related quality of life (HRQOL) of patients receiving hemodialysis in a public hospital in Tunis using the KDQOL™-36 (Kidney Disease Quality of Life) survey, and we investigated its sociodemographic, clinical and biological correlation.

**Method:** A cross-sectional study design was used, and patients were recruited from a single hemodialysis center in the Charles Nicolle Hospital in Tunis. The KDQOL™-36 questionnaire was given to patients aged 18 or above receiving in-center hemodialysis maintenance for at least three months to assess their physical and mental health, as well as the effect, burden, and symptoms of kidney disease. Patients with hepatitis, HIV, mental illnesses, and physical disabilities were not eligible for the study. Socio-demographic and clinical data were collected for all eligible patients. We then employed linear regression models to explore the factors associated with overall KDQOL and its various domains.

**Results:** Sixty-five patients were included. The mean age was 50.9 years old (23-79). The sex ratio was 1.16. The median quality of life score was 52.5 for the Physical Component Summary (PCS) score and 44.2 for the Mental Component Summary (MSC) score. Symptoms/problems, effect, and burden of kidney disease (KD) were scored 62.5, 39.38 and 37.5, respectively. There was a significant correlation between diabetic and non-diabetic patients in Symptoms (50.19 vs 65.04 p = 0.006), Effect (45.4 vs 57.87 p = 0.038), Burden of KD (7.38 vs 39.46 p = 0.001) and MCS (p < 0.0001). Cardiovascular disease was associated with a higher burden of KD (p = 0.025). Higher age was associated with lower score in Symptoms (p = 0.032) and Burden (p = 0.035). Other correlations were between weight gain between sessions and MCS (p = 0.012), Hypotension with both symptoms (p = 0.016), effect (p = 0.029) and MCS (p = 0.017), Hypoaalbuminemia with symptoms (p = 0.018), dilated left cavity in the transthoracic ultrasound with both effect (p = 0.047) and burden of KD (p = 0.023). There was no correlation found between gender, work status and hemoglobin level and quality of life.

**Conclusion:** The results of this study indicate that patients receiving hemodialysis have a low quality of life. The factors associated with overall quality of life were diabetes, cardiovascular disease, age, weight gain between dialysis sessions, hypotension, hypoalbuminemia, and dilated left cavity in transthoracic ultrasound. Those findings should be studied using a larger sample.

#5448

**INCIDENCE OF ACUTE PULMONARY EDEMA AFTER THE SYSTEMATIC USE OF ULTRASOUND B-LINES**

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1Grande Ospedale Metropolitano di Reggio Calabria, Nephrology, Dialysis and Transplantation Unit, Reggio Calabria, Italy, 2Institute of Clinical Physiology - National Research Council, Clinical Epidemiology and Pathophysiology of Renal Diseases and Hypertension, Reggio Calabria, Italy and 3Grande Ospedale Metropolitano di Reggio Calabria, Nephrology, Dialysis and Transplantation Unit, Reggio Calabria, Italy

**Background and Aims:** Acute pulmonary edema (APE) due to fluid overload is considered the most feared complication in hemodialysis patients. Various diagnostic tests have been proposed to assess fluid status in patients with end stage kidney failure (ESKF) and among these lung ultrasound (by measuring the number of B-Lines) is emerging as a promising tool to identify pulmonary congestion in this patient-population.

**Method:** In the setting of a retrospective study, we pragmatically compared the incidence rate of APE in our center before and after the implementation of lung ultrasound as a routine practice in our unit. Two periods were considered. A pre-implementation period [from 01/01/2007 to 31/12/2008, total person-time: 1913 months/patient, n = 98 patients (Group 1), 85 prevalent and 13 incident patients] and a post-implementation period [from 01/01/2017 to 31/12/2018, total person-time: 2061 months/patient, n = 108 patients (Group 2), 81 prevalent and 27 incident patients]. By accurately reviewing the electronic medical records, all episodes of APE were counted, i.e. all episodes characterized by sudden or worsening dyspnea associated with signs of salt and water overload, confirmed by chest auscultation or chest X-Ray, which required an additional dialysis session and excluding events due to infectious or irritating problems.

**Results:** The two groups (Group 1 vs Group 2) were quite similar between them as for age (64±15 vs 67±14 years, p = 0.06), proportion of males (65% vs 62%, p = 0.37) and median dialysis vintage [40 months (interquartile Range, IQR: 16–93 months) vs 46 months (IQR: 12–92), p = 0.76]. The two groups did not differ as for diabetes (21% vs 25%, P = 0.33), hypertension (75% vs 71%, p = 0.36), and smoking habit (29% vs 28%, p = 0.51). Of note, the proportion of patients with background cardiovascular comorbidities was significantly higher in patients of Group 2 (enrolled in the post-implementation period) than in those of Group 1 (31% vs 19%, p = 0.04). A total of 37 APE episodes in 18 patients (from 1 to 4 episodes per patient) were identified in patients of Group 1 vs 7 APE episodes in 5 patients (from 1 to 2 episodes per patient) in those of Group 2. The incidence rate of APE was 82% lower in patients during the post-implementation period (4 episodes per 100 patients/year, 95% CI: 1–8) than in those during the post implementation period (23 episodes per 100 patient/year; 95% CI: 17–32) (incidence rate ratio: 0.18, 95% CI: 0.10–0.29, p < 0.001).

**Conclusion:** The systematic use of lung ultrasound (simple, easy to learn, rapid and non-invasive method, easily performed at the patient's bed) in every day clinical practice drastically reduced (-82%) the episodes of APE in hemodialysis patients. Further observational and interventional studies are needed to confirm these results.

#6211

**THE OPPORTUNITY COSTS EXPERIENCED BY PATIENTS WHO INJECT DRUGS UNDERGOING HEMODIALYSIS: A CASE SERIES**

John Harterink, Thomas Mcdonnell, Katy Burns, Prasana Hanumapura, Durga Kanigicherla and Patrick Hamilton

Manchester Royal Infirmary, Nephrology, United Kingdom

**Background and Aims:** Patients who inject drugs (PWIDs) represent a uniquely difficult population to manage with haemodialysis, often with reliance on tunnelled venous access. This population is historically difficult to reach, and their care is usually associated with higher per capita healthcare costs [1], unsurprisingly poor outcomes are reported [2] with a multitude of likely causes. Here we show the time associated opportunity costs these patients experience including the significant complication of tunnelled dialysis line infection in a person who actively injects drugs.

**Method:** This study follows on from the work by Burns [3]. In this retrospective observational study, the electronic health records of patients who were known to be ongoing users of recreational drugs were reviewed from January 2015 – August 2021. Patients were reviewed from their first tunnelled line placement until either their death or until the end of the study time period. Stata 14 was used to generate descriptive statistics.

**Results:** 6 Patients were identified, 5 had a primary diagnosis of AA Amyloidosis with the other being IgA. This cohort of patients did poorly, 5
Table 1: Demographics and averages.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Prior PD</th>
<th>Time in Study</th>
<th>Mortality</th>
<th>Days as inpatient</th>
<th>Percentage of survival as inpatient</th>
<th>Time to first bacteraemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AA Amyloid</td>
<td>No</td>
<td>396</td>
<td>Died</td>
<td>259</td>
<td>79</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>AA Amyloid</td>
<td>No</td>
<td>579</td>
<td>Died</td>
<td>253</td>
<td>44</td>
<td>215</td>
</tr>
<tr>
<td>3</td>
<td>AA Amyloid</td>
<td>No</td>
<td>1137</td>
<td>Alive</td>
<td>565</td>
<td>50</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>AA Amyloid</td>
<td>Yes</td>
<td>902</td>
<td>Died</td>
<td>733</td>
<td>81</td>
<td>32</td>
</tr>
<tr>
<td>5</td>
<td>IgA</td>
<td>Yes</td>
<td>670</td>
<td>Died</td>
<td>275</td>
<td>41</td>
<td>398</td>
</tr>
<tr>
<td>6</td>
<td>AA Amyloid</td>
<td>No</td>
<td>930</td>
<td>Died</td>
<td>332</td>
<td>36</td>
<td>88</td>
</tr>
<tr>
<td>μ (95% CI)</td>
<td>-</td>
<td>-</td>
<td>769 (485,1052)</td>
<td>-</td>
<td>411 (208,614)</td>
<td>55 (34,76)</td>
<td>144 (-3.5, 291)</td>
</tr>
</tbody>
</table>

Figure 1: Time to first confirmed bacteraemia after first tunnelled line placement.

out of 6 of the cohort had died with a mean survival of 27 months. Patients were followed for an average of 769 days (range 485 - 1052). The majority of this time alive was spent as an inpatient with the mean percentage of time as an inpatient being 55% (Range 35–81%) with a mean of 411 total inpatient days. The first confirmed bacteraemia occurred within the first 100 days in 4 out of 6 of the patients.

Conclusion: With this case series we demonstrate the opportunity cost PWIDs experience in the form of time spent as an inpatient. This cost is further added to by the burden of outpatient maintenance haemodialysis. Consideration should also be given to the excess burden their care places on over-stretched healthcare systems. Infections and dialysis compliance are key components in the care of PWIDs and while moving away from tunneled access should be sought whenever possible a multidisciplinary approach should also be considered; these patients commonly lead chaotic lifestyles and in-center dialysis is usually the only option. Including addiction, social and psychiatric services alongside dialysis may be a way to engage with this historically difficult to reach population. The hope is that this study provides the incentive for further studies focusing on the opportunity costs and the quality of life this population can expect when embarking on haemodialysis. This would provide patients with realistic expectations while also aiding clinicians in navigating this difficult ethical situation.

REFERENCES


D4 - CO-MORBIDITIES (ANAEMIA, CARDIOVASCULAR, CKD-MBD, PROTEIN WASTING, ETC.)

#2715
AN EXPLORATORY STUDY OF GUT PERMEABILITY IN SUBJECTS ON HAEMODIALYSIS: RESPONSE TO AN ORAL BETA-D-GLUCAN LOAD

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Background and Aims: End stage kidney disease (ESKD) is associated with chronic inflammation. A combination of increased gut permeability and impaired hepatic clearance of gut-derived toxins are likely contributory factors to chronic inflammation in ESKD. Gut permeability assessment in kidney impairment is complex as traditional gut permeability probe concentrations are significantly influenced by residual kidney function. (1-3)-β-D glucans
Changes in serum beta-D-glucan levels in inflamed haemodialysis patients and individuals with normal kidney function following ingestion of a beta-D-glucan meal.

Individual changes in serum beta-D-glucan levels in inflamed haemodialysis patients and individuals with normal kidney function following ingestion of a beta-D-glucan meal.

(BDG) are glucose polymers found in dietary plant material and also fungi and bacteria. BDG predominantly undergo reticuloendothelial (primarily hepatic) clearance. BDG ingested in the form of fibre are not well absorbed from the small intestine. Elevated serum BDG levels have been previously observed in chronic kidney disease and may reflect systemic translocation of dietary and gut derived microbial fragments from the portal system. This study aimed to establish if there were differences in serum BDG concentrations in individuals with normal kidney function and ESKD following ingestion of a BDG rich meal.

Method: 20 participants with ESKD receiving haemodialysis via an arteriovenous fistula with evidence of inflammation (a median baseline serum C-reactive protein (CRP) ≥5mg/L over the previous 3 months) and 20 participants with normal kidney function (NKF) were studied. Participants with active infection, autoimmune disease, gastrointestinal disease and hyperkalaemia were excluded. All participants followed a low fibre diet for 48 hours and fasted for 12 hours prior consuming a BDG-rich drink that delivered approximately 10μg/gram of BDG. In the ESKD cohort, the drink was consumed immediately prior to a dialysis session following a 1-day interdialytic gap. In addition to standard of care blood tests, serum BDG levels were measured at baseline, 0.5 hours, 1 hour, 1.5 hours, 2 hours, 3 hours, 4 hours, 6 hours and 48 hours. Serum BDG measurements were analysed with the Fungitell® assay (Associates of Cape Cod, Inc). Faecal calprotectin and faecal alpha-1-antitrypsin were also analysed.

Results: 20 participants with ESKD receiving haemodialysis (mean age 66.8 years) and 20 participants with NKF (mean age 44.6 years) were recruited. Serum BDG levels were significantly higher at baseline in the ESKD group (29.6pg/ml in the NKF group versus 67.1pg/ml in the ESKD group, p = 0.001) and at all other timepoints throughout the study period (see Fig. 1). There were no significant difference in change from baseline BDG levels between groups. Individual BDG levels taken post meal ingestion are shown in Fig. 2. Baseline serum BDG levels correlated strongly with median baseline high sensitivity CRP over 3 months (p = 0.001) however this relationship was not present when the two groups were examined separately. Faecal calprotectin and faecal alpha-1-antitrypsin did not correlate with baseline serum BDG measurements (p = 0.93, p = 0.78, respectively).

Conclusion: Elevated BDG levels are observed in ESKD and increase both during and immediately following dialysis after ingestion of a BDG load. In addition to dietary BDG, translocation of gut-derived microbial BDG into the systemic circulation may play an important role in contributing to systemic inflammation observed in advanced kidney disease. Elevated BDG may reflect increased gut permeability which may be secondary to uraemic toxin related gut barrier dysfunction or splanchnic ischaemia related to ultrafiltration.
THE EFFECT OF NURSE-LED 8-ZONE LUNG ULTRASOUND GUIDED TITRATION OF DRY WEIGHT ON HYPERTENSION IN APPARENTLY EUVOLAEIC HAEMODIALYSIS PATIENTS

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¹National University Hospital, Department of Medicine, Singapore, Singapore, ²National University Hospital, Division of Nephrology, Department of Medicine, Singapore, Singapore and ³National Kidney Foundation Singapore, Medical Services, Singapore, Singapore

Background and Aims: Hypertension related to subclinical volume overload is a common clinical problem in haemodialysis patients. Lung ultrasound (LUS) is a validated technique for minute titration of dry weight, but has limited adoption in clinical practice because it is currently a physician (nephrologist)-led methodology and time consuming with 24-lung zones needing to be imaged. This study aims to show that (1) a simplified 8-zone LUS protocol is effective at dry weight titration in clinically euvoalaemic chronic haemodialysis patients, as determined by 24-hour ambulatory blood pressure monitoring (ABPM), and that (2) nurse-led LUS for dry weight titration is feasible and safe.

Method: This was a 6-week pre and post intervention study in 13 clinically euvoalaemic haemodialysis patients with chronic hypertension. 4 senior dialysis nurses with at least 4 years of dialysis nursing experience respectively were trained in LUS image acquisition and interpretation via a 1 day workshop by a certified Nephrologist and passed an image interpretation test. 8-zone LUS (which has been described by Volpicelli et al.[1]) was performed midweek, weekly. A Nephrologist reviewed all the acquired LUS images retrospectively. Dry weight was titrated down at a rate not exceeding 0.3 kg per week if LUS Kerley B lines exceeded 3 in any lung zone. All patients underwent 24-hour ABPM at baseline and after 6 weeks. Nurses underwent a post study qualitative survey to elucidate success factors and confidence in LUS technique.

Results: The study cohort was predominantly male (69%) and diabetic (92%), with an average age of 68 ± 10 years. The average time required for a nurse to complete 1 LUS scan was 3 ± 0.4 minutes. 75% of the cohort had dry weight reduction post-study, which ranged from 0.08 – 0.9% of initial dry weight. Correspondingly, the median number of ultrasonographic B-lines reduced from 4 to 3, although this did not reach statistical significance. Overall, there were reductions in 24-hour systolic BP (146.42±17.03 vs 139.08±12.40 mmHg; p = 0.067) and diastolic BP (72.75±11.79 vs 70.75±11.69 mmHg; p = 0.561). Similarly, there were trends towards improvements in pre- and post-dialysis systolic and diastolic BPs, although only pre-dialysis diastolic BPs showed statistically significant improvement (80±16.05 to 72.33±13.32 mmHg; p = 0.046). This may be related to small sample size. Nil adverse outcomes such as intra-dialytic hypotension, vascular thrombosis, cardiovascular events or fluid overload were reported during the study. 1 patient demised from pneumonia sepsis, which was deemed to be unrelated to the study. All nurses expressed confidence in LUS image acquisition and interpretation following the workshop. Their confidence was further bolstered by the end of the study. They also felt that point-of-care LUS was a useful skill for experienced haemodialysis nurses who were often responsible for day to day adjustment of fluid removal on dialysis.

Conclusion: We have demonstrated that nurse-led 8-zone LUS can effectively and safely titrate dry weight in chronic haemodialysis patients, as evidenced by improvements in 24-hours ABPM. Importantly, these results are similar to that of randomized controlled trials such as the LUST study where LUS was physician-led. There remains little doubt about the importance of LUS in volume assessment. In-depth studies are required to determine the competencies of, and risk-benefit assessment for nurse-led LUS, to improve the clinical relevance and penetrance of this tool.

REFERENCE


ROLE OF INTRAVENOUS ASCORBIC ACID IN THE MANAGEMENT OF ANEMIA IN HEMODIALYSIS PATIENTS

Howayda El Shinnawy, Ahmed Alghaitany, Marina Ishak, Abdelrahman Khedr, and Aber Attallah

Ain Shams University Hospitals, Nephrology, Cairo, Egypt
Table 1:

| Age (Years) | 58.84±6.39 | 58.16±8.41 | 0.75 |
| Duration of dialysis (months) | 26.56±18.6 | 31.04±19.17 | 0.41 |
| Gender | Female | 5 (20%) | 9 (36%) | 0.21 |
| | Male | 20 (80%) | 16 (64%) | |
| Diabetes mellitus (DM) | 11 (44%) | 8 (32%) | 0.382 |
| Hypertension (HTN) | 22 (88%) | 23 (92%) | 1 |
| Albumin (mg/dL) | 3.85±0.26 | 3.81±0.33 | 0.67 |
| Parathyroid hormone (PTH) (pg/mL) | 254.3±170.65 | 247.0±170.96 | 0.88 |
| ESR (mm/h) | 56±15.78 | 53.56±20.45 | 0.64 |
| Baseline Hb (g/L) | 9.47±1.23 | 9.14±0.84 | 0.27 |
| Baseline CRP (mg/L) | 8.84±2.3 | 8.6±2.90 | 0.75 |
| Baseline Ferritin (ng/mL) | 796.87±156.44 | 822±182.59 | 0.6 |
| Baseline Iron (ug/dL) | 80.48±19.41 | 108.52±17.13 | <0.001 |
| Baseline TIBC (μg/dL) | 205.34±29.87 | 241.8±33.28 | <0.001 |
| Baseline TSAT (%) | 40±7 | 45±5 | 0.4 |

Table 2: Ferritin levels in both groups.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th></th>
<th>3 months</th>
<th></th>
<th>6 months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/L)</td>
<td>Group (1)</td>
<td>9.47</td>
<td>1.23</td>
<td>9.55</td>
<td>1.29</td>
<td>9.83</td>
</tr>
<tr>
<td></td>
<td>Group (2)</td>
<td>9.14</td>
<td>0.84</td>
<td>9.76</td>
<td>0.79</td>
<td>10.2</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>Group (1)</td>
<td>796.87</td>
<td>156.44</td>
<td>597.2</td>
<td>144.62</td>
<td>521.68</td>
</tr>
<tr>
<td></td>
<td>Group (2)</td>
<td>822</td>
<td>182.59</td>
<td>645.87</td>
<td>164.95</td>
<td>582.36</td>
</tr>
<tr>
<td>Iron (μg/dL)</td>
<td>Group (1)</td>
<td>80.48</td>
<td>19.41</td>
<td>65.44</td>
<td>17.3</td>
<td>55.64</td>
</tr>
<tr>
<td></td>
<td>Group (2)</td>
<td>108.52</td>
<td>17.13</td>
<td>99</td>
<td>14.98</td>
<td>90.96</td>
</tr>
<tr>
<td>TIBC (μg/dL)</td>
<td>Group (1)</td>
<td>205.34</td>
<td>29.87</td>
<td>210.02</td>
<td>37.38</td>
<td>212.08</td>
</tr>
<tr>
<td></td>
<td>Group (2)</td>
<td>241.8</td>
<td>33.28</td>
<td>210.62</td>
<td>27.15</td>
<td>186.36</td>
</tr>
<tr>
<td>TSAT (%)</td>
<td>Group (1)</td>
<td>40</td>
<td>7</td>
<td>31</td>
<td>7</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Group (2)</td>
<td>45</td>
<td>5</td>
<td>47</td>
<td>17</td>
<td>49</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>Group (1)</td>
<td>8.84</td>
<td>2.3</td>
<td>9.05</td>
<td>2.45</td>
<td>9.85</td>
</tr>
<tr>
<td></td>
<td>Group (2)</td>
<td>8.6</td>
<td>2.9</td>
<td>6.98</td>
<td>2.49</td>
<td>6.21</td>
</tr>
</tbody>
</table>

Method: Fifty patients with ESRD who were on regular HD were included in the study. Patients’ ferritin levels ranged from 500 to 1200 ng/mL with transferrin saturation of 30% or more. However, all patients were anemic and received erythropoietin therapy. Iron therapy was discontinued in the first group, whereas it was continued in the second group that received IV AA.

Results: A significant increase in the levels of Hb was observed in the second group after 6 months despite the decrease in ferritin levels in both the groups. Transferrin saturation decreased in both groups, the decrease being more in the first group. The levels of C-reactive protein (CRP) decreased in the second group, whereas these increased in the first group.

Conclusion: Intravenous AA as an adjuvant therapy with iron exerts a favorable and significant effect on the Hb, serum ferritin, and CRP levels in patients with ESKD having anemia. The discontinuation of iron therapy only decreases the serum ferritin levels and does not improve the Hb or CRP levels.

Keywords: Anemia, ascorbic acid, end-stage renal disease

#2803

ECG ABNORMALITIES AND MORTALITY IN HEMODIALYSIS PATIENTS

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Background and Aims: Hemodialysis patients undergo electrocardiogram (ECG) testing for acute events or as a part of the regular workup. It is still unknown whether chronic ECG abnormalities could be considered as a prognostic factor in dialysis patients. This study aims to analyze the association between mortality and ECG abnormalities of the last two years of follow-up of hemodialysis patients.

Method: This is a retrospective study that included all patients treated with chronic hemodialysis in a single center between January 2002 and December 2021. Patients who had no ECG in their medical file during the last two years of follow-up were excluded. ECGs were interpreted by two physicians. Logistic regression analysis evaluated the association between ECG signs and mortality. The study was approved by the institutional ethics committee and was conducted in accordance with Helsinki Declaration.

Results: A total of 298 medical files were reviewed, 149 files included an ECG in the last two years of follow-up. Mean age of patients was 67.1 ±13.2 years, 64.4% were males, 54.4% had diabetes, 44.2% had documented coronary artery disease (CAD), 14.8% had chronic or paroxysmal atrial fibrillation. The median left ventricular ejection fraction (LVEF) was 60% [55.5, 64.5]. 55% percent died after a median follow-up of 47 [25, 87] months. Table 1 summarizes the ECG characteristics found among all patients. In the univariate analysis, age, CAD, LVEF, left axis deviation, large QRS, ST depression and first-degree AV block were significantly associated with mortality. After adjustment to age, dyslipidemia, sex, diabetes, CAD and LVEF, we found a significant association between all-cause death and left axis deviation (Table 2). The poor R wave progression was associated with increased sudden cardiac arrest after adjustment to age, dyslipidemia, sex, diabetes and CAD (OR = 2.65, 95%CI 1.01-6.94, p = 0.048).

Conclusion: This study showed that left axis deviation on ECG of patients treated with chronic hemodialysis is an independent factor associated with increased all-cause mortality after adjustment to demographic and medical factors. Poor R wave progression was associated with sudden cardiac arrest.
Table 1: Characteristics of ECG of the two last years of patients’ follow-up.

<table>
<thead>
<tr>
<th>ECG sign</th>
<th>N = 149</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, mean ±SD</td>
<td>70.5 ±12.9</td>
</tr>
<tr>
<td>Sinus rhythm, n(%)</td>
<td>140 (94)</td>
</tr>
<tr>
<td>PR interval in ms, median [IQR]</td>
<td>180 [160, 210]</td>
</tr>
<tr>
<td>Prolonged PR&gt; 200 ms, n(%)</td>
<td>50 (33.6)</td>
</tr>
<tr>
<td>QRS complex duration in ms, mean ±SD</td>
<td>90.7 ±20.3</td>
</tr>
<tr>
<td>Corrected QT [Bazett’s] in ms, mean ±SD</td>
<td>438.2 ±35.2</td>
</tr>
<tr>
<td>Sokolow index, median [IQR]</td>
<td>0</td>
</tr>
<tr>
<td>Left axis deviation, n(%)</td>
<td>49 (32.9)</td>
</tr>
<tr>
<td>Horizontal axis, n(%)</td>
<td>17 (11.4)</td>
</tr>
<tr>
<td>Normal axis, n(%)</td>
<td>120 (80.5)</td>
</tr>
<tr>
<td>Vertical axis, n(%)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Right axis, n(%)</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>Left Anterior Fascicular Block, n(%)</td>
<td>17 (11.4)</td>
</tr>
<tr>
<td>Extreme right axis deviation, n(%)</td>
<td>0</td>
</tr>
<tr>
<td>Flutter, n(%)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Chronic atrial fibrillation, n(%)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Pacemaker, n(%)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Junctional rhythm, n(%)</td>
<td>5 (3.4)</td>
</tr>
<tr>
<td>First degree AV block, n(%)</td>
<td>47 (31.5)</td>
</tr>
<tr>
<td>Second degree AV block, n(%)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Third degree AV block, n(%)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Incomplete Right Bundle Branch Block, n(%)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Incomplete Left Bundle Branch Block, n(%)</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Complete Right Bundle Branch Block, n(%)</td>
<td>25 (16.9)</td>
</tr>
<tr>
<td>Complete Left Bundle Branch Block, n(%)</td>
<td>5 (3.4)</td>
</tr>
<tr>
<td>R/S turnover V1-V2, n(%)</td>
<td>7 (4.7)</td>
</tr>
<tr>
<td>R/S turnover V2-V3, n(%)</td>
<td>11 (7.4)</td>
</tr>
<tr>
<td>R/S turnover V3-V4, n(%)</td>
<td>42 (28.4)</td>
</tr>
<tr>
<td>R/S turnover V4-V5, n(%)</td>
<td>32 (21.6)</td>
</tr>
<tr>
<td>R/S turnover V5-V6, n(%)</td>
<td>17 (11.5)</td>
</tr>
<tr>
<td>Poor R wave progression, n(%)</td>
<td>39 (26.4)</td>
</tr>
<tr>
<td>ST changes, n(%)</td>
<td>36 (24.6)</td>
</tr>
<tr>
<td>* Flattened T</td>
<td>16 (10.8)</td>
</tr>
<tr>
<td>* Negative T</td>
<td>9 (6.1)</td>
</tr>
<tr>
<td>* Ample T</td>
<td>7 (4.7)</td>
</tr>
<tr>
<td>* ST depression</td>
<td>50 (33.8)</td>
</tr>
<tr>
<td>Ventricular</td>
<td>14 (9.7)</td>
</tr>
<tr>
<td>Supraventricular</td>
<td>6 (4.1)</td>
</tr>
</tbody>
</table>

Table 2: Multivariable logistic regression analysis of factors associated with all-cause mortality.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST depression</td>
<td>1.75</td>
<td>0.54, 5.66</td>
<td>0.552</td>
</tr>
<tr>
<td>QRS complex duration in ms</td>
<td>0.99</td>
<td>0.97, 1.02</td>
<td>0.597</td>
</tr>
<tr>
<td>First degree AV block</td>
<td>2.13</td>
<td>0.82, 5.50</td>
<td>0.119</td>
</tr>
<tr>
<td>Poor R wave progression</td>
<td>2.63</td>
<td>0.55, 12.63</td>
<td>0.228</td>
</tr>
<tr>
<td>Left axis deviation</td>
<td>3.66</td>
<td>1.46, 9.16</td>
<td>0.006</td>
</tr>
<tr>
<td>Complete Right Bundle Branch Block</td>
<td>0.88</td>
<td>0.40, 2.02</td>
<td>0.795</td>
</tr>
<tr>
<td>Age at dialysis initiation</td>
<td>0.71</td>
<td>0.99, 1.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Dialysis vintage in months</td>
<td>0.92</td>
<td>0.99, 1.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Sex (Reference = Male)</td>
<td>0.95</td>
<td>0.40, 2.23</td>
<td>0.899</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.14</td>
<td>0.92, 9.01</td>
<td>0.079</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.89</td>
<td>0.81, 4.45</td>
<td>0.142</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.95</td>
<td>0.92, 0.99</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Background and Aims: Chronic kidney disease is associated with the accumulation of so-called middle molecules in the blood, in particular parathyroid hormone, and the formation of secondary hyperparathyroidism with a tendency to extra-bone calcification. The most vulnerable organ in relation to calcification is the vascular wall. The all of the study to study the features of vascular wall remodeling in patients with chronic kidney disease who are being treated with programmed hemodialysis.

Method: The study included 86 patients with CKD 5 (mean age 47.4±5.04 years) who had been on programmed hemodialysis for at least 6 months. All patients underwent examination, including multislice spiral computed tomography (MSCT) with an assessment of the calcium content in the coronary arteries (Agatston index), ultrasound examination of the carotid arteries with determination of the thickness of the intima-media complex, the degree of endothelium-dependent vasodilation in a sample with 5-minute compression of the brachial artery and determination of changes in the diameter of the brachial artery. The data obtained (presented in the form of an arithmetic mean and its standard error) were compared with normal values typical for a healthy population.

Results: There was an accumulation of calcium in the coronary vessels with an average Agatston index of 146.83 ± 13.26 units. Also, during MSCT, calcifications were found in the aortic wall in 86 out of 57 patients. The intima-media complex in patients with CKD was significantly increased and averaged 1.21±0.06mm. The degree of endothelium-dependent vasodilation in patients with CKD was reduced and amounted to 5.48±0.03% of the initial diameter of the brachial artery. Correlation analysis revealed significant positive associations of average strength between the value of the Agatston index, the thickness of the intima-media complex of the carotid arteries and the concentration of parathyroid hormone in peripheral blood (g = 0.49, P<0.05 with the Agatston index and P = 0.42, P<0.05 with the thickness of the intima-media complex), as well as a significant negative relationship between the product of the concentration of calcium and phosphorus in peripheral blood and the degree of endothelium-dependent vasodilation (g = -0.49, P<0.05).

Conclusion: In patients with CKD, against the background of programmed hemodialysis, there is a remodeling of the heart with an increase in the size of the heart cavities and LV myocardial mass, a violation of regional and general LV contractile function, LV diastolic dysfunction and an increase in pressure in the pulmonary artery system. The introduction of sevelamer hydrochloride into the therapy regimen is associated with the prevention of the progression of cardiac remodeling. Calcification of the aortic valve progresses, regardless of the therapy used. Vascular remodeling in patients with CKD on the background of programmed hemodialysis is manifested by an increase in the thickness of the intima-media complex of the carotid arteries and a violation of endothelium-dependent vasodilation in favor of paradoxical vasoconstriction. Against the background of calcium carbonate therapy, structural disorders of the vascular wall progress. The introduction of sevelamer phosphate binder into the therapy regimen allows to prevent the progression and improve the functional state of endothelial function.
first reported result within 3 months of starting HD. Cohorts were grouped according to biomarker-specific thresholds and 1:1 propensity-score matched for age, gender, and co-morbidities (hypertension, diabetes mellitus and smoking status). Logistical regression produced odds ratios with 95%CI for 5- year incident MACE. MACE was defined, a priori, as a composite of ischaemic heart disease, angina pectoris, acute myocardial infarction, heart failure, AF, stroke, and all-cause mortality. All statistical analysis was performed on the TriNetX online platform.

Results: The results are shown in Table 1. Results that reached statistical significance (p<0.05) are shown.

Conclusion: Routinely available cardiac biomarkers can predict incident MACE and outcomes in incident HD, although results differ between markers of myocyte injury (troponin) and stress (NTproBNP). The results suggest the clinical need for CV mortality and morbidity risk profiling in incident dialysis using a combination of clinical and laboratory variables.

Table 1:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number with outcome</th>
<th>Odds Ratio 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-sensitivity Troponin I &lt; 50 ng/L or Troponin I &lt; 0.05 ng/ml = ref group (N = 38244; mean age 60[14]; 60% male)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>5751</td>
<td>1.29</td>
<td>1.19-1.42</td>
</tr>
<tr>
<td>Death</td>
<td>14796</td>
<td>1.34</td>
<td>1.28-1.39</td>
</tr>
<tr>
<td>AF</td>
<td>4197</td>
<td>1.12</td>
<td>1.04-1.19</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>5743</td>
<td>1.12</td>
<td>1.06-1.19</td>
</tr>
<tr>
<td>AMI</td>
<td>4640</td>
<td>1.29</td>
<td>1.21-1.37</td>
</tr>
<tr>
<td>High-sensitivity Troponin T &lt;50 ng/L or Troponin T &lt; 0.05 ng/ml = ref group (N = 11876; mean age 61[15]; 50% male)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>4351</td>
<td>1.23</td>
<td>1.42-1.33</td>
</tr>
<tr>
<td>NT-pro BNP &lt; 400 pg/ml = ref group (N = 1254; mean age 56[15]; 59% male)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>381</td>
<td>1.34</td>
<td>1.05-1.71</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>216</td>
<td>1.78</td>
<td>1.27-2.49</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>196</td>
<td>1.59</td>
<td>1.13-2.23</td>
</tr>
<tr>
<td>BNP &lt; 35 pg/ml = ref group (N = 3414; mean age 56[15]; 57% male)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>566</td>
<td>1.47</td>
<td>1.34-1.90</td>
</tr>
<tr>
<td>AF</td>
<td>356</td>
<td>1.39</td>
<td>1.11-1.74</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>482</td>
<td>1.44</td>
<td>1.66-1.78</td>
</tr>
</tbody>
</table>

Conclusion: PC is common in HD patients even after reaching their dry weight at the end of their two consecutive sessions. It is not only correlated to volume status and cardiac function. Chronic inflammation may be involved in PC pathophysiology. A better management strategy is thus needed to better reduce PC in HD patients.

Ezzeledin Shalaby
Faculty of Medicine Cairo University, Cairo, Egypt

Background and Aims: Proton Pump Inhibitors are widely used in haemodialysis patients for the prevention and treatment of uremic gastritis, peptic ulcer, gastritis, esophagitis and gastro oesophageal reflux. Hypomagnesaemia is reported recently in some patients who abuse intake of Proton Pump Inhibitors (PPIs) but this problem is still not well studied yet. Our study aims to evaluate the chronic toxic effect of Proton Pump Inhibitor on Magnesium level in Egyptian haemodialysis patients, especially those who suffer from abuse of intake without medical prescriptions.

Method: The study was conducted at the haemodialysis centre and clinic of Alzawya One-Day Surgery Hospital in Cairo including 60 end stage renal disease patients after their consents and approval of ethical committee in our hospital. PPIs use and duration were investigated. The patients were dialyzed using a diализate magnesium level of 0.5 mmol/L and Calcium level 1.5 mmol/L in all groups, after at least one month of haemodialysis with the mentioned diализate, laboratory tests were performed. The patients participating in this study after their consents were divided into 3 groups:

• Group A: -20 patients on Proton Pump Inhibitors regularly with long term intake for more than 6 months on high dose above or equal 280 mg/week [1]
• Group B: -20 patients on Proton Pump Inhibitors irregularly for less than 6 months on low dose below 280 mg/week.
• Group C: -20 patients not intake Proton Pump Inhibitors.

The magnesium level in haemodialysis patients was evaluated by comparison between the 3 groups and its correlation with duration of its use, Calcium and Phosphorus level in blood. Dialysate magnesium and calcium concentration in all groups were fixed and abuse of intake of PPIs without medical prescription in the participated patients was evaluated.

Results: Show highly statistically significant higher mean value in Non-intake of PPI group, followed by PPI intake ≤6m group and the lowest value in PPI intake >6m group according to magnesium "mg/dl", with p-value (p<0.001). There is no statistically significant difference between groups according to calcium "mg/dl"; with p-value (p>0.05).

Conclusion: Proton Pump Inhibitors regularly with long term intake for more than 6 months on high dose above or equal 280 mg/week associated with hypomagnesaemia. So we recommend stoppage of abuse intake of PPIs in haemodialysis patients.

Table 1:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number with outcome</th>
<th>Odds Ratio 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-pro BNP &lt; 400 pg/ml = ref group (N = 1254; mean age 56[15]; 59% male)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>381</td>
<td>1.34</td>
<td>1.05-1.71</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>216</td>
<td>1.78</td>
<td>1.27-2.49</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>196</td>
<td>1.59</td>
<td>1.13-2.23</td>
</tr>
<tr>
<td>BNP &lt; 35 pg/ml = ref group (N = 3414; mean age 56[15]; 57% male)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MACE</td>
<td>566</td>
<td>1.47</td>
<td>1.34-1.90</td>
</tr>
<tr>
<td>AF</td>
<td>356</td>
<td>1.39</td>
<td>1.11-1.74</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>482</td>
<td>1.44</td>
<td>1.66-1.78</td>
</tr>
</tbody>
</table>
MAGNETIC RESONANCE IMAGING ASSESSMENT OF SKIN AND MUSCLE SODIUM IN HAEMODIALYSIS

Rebecca Noble1,2, Ben Prestwich1, Kelly White3, Maarten Taal1,2, Nick Selby1,3 and Susan Francis3

1University of Nottingham, United Kingdom and 2Centre of Kidney Research and Innovation, Derby, United Kingdom

Background and Aims: Haemodialysis (HD) is life sustaining for patients with end-stage kidney disease (ESKD) but is associated with a marked increase in incidence of cardiovascular disease (CVD) and high annual mortality rates. Sodium balance is regulated by the kidneys in health but has to be achieved by sodium removal during HD for those with ESKD. Recent evidence suggests that non-osmotically stored sodium in the muscle and/or skin may be a critical factor impacting the development of hypertension and CVD. Sodium magnetic resonance imaging ($^{23}$Na MRI) allows assessment of skin and muscle sodium storage and may provide a valuable tool in evaluating sodium storage in dialysis patients. In this study, we used $^{23}$Na MRI to measure muscle and skin sodium content in younger and older healthy individuals and people receiving HD, and investigated the effect of a single dialysis session on muscle and skin sodium content.

Method: $^{23}$Na MRI was acquired on a 3T Philips Ingenia scanner using a custom-made $^{23}$Na RF coil. 3D GRE $^{23}$Na scans ($3 \times 3 \times 30\text{mm}^3$, 10 slices) were acquired in a 15-minute scan. Four reference bottles of increasing sodium concentration were placed in the RF coil above the leg to calibrate sodium concentration. In the same imaging session, 1H MR images were acquired to delineate muscle groups, skin structures and tissue water content. $^{23}$Na concentration maps were generated using custom software and regions of interest of each muscle and the skin were manually segmented. Data was collected on 14 younger (23-38yrs,7M:7F) and three older (66-77yrs,3M:1F) healthy volunteers (HVs), and 5 male HD patients (55-68yrs) who had been on HD for more than 3-months. HD patients underwent a pre-dialysis $^{23}$Na MRI calf scan, then had their usual dialysis session with a dialysate Na prescription of 137 mmol/L, followed by a repeat $^{23}$Na MRI calf scan post dialysis. Patient demographics, dialysis vintage, residual renal function, and ultrafiltration volume were collected, along with blood samples at the start and end of the dialysis session, including serum sodium.

Results: Figure 1 shows $^{23}$Na images in the younger and older HV group and HD patients pre-dialysis. Muscle and skin sodium was increased in older HVs compared to younger, with HD patients pre-dialysis tending to be lower than older HVs (Fig. 2). HD patients’ demographics and clinical measures pre- and post-dialysis are shown in Table 1. HD treatment reduced muscle sodium whilst skin sodium showed little change (Fig. 3).

Conclusion: We have optimised methods for measuring muscle and skin sodium. $^{23}$Na concentration in muscle and skin is higher in older subjects. HD patients’ $^{23}$Na values fall between those observed in the older and younger HV groups. These values are consistent with published data from patients dialysed against 137mmol/l sodium dialysate, but lower than other studies in which dialysate sodium levels were higher. Further studies are planned to study...
Our study cohort was well representative of general dialysis population. Median Age was 65 years, with 65.6% Males and 34.4% Females. All sleep quality parameters were considerably poor compared to age matched general population. Mean Sleep Efficiency was 77.5% (Normal for age matched general population is 83.2%), Mean TST was 318 minutes (Normal 372 minutes), Mean WASO was 83 minutes (Normal 64 minutes), Mean Sleep Fragmentation index was 43. None of the sleep quality parameters had significant difference in different dialysis modalities in our study.

#4268
RELATIONSHIP BETWEEN MEASURED SLEEP QUALITY AND CLINICAL PARAMETERS IN DIALYSIS PATIENTS
Usama Butt, Enric Vilar, Sivakumar Sridharan, Kenneth Farrington and Jocelyn Berdeprado
Lister Hospital, Stevenage, United Kingdom

Background and Aims: Poor sleep quality in dialysis patients has been well reported and has deleterious effects on quality of life. Factors affecting the sleep quality in these patients have not been very well explored. Actigraphy using wearable devices with 3D accelerometers is a well-recognised method of analysing the sleep quality. We set out to determine the relationship of sleep quality parameters measured using actigraphy with dialysis related factors in patients on dialysis.

Method: We conducted a prospective analysis of 95 patients, involving 75 In Centre Haemodialysis (ICHD), 15 Home Haemodialysis (HHD) and 8 Peritoneal dialysis (PD) patients. Sleep data was collected using Actigraph wrist device. Participants were instructed to wear the device 24 hours a day for consecutive 7 days. Sleep data analysis was conducted with Actilife software using Cole-Kripke sleep-wake algorithm. Sleep quality parameters used for assessment included Sleep Efficiency, Average Total sleep time (TST), Wake after sleep onset (WASO), Number of Awakenings, Sleep Fragmentation index. Demographic and clinical information was collected prospectively from medical records.

Results: Our study cohort was well representative of general dialysis population. Median Age was 65 years, with 65.6% Males and 34.4% Females. All sleep quality parameters were considerably poor compared to age matched general population. Mean Sleep Efficiency was 77.5% (Normal for age matched general population is 83.2%), Mean TST was 318 minutes (Normal 372 minutes), Mean WASO was 83 minutes (Normal 64 minutes), Mean Sleep Fragmentation index was 43. None of the sleep quality parameters had significant difference in different dialysis modalities in our study. Amongst the predictors of sleep quality, serum phosphate had significant association with increased WASO (p = 0.002). Mean WASO was 99 minutes for patients with serum Phosphate > 1.8 mmol/L compared to 74 minutes for those with serum phosphate of < 1.8 mmol/L. Serum phosphate had a borderline significant positive correlation with Number of Awakenings (p = 0.06) and borderline significant negative correlation with Sleep Efficiency (p = 0.06). Renal urea clearance (KRU) had statistically significant positive correlation with sleep efficiency (p = 0.013) but didn’t reach statistical significance in relation to the other sleep quality parameters. Urine volume also had positive correlation with sleep efficiency nearly reaching statistical significance (p = 0.055). Other factors analysed during the study didn’t appear to have any significant associations with sleep quality.

Conclusion: Actigraphy is non-invasive, less cumbersome, and reliable method of sleep assessment in dialysis patients. Compared to the age matched general population, dialysis patients have objectively measured poor sleep quality. Serum phosphate has significant negative impact on sleep quality possibly secondary to hyperphosphatemia-related side effects. Residual kidney function has positive association with sleep efficiency. This study highlights the potential importance of preserving residual kidney functions and treating hyperphosphatemia in dialysis patients which warrants further research.

#2567
ASSOCIATION OF IMBALANCE OF MYOCARDIAL OXYGEN SUPPLY/Demand WITH MYOCARDIAL INJURY IN END STAGE KIDNEY DISEASE PATIENTS
Kenji Nakata, Minako Harada, Mai Hitaka, Yuri Tanaka and Nobuhiko Joki
Toho University Ohashi Hospital, Division of Nephrology, Meguro-ku, Japan

Background and Aims: It is well known that oxygen transport ability is impaired in patients with anemia, low hemoglobin (Hb) level, whereas the double product (DP, bpm*mmHg), consisting of the systolic blood pressure (SBP) multiplied by the heart rate (HR), is an index of myocardial oxygen consumption. The combination of these two markers could be a potential marker for balance of myocardial oxygen supply and demand. Therefore, we hypothesized that the balance of these two markers may lead to myocardial damage in end-stage kidney disease (ESKD) patients who is susceptible to vulnerable heart in oxygen balance. The purpose of this study is to examine the association of balance of DP and Hb with myocardial injury in ESKD patients.

Method: A single-center, cross-sectional study has conducted. From December 2010 to November 2021, 327 consecutive ESKD patients started maintenance hemodialysis (HD). Among them, 44 patients met the exclusion criteria as follows: (1) missing data of cardiac troponin T (cTnT); (2) complicating acute cardiac syndrome; (3) death during hospitalization for HD initiation, a total of 283 ESKD patients were enrolled into the study finally. The patients were divided four groups according to the high or low of Hb level of 9 g/dL and DP 12500, a median of our patients, and named low-DP/high-Hb; G1, low-DP/low-Hb; G2, high-DP/high-Hb; G3, and high-DP/low-Hb; G4. The patients with G1 group were defined as a well oxygen balanced group, whereas those with G4 was defined as an imbalance of oxygen supply and demand group. Based on the results of previous study, cTnT cut off for myocardial injury was serum cTnT ≥0.15 ng/mL. Odds ratio (OR) for myocardial injury was calculated in each group compared with well oxygen balanced group by logistic regression analysis.

Results: Median age was 72 years, 71% of them were male, 52.6% had diabetes. Mean Hb level was 9.09 ± 1.61, and median DP was 12144 (25% tile 10540, 75% tile 14688). Median cTnT was 0.083 (25% tile 0.057 and 75% tile 0.13), and 20.4% of patients were defined as suffering from myocardial injury latently. In the adjusted model, the odds for myocardial injury was significantly increasing in high-DP compared with low-DP (OR: 1.87, p = 0.049), while low-Hb did not show significant increment of odds for myocardial injury compared with high-Hb. As shown in the Table 1, compared to well-balanced group (G1), OR increased by exposing only high-DP (G3), however it was
Table 1: Cut off Hb level < 9 g/dL.

<table>
<thead>
<tr>
<th>Group</th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>DP ≥12500</td>
<td>1.87</td>
<td>1.00-3.58</td>
<td>0.049</td>
</tr>
<tr>
<td>Hb &lt; 9, g/dL</td>
<td>1.58</td>
<td>0.84-2.98</td>
<td>0.15</td>
</tr>
<tr>
<td>DP &lt;12500</td>
<td>1.96</td>
<td>0.95-3.96</td>
<td>0.066</td>
</tr>
<tr>
<td>Hb ≥9</td>
<td>1.27</td>
<td>0.87-6.45</td>
<td>0.089</td>
</tr>
<tr>
<td>DP ≥12500</td>
<td>2.13</td>
<td>0.94-4.55</td>
<td>0.051</td>
</tr>
<tr>
<td>Hb &lt; 8</td>
<td>3.91</td>
<td>1.34-11.37</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Table 2: Cut off Hb level < 8 g/dL.

<table>
<thead>
<tr>
<th>Group</th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>DP ≥12500</td>
<td>1.87</td>
<td>1.00-3.58</td>
<td>0.049</td>
</tr>
<tr>
<td>Hb &lt; 8, g/dL</td>
<td>1.96</td>
<td>0.95-3.96</td>
<td>0.066</td>
</tr>
<tr>
<td>DP &lt;12500</td>
<td>1.27</td>
<td>0.87-6.45</td>
<td>0.089</td>
</tr>
<tr>
<td>Hb ≥8</td>
<td>2.13</td>
<td>0.94-4.55</td>
<td>0.051</td>
</tr>
<tr>
<td>DP ≥12500</td>
<td>3.91</td>
<td>1.34-11.37</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Table 3: Cut off Hb level < 10 g/dL.

<table>
<thead>
<tr>
<th>Group</th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>DP ≥12500</td>
<td>1.87</td>
<td>1.00-3.58</td>
<td>0.049</td>
</tr>
<tr>
<td>Hb &lt; 10, g/dL</td>
<td>1.01</td>
<td>0.51-2.09</td>
<td>0.96</td>
</tr>
<tr>
<td>DP &lt;12500</td>
<td>1.27</td>
<td>0.87-6.45</td>
<td>0.089</td>
</tr>
<tr>
<td>Hb ≥10</td>
<td>1.96</td>
<td>0.94-4.55</td>
<td>0.051</td>
</tr>
<tr>
<td>DP ≥12500</td>
<td>2.13</td>
<td>0.94-4.55</td>
<td>0.051</td>
</tr>
<tr>
<td>Hb &lt; 10</td>
<td>3.91</td>
<td>1.34-11.37</td>
<td>0.012</td>
</tr>
</tbody>
</table>

HEMOGLOBIN VARIABILITY IS ASSOCIATED WITH NUTRITIONAL STATUS IN HEMODIALYSIS PATIENTS UNDERGOING DARBEPOETIN-ALFA TREATMENT

Do Hyoung Kim1, Jungho Shin2 and Dong-Jin Oh3

1Hallym University Kangnam Sacred Heart Hospital, Department of Internal Medicine, Seoul, Rep. of South Korea, 2Chung-Ang University Hospital, Department of Internal Medicine, Seoul, Rep. of South Korea, 3Myongji Hospital, Hanyang University College of Medicine, Department of Internal Medicine, Gyeonggi-do, Rep. of South Korea

Background and Aims: Anemia is the most common finding in hemodialysis (HD) patients. A significant proportion of patients are taking erythropoietin (EPO) or other erythroid-stimulating agents (ESA), yet the response to treatment is unsatisfactory, and EPO responsiveness is inconsistent in HD patients. Further, although the introduction of EPO has led to a dramatic reduction in blood transfusion requirements and is associated with improved quality of life, fluctuations in hemoglobin (Hb) levels, known as Hb variability, during EPO treatment is a well-documented phenomenon. Malnutrition is a well-known risk factor in the general population and in HD patients. However, few studies have evaluated the association between EPO responsiveness/Hb variability and nutritional status in HD patients. Therefore, our aim was to investigate whether EPO responsiveness and Hb variability can be associated with nutritional status in HD patients undergoing darbepoetin-alfa (darbepoetin-alfa; Kyowa Kirin Korea Co., Ltd.) treatment.

Method: In this prospective study, we included adult ninety-eight patients aged over 20 years who had been undergoing HD over 6 months. The target hemoglobin (Hb) level is 10–11 g/dL according to the Korean reimbursement guideline. Dose adjustments of NESP® were made according to the Hb level measured monthly in our facility. Every study population have more than 24 monthly Hb data points. We checked average darbepoetin-alfa dose weekly and the EPO resistance index (ERI) as a marker of EPO responsiveness was calculated by dividing the weekly average darbepoetin-alfa dose by the Hb level. In addition, we evaluated the more than 24 month Hb variability, which was expressed by Hb-Coefficient of Variation (Hb-CV). All of them were measured by BCM® (Fresenius Medical Care a Deutschland GmbH, Germany) three times (Baseline (12 Mos), 12 Mos). Nutritional parameters obtained by BCM® were body mass index (BMI), fat tissue index (FTI), lean tissue index (LTI), body cell mass index, phase angle (PhA). Clinical parameters and routine biochemical tests such as dose of erythropoietin, Kt/Vurea, iron and lipid profiles, C-reactive protein, albumin, calcium, phosphorus, intact-parathyroid hormone were also taken into account.

Results: In this study, the mean age of the patients was 64.0 ± 11.9 years, and 55.0% were male. Dialysis vintage was 54.9 ± 46.8 months. Follow-up duration was 79.3 ± 47.9 months. Mean Hb was 10.7 ± 1.3 g/dL. We divided into tertiles (T) according to the ERI. The average ERI was 0.02 ± 0.01, 0.04 ± 0.01, and 0.07 ± 0.03 in ERI-T1, ERI-T2, and ERI-T3, respectively. The ERI-T3 group had the lower Hb level (p = 0.038) whereas administration dose of EPO were higher in ERI-T3 (p = 0.001). The ERI-T3 group had the lower Pha (p = 0.044), BMI (p = 0.001) and FTI (p = 0.046) values. We divided into tertiles (T) according to the Hb-CV. The average Hb-CV was 0.06 ± 0.01, 0.08 ± 0.05, and 0.12 ± 0.02 in Hb-CV-T1, Hb-CV-T2, and Hb-CV-T3, respectively. When comparing the three groups, the Hb-CV-T3 group had the lower BMI (p = 0.002) and lower FTI (p = 0.002). Age (r = 0.203, p = 0.036), female sex (r = 0.376, p = 0.001), presence of diabetes mellitus (r = 0.191, p = 0.049), total iron binding capacity (r = 0.205, p = 0.035) and triglyceride (r = 0.227, p = 0.018) were positively correlated with FTI. BMI (r = 0.193, p = 0.046) and Hb-CV (r = -0.268, p = 0.005) were negatively correlated with FTI. In multiple linear regression analysis, FTI was negatively associated with ERI (β = -0.218, p = 0.014), Hb-CV (β = -0.181, p = 0.039), whereas FTI was positively associated with age (β = 0.197, p = 0.017) and female sex (β = 0.386, p = 0.001).

Conclusion: In HD patients with higher ERI, Pha, BMI and FTI were significantly decreased. Furthermore, in patients with high Hb-CV, BMI and FTI were decreased. In addition, FTI was negatively associated with ERI and Hb-CV. Therefore, EPO responsiveness and Hb-variability is associated with nutritional status, especially fat tissue in hemodialysis patients undergoing darbepoetin-alfa treatment.

#2513 EFFECT OF HEMODIALYSIS WITH MEDIUM CUT-OFF VERSUS HIGH-FLOW MEMBRANES ON ENDOTHELIAL FUNCTION OF CHRONIC KIDNEY DISEASE PATIENTS

Rachel Armani1, Aluizio Carvalho2, Monique Vercia1, Luiz Aparecido Bortolotto2 and Maria Eugênia Cianzani2

1Escola Paulista de Medicina, Nephrology, São Paulo, Brazil and 2InCor - Instituto do Coração do Hospital das Clínicas da FMUSP, Cardiology, Brazil

Background and Aims: Endothelial dysfunction (ED) is considered a marker of vascular complications, especially in patients with chronic kidney disease (CKD). Inflammation and the uremic state contribute to ED in hemodialysis (HD) patients. Recently, the medium cut-off (MCO) HD membrane has been proposed to efficiently remove inflammatory cytokines and higher molecular weight uremic toxins. This study aimed to compare the effect of dialysis with medium cut-off (MCO) or high-flow (HF) membranes on the endothelial function of patients on chronic HD.

Method: A prospective, randomized, crossover study in which 32 patients with CKD were dialyzed for 12 weeks with each membrane, including a 4-week washout period between treatments. Endothelial function was assessed by flow-mediated dilation (FMD) using brachial artery ultrasound at weeks 1, 12, 16, and 28.

Results: The population consisted of 59% men, 52.7 ± 13.4 years, 16% non-black, on HD for 8.6 (4.1-15.1) years, 72% with arteriogenous fistula. Hypertension was the most common etiology of CKD and 34% of patients had previous cardiovascular disease. Table 1 shows clinical and demographic characteristics of all subjects. The Patients were grouped, regardless of treatment sequence, into MCO or high flow groups, since no drag (p = 0.634) or sequence (p = 0.998) effects were observed in the FMD assessment. The ANOVA model with repeated measures showed no effects of treatment (p = 0.426), time (p = 0.972) or interaction (p = 0.413) in the comparison of FMD, between the MCO and high flow groups.

Conclusion: Dialysis performed with MCO, or HF membranes did not influence endothelial function in patients undergoing chronic HD.
#3330

**INFLAMMATION SECONDARY TO CHRONIC KIDNEY DISEASE AND PERITONEAL DIALYSIS ACCELERATES ATHEROSCLEROSIS IN A NEW MOUSE MODEL**

Jamie Kane1,2, Myriam den Toom1, Laura Bosmans1, Bram van Os1, Winnie Vos1, Linda Beckers1, Lily Jakulj2, Esther Lutgens4, Marc Vervloet2 and Etto Eringa1,5

1Amsterdam UMC, Medical Biochemistry, Amsterdam, Netherlands, 2Amsterdam UMC, Nephrology, Amsterdam, Netherlands, 3Amsterdam UMC, Physiology, Amsterdam, Netherlands, 4Mayo Clinic, Cardiovascular Medicine, Rochester, United States of America and 5Maastricht University, Physiology, Maastricht, Netherlands

**Background and Aims:** Inflammation is an established contributor to accelerated atherosclerosis, which is highly prevalent in people with chronic kidney disease (CKD) and even more so in those treated with peritoneal dialysis (PD). We therefore hypothesised that PD-induced systemic inflammation is essential in the development of atherosclerosis. To study this we developed a novel mouse model of CKD and PD accelerated atherosclerosis.

**Method:** We performed a 5/6ths nephrectomy in ApoE deficient "black 6" mice, fed these mice a high-cholesterol diet (HCD), and intraperitoneally administered 3.6% Physioneal daily for 67 days. There were three groups of mice: control (HCD-only), CKD+HCD, and CKD+HCD+PD, with relevant shams. Tissues were harvested twelve weeks after the nephrectomy. Assessments of residual kidney function, atherosclerotic plaque pathology and immunology, and systemic immune responses were performed.

**Results:** Atherosclerotic plaque size in the aortic arch was larger in the PD group compared to the control, increasing from 83.779 ±μm² ±18.430 to 109.973 ±μm² ±25.602 (p = 0.0349), whilst plaque size was unchanged in the CKD group. In contrast, both the CKD and PD groups displayed altered plaque stability. There was less collagen in the plaque vs control, decreasing from 43.54% ±10.65 to 29.71% ±9.43 and 29.73% ±10.18 respectively. Additionally, fibrous cap thickness decreased in both groups vs control. These plaques from only the PD group showed infiltration by T-cells compared to control, with no changes in macrophage content in either the CKD or PD group. In the spleen in the CKD and PD groups, naïve CD4 cells increased and effector CD4 cells decreased compared to control, with the latter change also occurring in the circulation. Central memory CD4 cells, terminally differentiated Th1 cells, Th17 cells, and 'vascular homing' cells all increased in the PD group compared to control mice. These homing cells also increased in circulation. The PD group showed decreases in the spleen of regulatory T-cells, effector Th1 cells, and effector CD8 cells. Notably, all of these changes were absent from the mesenteric lymph node. There was a large drop in monocytes in the spleen and a loss of immature and mature dendritic cells in the PD group.

**Conclusion:** Combining CKD, a high-cholesterol diet, and exposure to PD fluids in ApoE−/− mice successfully generated a new model for cardiovascular disease in human PD patients. This new model is in a widespread and well-understood mouse line representative of human atherosclerosis. Here we demonstrate the pronounced effects of CKD and PD on the innate and adaptive immune response which increases atherosclerotic burden and leads to larger more vulnerable plaques

#6158

**UREMIC TOXINS ARE ASSOCIATED WITH IMMUNE-SENEGENCE AND IMMUNE-EXHAUSTION IN HEMODIALYSIS PATIENTS**

Theodores Tourountzis1, Georgios Liolios2, Steven Van Laecke3, Michalis Christodoulou2, Eleni Moysidou2, Stamatis Star2, Asimina Pylakiotou2, Griet Glericusx4 and Maria Stangou2

1Protypo Dialysis Center of Thessaloniki, Greece, 2General Hospital of Thessaloniki "Ippokrateio", Thessaloniki, Greece and 3Ghent University Hospital, Gent, Belgium

**Background and Aims:** Immune-senescence and exhaustion have been described in hemodialysis (HD) patients, with changes in lymphocyte phenotype possibly stimulated by the uremic environment, independent of age and comorbid conditions. We evaluated the potential association of uremic toxin accumulation with changes in lymphocyte count and phenotype in HD patients.

**Method:** In the peripheral blood of 54 HD patients (23 female, mean age 51±16.91 years) and 31 age-matched healthy controls, lymphocytes surface molecules were determined by flow cytometry: T cells (CD4, CD8, CD31,
CD45RA, CCR7, CD28, CD57, PD1) and B cells (CD27, IgD). Plasma levels of the protein bound uremic toxins [hippuric acid (HA), indoxyl sulfate (IxS) and p-cresyl sulfate (pCS)] were measured by ultra-performance liquid chromatography. Lymphocyte phenotypes were correlated with uremic toxins levels using Spearman's correlation coefficient test. Patients with recent or active infection, malignancy, autoimmune disease and/or diabetes mellitus were excluded. 

Results: A higher concentration of uremic toxins was observed in HD patients, compared to healthy controls, namely: total HA 3.05 (1.66-5.37) vs 0.102 (0.04-0.2) mg/dl (p < 0.001), free HA 1.482 (0.7-2.8) vs 0.029 (0.03-0.04) mg/dl (p < 0.001); total IxS 2.207 (1.27-3.34) vs 0.063 (0.04-0.09) mg/dl (p < 0.001), free IxS 0.146 (0.09-0.27) vs 0.0004 (0.0004-0.0004) mg/dl (p < 0.001); total pCS 1.248 (0.84-1.66) vs 0.066 (0.04-0.13) mg/dl (p < 0.001), free pCS 0.089 (0.06-0.13) vs 0.004 (0.004-0.005) mg/dl (p < 0.001); respectively. There was a positive correlation between hemodialysis vintage and total as well as free HA (p = 0.005, p = 0.003, respectively). No significant differences in uremic toxin levels were found in HD patients according to sex, age, dialysis prescription and method. Patients with residual urine output had reduced total and free HA levels 1.739 (3.5) vs 3.437 (4.16) mg/dl (p = 0.05), and 0.717 (1.9) vs 1.901 (3.5) mg/dl (p = 0.04), respectively and free IxS levels, 0.117 (0.1) vs 0.177 (0.2) mg/dl (p = 0.02), respectively. Total lymphocyte count and absolute number of CD4 cells were negatively correlated with total (p = 0.018 and p = 0.02 respectively) and free HA levels (p = 0.024 and p = 0.017 respectively). Several naive and less differentiated CD4 subpopulations also demonstrated a negative correlation with total and free HA levels, most importantly CD4CD31+ (p = 0.037 and p = 0.027 respectively), CD8CD28+CD57- (p = 0.018 and p = 0.014 respectively) CD4CD45+CD57- (p = 0.039 and p = 0.027 respectively) and naive B cells (CD19+IgD+CD27-)(p = 0.042 and p = 0.032 respectively). Advanced differentiated lymphocyte subtypes, CD4CD28+CD57+ and CD4CD45-CD57+ had a positive correlation with free HA levels (p = 0.036 and p = 0.045 respectively). Exhausted CD4 cells, defined as CD4+PD1+ had positive correlations with total and free IxS levels (p = 0.004 and p = 0.011 respectively) and total and free pCS (p = 0.027 and p = 0.018 respectively), but not with HA levels. Moreover, further divided exhausted lymphocytes, according to CD45RA expression, CD4CD45RA- PD1+ cells correlated positively with total and free IxS levels (p = 0.004 and p = 0.01 respectively) and CD4CD45RA+PD1+ with pCS total and free levels (p = 0.039 and p = 0.045 respectively).

Conclusion: Uremic toxins are increased in hemodialysis patients and may influence adaptive immunity. HA is associated with an immune-senescent, while IxS and pCS to an immune-exhausted lymphocyte phenotype.

#2616
Diagnostic Value of the Handgrip Strength in Detecting Protein-Energy Wasting among Hemodialysis Patients at National Kidney and Transplant Institute

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1National Kidney and Transplant Institute, Adult Nephrology, Quezon City, The Philippines and 2National Kidney and Transplant Institute, Quezon City, The Philippines

Background and Aims: Protein energy wasting (PEW) is a syndrome of adverse nutritional and catabolic changes common among chronic kidney disease (CKD) patients. Handgrip strength (HGS) was one of the methods of screening PEW mentioned in Kidney Disease Outcomes Quality Initiative guidelines. However, only few studies determined the validity of HGS in detecting PEW among maintenance hemodialysis (MHD) patients. The study aimed to determine the diagnostic validity of HGS in detecting PEW among MHD patients in a tertiary government hospital, with the following specific objectives: to determine the prevalence of PEW among MHD patients, to compare the demographic and clinical profile by PEW status, to identify the optimal cut-off point of HGS pre- and post-HD sessions in detecting PEW by sex, and to determine the following diagnostic value parameters of HGS pre- and post-HD sessions in detecting PEW by sex in terms of discriminative ability, accuracy, sensitivity, specificity, positive predictive value and negative predictive value.

Method: Participants included in this cross-sectional study are randomly selected patients undergoing MHD in National Kidney and Transplant Institute (NKTI) from September to October, 2022. Diagnosis of PEW was based on the Malnutrition Inflammation Score (MIS) ≥5. HGS was measured using a dynamometer pre- and post-dialysis sessions.

Results: A total of 143 patients were included in the study, and 53% were diagnosed with PEW. Pre-HD and post-HD HGS have acceptable discriminative ability based on Area Under the Curve >0.70 in detecting PEW regardless of patient sex. In males, a pre-hemodialysis cut-off of <17.9 showed 72% sensitivity and 71% specificity in detecting PEW. Meanwhile, a
pre-hemodialysis cut-off of <18.6 in females showed 83% sensitivity and 65% specificity in detecting PEW.

**Conclusion:** PEW is common among MHD patients in NKTI. The diagnostic performance of HGS in detecting PEW was found to be acceptable in both males and females. While both pre- and post-HD measures can be used in males, only the pre-HD measures are recommended for females. HGS can, therefore, be used as a non-expensive, accurate and objective screening assessment tool in detecting PEW for MHD patients. External validation of the proposed HGS cut-off values is still recommended.
Table 3: Diagnostic value of HGS in detecting PEW among males.

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Pre-HD</th>
<th>Post-HD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With PEW</td>
<td>Without PEW</td>
</tr>
<tr>
<td>&lt;18.3</td>
<td>37</td>
<td>7</td>
</tr>
<tr>
<td>≥18.3</td>
<td>21</td>
<td>43</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Discriminative ability</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>(0.67-0.83)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Accuracy</td>
<td>74.07%</td>
</tr>
<tr>
<td></td>
<td>Sensitivity</td>
<td>63.79%</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td>Positive predictive value</td>
<td>84.09%</td>
</tr>
<tr>
<td></td>
<td>Negative predictive value</td>
<td>67.19%</td>
</tr>
<tr>
<td></td>
<td>Likelihood ratio +</td>
<td>4.56</td>
</tr>
<tr>
<td></td>
<td>Likelihood ratio -</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Table 4: Diagnostic value of HGS in detecting PEW among females.

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Pre-HD</th>
<th>Post-HD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With PEW</td>
<td>Without PEW</td>
</tr>
<tr>
<td>&lt;18.6</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>≥18.6</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Discriminative ability</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>(0.59-0.89)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Accuracy</td>
<td>74.29%</td>
</tr>
<tr>
<td></td>
<td>Sensitivity</td>
<td>83.33%</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>64.71%</td>
</tr>
<tr>
<td></td>
<td>Positive predictive value</td>
<td>71.43%</td>
</tr>
<tr>
<td></td>
<td>Negative predictive value</td>
<td>78.57%</td>
</tr>
<tr>
<td></td>
<td>Likelihood ratio +</td>
<td>2.36</td>
</tr>
<tr>
<td></td>
<td>Likelihood ratio -</td>
<td>0.26</td>
</tr>
</tbody>
</table>
Table 5: Diagnostic value of HGS in detecting PEW among males excluding T2DM.

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Pre-HD With PEW</th>
<th>Pre-HD Without PEW</th>
<th>Total</th>
<th>Post-HD With PEW</th>
<th>Post-HD Without PEW</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16.3</td>
<td>23</td>
<td>4</td>
<td>27</td>
<td>26</td>
<td>9</td>
<td>35</td>
</tr>
<tr>
<td>≥16.3</td>
<td>14</td>
<td>32</td>
<td>46</td>
<td>11</td>
<td>27</td>
<td>38</td>
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<tr>
<td>Total</td>
<td>37</td>
<td>36</td>
<td>73</td>
<td>37</td>
<td>36</td>
<td>73</td>
</tr>
</tbody>
</table>

Discriminative ability 0.76 (0.66-0.85) 0.73 (0.62-0.83)

Accuracy 75.34% 72.60%
Sensitivity 62.16% 70.27%
Specificity 88.89% 75%
Positive predictive value 85.19% 74.29%
Negative predictive value 69.57% 71.05%
Likelihood ratio + 5.59 2.81
Likelihood ratio - 0.43 0.40

Table 6: Diagnostic value of HGS in detecting PEW among females excluding T2DM.

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Pre-HD With PEW</th>
<th>Pre-HD Without PEW</th>
<th>Total</th>
<th>Post-HD With PEW</th>
<th>Post-HD Without PEW</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.6</td>
<td>12</td>
<td>6</td>
<td>18</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>≥18.6</td>
<td>3</td>
<td>10</td>
<td>13</td>
<td>9</td>
<td>14</td>
<td>23</td>
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<tr>
<td>Total</td>
<td>15</td>
<td>16</td>
<td>31</td>
<td>15</td>
<td>16</td>
<td>31</td>
</tr>
</tbody>
</table>

Discriminative ability 0.71 (0.55-0.87) 0.64 (0.48-0.79)

Accuracy 70.97% 64.52%
Sensitivity 80% 40%
Specificity 62.50% 87.50%
Positive predictive value 66.67% 75%
Negative predictive value 76.92% 60.87%
Likelihood ratio + 2.13 3.20
Likelihood ratio - 0.32 0.69

Table 7: Diagnostic value of HGS in detecting PEW among males excluding patients that used the non-dominant arm.

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Pre-HD With PEW</th>
<th>Pre-HD Without PEW</th>
<th>Total</th>
<th>Post-HD With PEW</th>
<th>Post-HD Without PEW</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16.3</td>
<td>31</td>
<td>5</td>
<td>36</td>
<td>34</td>
<td>10</td>
<td>44</td>
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<tr>
<td>≥16.3</td>
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<tr>
<td>Total</td>
<td>48</td>
<td>35</td>
<td>83</td>
<td>48</td>
<td>35</td>
<td>83</td>
</tr>
</tbody>
</table>

Discriminative ability 0.75 (0.66-0.84) 0.71 (0.61-0.81)

Accuracy 73.49% 71.08%
Sensitivity 64.56% 70.83%
Specificity 85.71% 71.43%
Positive predictive value 86.11% 77.27%
Negative predictive value 63.83% 64.10%
Likelihood ratio + 4.52 2.48
Likelihood ratio - 0.41 0.41
Table 8: Diagnostic value of HGS in detecting PEW among females excluding patients that used the non-dominant arm.

<table>
<thead>
<tr>
<th>C-statistic</th>
<th>E-O ratio</th>
<th>Slope</th>
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<tbody>
<tr>
<td>PRE-HD</td>
<td>POST-HD</td>
<td>PRE-HD</td>
</tr>
<tr>
<td>0.746</td>
<td>0.85</td>
<td>0.990</td>
</tr>
<tr>
<td>0.735</td>
<td>0.991</td>
<td>1.015</td>
</tr>
<tr>
<td>0.698</td>
<td>0.956</td>
<td></td>
</tr>
</tbody>
</table>

Table 9: Internal validity parameters of HGS in detecting PEW.

### MALES

<table>
<thead>
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<th>C-statistic</th>
<th>E-O ratio</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE-HD</td>
<td>POST-HD</td>
<td>PRE-HD</td>
</tr>
<tr>
<td>0.746</td>
<td>0.85</td>
<td>0.990</td>
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<tr>
<td>0.735</td>
<td>0.991</td>
<td>1.015</td>
</tr>
<tr>
<td>0.698</td>
<td>0.956</td>
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</tbody>
</table>

### FEMALES

<table>
<thead>
<tr>
<th>C-statistic</th>
<th>E-O ratio</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE-HD</td>
<td>POST-HD</td>
<td>PRE-HD</td>
</tr>
<tr>
<td>0.746</td>
<td>0.85</td>
<td>0.990</td>
</tr>
<tr>
<td>0.735</td>
<td>0.991</td>
<td>1.015</td>
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<tr>
<td>0.698</td>
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</tbody>
</table>

#3517

**BRAIN MAGNETIC RESONANCE IMAGING AND COGNITIVE FUNCTION IN PATIENTS RECEIVING HEMODIALYSIS**

Mei-Chuan Kuo1,2, Ping-Hsun Wu1,2, Hsiu-Fen Lin1,2, Tsai-Shan Wu1,4 and Yi-Ting Lin2,5

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**Background and Aims:** Chronic kidney disease is high risk to adverse events including stroke, cardiovascular diseases and cognitive decline. Cognitive function was known to be linked to chronic kidney disease. The Fazekas's scale, which was used for assessing white matter hyperdensities (WMH), has been reported to associate with poor cognitive performance. We aim to investigate the associations between mini-mental status examination (MMSE), Montreal cognitive assessment (MoCA), cognitive abilities screening instrument (CASI) and Fazekas's scale in patients under hemodialysis (HD).

**Method:** The periventricular (PV) and deep white matter (DWM) lesions in brain MR images of 59 patients under dialysis for at least 90 days were graded by Fazekas’s scale. Cognition function tests including MMSE, MoCA, and CASI were performed. Multivariable ordinal regression and logistic regression were used for identifying the associations between cognitive performance and Fazekas scale.

**Results:** Inverse associations were found between three cognitive function tests across the Fazekas scale of PV lesions (p = 0.037, 0.006 and 0.008 for MMSE, MoCA, and CASI respectively), and higher scales were associated with lower cognitive function scores in trend; however, the association attenuated in the DWM group. In subdomains of CASI, significant differences were identified in five subdomains, including short-term memory, mental manipulation, abstract thinking, spatial construction, and name fluency; nevertheless, in DWM hyperdensities, only abstract thinking and short-term memory showed obvious correspondence.

**Conclusion:** Inverse correlation between the Fazekas’s scale, predominantly in PV lesions, and cognition was detected in HD patients. The Fazekas’s scale of PV lesions was associated with cognitive performance assessed by MMSE, MoCA and CASI, as well as with subdomains of CASI such as memory, language, and name fluency in HD patients.

#3892

**AGE-RELATED TRAJECTORY PATTERN OF HANDGRIP STRENGTH AND MORTALITY IN PATIENTS ON HEMODIALYSIS**

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**Background and Aims:** Muscle weakness is a factor known to worsen prognosis in patients on hemodialysis [1], and the prevention of muscle weakness is extremely important in disease management. In particular, understanding age-related changes in muscle strength can be advantageous for long-term interventions. A previous study on community-dwelling older adults examined sex-specific age trends in muscle strength in order to identify potential trajectory patterns, and it showed that muscle strength tended to display similar age-related changes later in life regardless of the baseline level. Additionally, individuals in the low trajectory group had a higher mortality risk than did the high trajectory group [2]. However, reports examining longitudinal trajectories of muscle strength in patients on hemodialysis are limited, and their association with life prognosis remains unclear. Therefore, this study aimed to identify sex-specific aging patterns of handgrip strength as an indicator of muscle strength in patients on hemodialysis and to further investigate their association with life prognosis.

**Method:** Patients on hemodialysis with a minimum of two available measurements of handgrip strength between the years 2002 and 2022 were classified by sex using group-based semiparametric mixture modeling. The association between typed aging patterns of handgrip strength and all-cause mortality was examined using Cox regression analysis after adjusting for the baseline age, body mass index, dialysis history, comorbidity index score, and hemoglobin and albumin levels. The statistical significance level was set at 5%.

**Results:** Age-related trajectory patterns of handgrip strength in men and women were categorized into three groups, low, middle, and high, as shown in Fig. 1. All three groups showed an age-related decline. The “low group” showed a reduction in handgrip strength (< 28 kg for men and < 18 kg for women) from baseline and continued to decline thereafter. The “middle group” did not show...
any decline at baseline, but decline was noted after 65 years of age. The “high group” displayed a decline in handgrip strength after 80 years of age, despite high handgrip strength at baseline. 23.9%, 60.1%, and 16.0% for men and 30.1%, 46.3%, and 23.7% for women were assigned to the low, middle, and high groups, respectively. When the high group was used as the reference group, the low groups showed a significantly higher mortality risk after adjusting for confounders in both men and women (men; p = 0.03, women; p < 0.001).

Conclusion: In patients on hemodialysis, age-related decline of handgrip strength was observed in both men and women, regardless of baseline values. Among the three patterns of decline, the low group had a higher mortality rate compared to the high group in both men and women. The results suggest that even if decline in muscle weakness over time can be expected, handgrip strength needs to be improved in order to improve life prognosis.

REFERENCES

TRAJECTORY OF ANTHROPOMETRIC INDICATOR AND CLINICAL EVENTS AMONG PATIENTS ON HEMODIALYSIS
Shun Yoshikoshi1, Yuta Suzuki2, Shohei Yamamoto3, Keigo Imamura1, Manae Harada4, Narumi Fukuzaki1, Asumi Tobita1, Sayaka Nikkawa1, Shiwori Osada5 and Atsuhiko Matsuanga5

1Kitasato University Graduate School of Medical Sciences, Rehabilitation Sciences, Sagamihara, Japan, 2National Institute of Public Health, Center for Outcomes Research and Economic Evaluation for Health, Wako, Japan, 3National Center for Global Health and Medicine, Epidemiology and Prevention, Center for Clinical Sciences, Shinjuku-ku, Japan, 4Sagami Circulatory Organ Clinic, Rehabilitation, Sagamihara, Japan and 5Tokyo Ayase Kidney Center, Nephrology, Katsushika-ku, Japan

Background and Aims: Low values for anthropometric indicators are risk factors for adverse clinical outcomes among patients on hemodialysis (HD). Anthropometric parameters are time-dependent; thus, reliance on only baseline measurements may not sufficiently capture important patient outcomes. Nonetheless, little is known about the associations between the trajectory of anthropometric indicators and prognosis. We examined associations between a one-year change in anthropometric indicators and hospitalization and mortality rates in patients undergoing HD.

Method: This retrospective study collected data from outpatients undergoing HD at two dialysis facilities between April 2018 and March 2022. The five anthropometric measurements were evaluated, including body mass index (BMI), mid-upper arm circumference (MUAC), mid-arm muscle circumference (MAMC), triceps skinfold (TSF), and calf circumference (CC). We defined baseline which was the date of the first measurement of anthropometric assessments. Thereafter, we evaluated their trajectories over one year. Change in anthropometric indicators over the 1-year was calculated by subtracting the baseline value from the second assessment value. Patients were divided into 2 groups according to a one-year change in anthropometric indicators: no decline (≥0) and decline (<0). The outcomes were all-cause death and the number and duration of all-cause hospitalizations. Death and hospitalizations were determined using the facilities’ records. Negative binomial regressions were used to examine the associations between anthropometric changes and clinical outcomes.

Results: We included 283 patients (mean age, 67.3 years; 60.4% males). During the follow-up period (median, 2.7 years), 30 deaths and 200 hospitalizations occurred. When considering anthropometric measurements trajectories as continuous variables, increasing BMI per 1 standard deviation (incident rate ratio [IRR]: 0.87; 95% confidence interval [CI]: 0.85–0.90), MUAC (IRR: 0.94; 95% CI: 0.88–0.99), TSF (IRR: 0.92; 95% CI: 0.84–0.99), and MAMC (IRR: 0.99; 95% CI: 0.98–0.99) were associated with a lower risk of all-cause hospitalizations and death regardless of their value at any one point in time. However, the CC trajectory was not associated with clinical events (IRR: 0.94; 95% CI: 0.83–1.07). Similarly, when the anthropometric changes were considered in the categorical models, the group with BMI decline (IRR: 1.36, 95% CI: 1.30–1.43), MUAC decline (IRR: 1.14, 95% CI: 1.02–1.28), TSF decline (IRR: 1.27, 95% CI: 1.05–1.53), and MAMC decline (IRR: 1.11, 95% CI: 1.03–1.19) had a higher risk of the clinical outcome than the no decline group. A significant association was not detected for CC decline (IRR: 0.93, 95% CI: 0.84–1.03) (Table 1).

Conclusion: We observed that decreasing BMI, MUAC, TSF, and MAMC over time were independently associated with clinical events. Routinely assessing these simple measures in clinical practice may be a useful management strategy for the prognostic stratification of patients undergoing HD.
Table 1: Associations between changes in anthropometric measures and clinical outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Person-years</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IRR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
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<td><strong>BMI models</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-decline group</td>
<td>419</td>
<td>1.30 (1.20 – 1.40)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Decline group</td>
<td>359</td>
<td>1.36 (1.30 – 1.43)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td><strong>MUAC models</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-decline group</td>
<td>356</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Decline group</td>
<td>422</td>
<td>1.10 (1.04 – 1.16)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>TSF models</strong></td>
<td></td>
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<tr>
<td>No-decline group</td>
<td>426</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
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<tr>
<td>Decline group</td>
<td>352</td>
<td>1.22 (0.92 – 1.61)</td>
<td>0.17</td>
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<tr>
<td><strong>MAMC models</strong></td>
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<td>No-decline group</td>
<td>371</td>
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<td>1.00 (reference)</td>
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<td>Decline group</td>
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<td>0.014</td>
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<td><strong>CC models</strong></td>
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<tr>
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<td>358</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Decline group</td>
<td>420</td>
<td>1.04 (0.82 – 1.31)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

**Note:** BMI, body mass index; CC, calf circumference; IRR, incidence rate ratio; MAMC, mid-arm muscle circumference; MUAC, mid-upper arm circumference; SD, standard deviation; TSF, triceps skinfold; 95% CI, 95% confidence interval. Adjusted for age, sex, hemodialysis vintage, atherosclerotic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, diabetes, comorbidity index score, serum albumin, serum hemoglobin, and anthropometric measures.

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PIVKA II IS A BIOMARKER FOR PREDICTING CORONARY CALCIFICATION IN HEMODIALYSIS PATIENTS WITH DIABETES
Mooyong Park, Byung Chul Yu and Soo Jeong Choi

Soonchunhyang University Bucheon Hospital, Division of nephrology, department of internal medicine, Bucheon-si, Rep. of South Korea

**Background and Aims:** Vascular calcification (VC) is a commonly occurring and serious complication in end-stage renal disease (ESRD) patients that increases mortality. Vitamin K deficiency is well known to cause the occurrence of VC through the inactivation of Vitamin K dependent proteins (VKDP). Therefore, a marker that can easily predict the risk of VC due to vitamin K deficiency is needed in clinical practice. In this study, we aim to investigate whether the easily measurable vitamin K absence II (PIVKA-II) can serve as a surrogate marker for predicting coronary artery calcification (CAC) in ESRD patients undergoing hemodialysis and what factors influence the prediction of CAC.

**Method:** This study is an observational study conducted on end-stage renal disease patients receiving hemodialysis treatment. Patients with liver cirrhosis, HCC, or a history of coronary artery disease with stent placement were excluded, as well as patients with active infectious diseases. CAC score was measured by Non-enhanced computed tomography; and before starting hemodialysis, blood samples were collected to measure PIVKA-II, osteocalcin (OC), and bone-specific alkaline phosphatase (BAP) among other bone markers. PIVKA-II was measured two times with 3 months interval, and the average value was calculated. Additionally, ankle-brachial index (ABI) and DEXA bone densitometry were also performed.

**Results:** In this study, 69 dialysis patients participated. Among them, 34 patients had diabetes mellitus (DM). The study compared two groups based on the presence of DM. The results showed that patients with DM had higher Body Mass Index (BMI) (p = 0.01) and a higher frequency of vascular diseases such as coronary artery disease or cerebrovascular disease (p = 0.004). The DM group also had higher LDL cholesterol levels (p = 0.03), but there was no significant difference between the two groups in terms of PIVKA-II, BAP, and Osteocalcin levels (Table 1). When analyzing the factors that had a correlation with the CAC score in all 69 patients, LDL cholesterol (r = -0.37, p = 0.002) and CRP (r = 0.28, p = 0.03) were found to have a significant correlation, but PIVKA-II (p = 0.063, Figure 1A), BAP (p = 0.57), and OC (p = 0.45) did not. In the DM group, there was a statistically significant correlation between CAC score and PIVKA-II (r = 0.283, p = 0.001), but there was no correlation between CAC score (Figure 1B) and CaxP, LDL cholesterol, CRP, BAP, and OC (p = 0.7, p = 0.4, p = 0.3, p = 0.7 and p = 0.4 respectively).

**Conclusion:** The results suggest that in patients with diabetes who undergo dialysis, PIVKA-II can be clinically useful as a surrogate marker for predicting CAC associated with vitamin K deficiency. This is because diabetic patients may have more pronounced VKDP inactivation and VC due to vitamin K deficiency, but additional research is needed to fully understand this relationship.

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Figure 1:
HEMODIALYSIS PATIENTS: A RANDOMIZED CONTROLLED TRIAL

NUTRITIONAL STATUS, COGNITIVE FUNCTION, AND BONE IN HEMODIALYSIS PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Background and Aims: Remote ischemic preconditioning (RIPC) is a process in which a brief period of ischemia is induced in one part of the body to protect another part from damage due to subsequent periods of more severe ischemia. Hemodialysis sessions are considered an ischemic process because it involves another part from damage due to subsequent periods of more severe ischemia. In which a brief period of ischemia is induced in one part of the body to protect another part from damage due to subsequent periods of more severe ischemia.

Method: Fifty patients who received regular hemodialysis for more than one year in our dialysis unit were included. The patients were randomized (single-blind) into two groups a control group (20 patients) and an intervention group (30 patients). Before each HD session, sphygmomanometer cuffs were placed around the non-vascular access arm. Three cycles of ischemia for five minutes were performed followed by reperfusion for five minutes. Ischemia was induced by inflating the sphygmomanometer cuffs to 200 mmHg. This maneuver was done before each HD session for 12 weeks. The Montreal Cognitive Assessment (MOCA) was used to assess cognitive function. The nutritional state was assessed by anthropometric measurement (body weight, BMI), laboratory (serum albumin and serum cholesterol), and Subjective Global Assessment Form (SGA). Serum calcium (s.Ca) and serum phosphorus (s.PO), serum alkaline phosphate (s. ALP) and intact parathyroid hormone (iPTH) were used as indices for bone profile.

Results: The intervention group include 30 patient with mean age (36.6±10), 19 male (66.7%) and 11 females (33.3%). The control group include 20 patient with mean age (46.9±9), 12 male (60%) and eight female (40%). None of these patients' demographic data (age, sex, original kidney disease, and duration of dialysis) were significantly different between the study groups (P>0.05). MOCA test score at baseline was (24.5±2.6) at intervention group and (24.4±3.2) at control group, and after 12 weeks intervention was (24.8±2.2) at intervention group and (24.4±2.8) at control group, there were no statistical significance regarding the difference between the two groups overall (P=0.4). NO significant Statistical changes in anthropometric measurements (Body weight (P=0.3) and BMI (P=0.6) were found between the two groups. Additionally, no significant changes (serum albumin and cholesterol) were detected. SGA score at baseline was at intervention group (1.2±0.4) and control group (1.1±0.3), and after 12 week was at the intervention group (1.4±0.5) and control group (1.6±0.3). SGA showed no statistical significance between the two groups overall (P=0.2). No significant statistical changes regarding bone profile (s.ca (P=0.5), s.PO (P=0.2), s.ALP (P=0.7) and iPTH (P=0.5)).

Conclusion: Although some studies showed a beneficial effect of RIPC on reduction of cardiovascular risk, our study found no significant effect on cognitive function, nutritional status, and bone disorders among hemodialysis patients.

#3724

CHANGES IN CARDIOVASCULAR CALCIFICATION AFTER PARATHYROIDECTOMY IN DIALYSIS-DEPENDENT PATIENTS

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Background and Aims: Vascular calcification (VC) is common in patients with end stage kidney disease on dialysis and with secondary hyperparathyroidism (SHPT). There is a lack of knowledge regarding dynamics of VC after surcrate treatment of SHPT. We aimed to evaluate evolution of coronary artery calcification (CAC) and abdominal aortic calcification (AAC) after parathyroidectomy (PTx) in dialysis patients with SHPT.

Method: The prospective cohort study included 33 dialysis-dependent patients (mean age of 50±13 years) with severe SHPT who underwent subtotal (n = 16) or total PTx with autotransplantation of parathyroid tissue (n = 17). Cardiac computed tomography scan (quantification of coronary calcium by Agatston method) and lateral lumbar X-ray (semi-quantitative Kaupilla score) were used to assess prevalence of VC before and 18 months after surgery. Levels of serum total calcium, phosphorus, parathyroid hormone (PTH), and alkaline phosphatase (AP) before and 18 months after surgery were also evaluated.

Results: In our cohort median dialysis vintage before surgery was 71 [Q1-Q3: 29.136] months, total serum Ca was 2.47±0.23 mmol/L, mean PTH was 139 [Q1-Q3: 90; 161] pg/ml. Prevalence of CAC before PTx was 79% (n = 26), and 61% (n = 20) of patients had AAC. Of note, 54.5% of the patients had severe coronary calcification (>400 AU), while only 12% were considered to have severe calcification using Kaupilla score (>12). We observed moderate positive correlation between CAC and AAC scores (Spearman’s ρ = 0.699 [95% CI: 0.48; 0.84], p=0.0001). Both CAC and AAC scores correlated moderately with age of the patients (ρ = 0.57 [95% CI: 0.3; 0.76], p=0.0002, and ρ = 0.64 [95% CI: 0.39; 0.8], p<0.0001, respectively), AAC had weak correlation with their dialysis vintage (ρ = 0.45 [95% CI: 0.14; 0.68], p=0.005). Median of baseline CAC was 458 [Q1-Q3: 23; 1585] AU, after 18 months - 491 [Q1-Q3: 58; 1956] AU, no statistically significant differences were observed (p = 0.91, Wilcoxon test). We did not find statistically significant differences between median of Kaupilla scores before and after PTx as well: 3 [Q1-Q3: 0; 10] and 2 [Q1-Q3: 0; 10], correspondingly, p = 0.17 (Wilcoxon test) – Fig. 1.

As it can be seen from Fig. 1, dynamics of both CAC and AAC values before and after PTx varied markedly across subjects. To investigate the factors that may affect VC progression less than 50 AU (n = 11) and after PTx and 61% (n = 20) with CAC progression of more than 50 AU (n = 14). Patients who had progression of coronary calcification by the end of the follow-up had higher age (59±11 vs 46±12 years in 2nd group, p = 0.0128) higher serum calcium levels (2.57±0.24 vs 2.29±0.32 mmol/L in 2nd group, p = 0.0267), and higher AP levels at follow-up (69.8 [Q1-Q3: 62.8, 96.0] vs 51.7 [Q1-Q3: 41.4; 57.1] U/ml in 2nd group, p = 0.003).UNivariate analysis showed no significant differences between groups

Table 1: Demographics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non-DM (N = 35)</th>
<th>DM (N = 34)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>17/18</td>
<td>16/18</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>61±11</td>
<td>61.10±1.9</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>21.2±3.7</td>
<td>24.2±3.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>8 (22.9)</td>
<td>4 (11.8)</td>
<td>NS</td>
</tr>
<tr>
<td>SBP</td>
<td>146.1±22.1</td>
<td>153.1±21.2</td>
<td>NS</td>
</tr>
<tr>
<td>DBP</td>
<td>73.1±14.7</td>
<td>68.2±15.0</td>
<td>NS</td>
</tr>
<tr>
<td>HTN</td>
<td>31 (88.6)</td>
<td>31 (91.2)</td>
<td>NS</td>
</tr>
<tr>
<td>CAD or CVA</td>
<td>12 (34.3)</td>
<td>20 (58.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>HD duration (months)</td>
<td>105.8±77.3</td>
<td>71.5±57.6</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Non-DM: Non-Dialysis; DM: Dialysis
Comparing dialysis vintage (p = 0.53), phosphate levels (p = 0.54), PTH levels (p = 0.32). In addition, CAC progression risk was not associated with type of surgery (total vs subtotal PTx RR = 1.11 [95% CI: 0.71; 1.8], OR = 1.48 [95% CI: 0.3; 5.7], p = 0.708).

Conclusion: Prevalence of vascular calcification in dialysis-dependent patients with severe SHPT is high. Progression of CAC by 18 months after PTx was associated with higher age of the patients, higher follow-up levels of serum total Ca and AP.

#3246
THE ASSOCIATION OF THE CO-OCCURRENCE OF MALNUTRITION AND SARCOPENIA WITH MORTALITY IN HEMODIALYSIS PATIENTS: A MULTICENTER PROSPECTIVE COHORT STUDY
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Background and Aims: Frailty is widely acknowledged as an age-related fragile state characterized by physiological vulnerability to stress, and it is prevalent among patients undergoing maintenance hemodialysis therapy. Various factors are interconnected and can be theoretically consolidated into a cycle of frailty, with malnutrition and sarcopenia at the core. These can result in numerous negative health outcomes in patients on hemodialysis and prompt identification and treatment are necessary. However, limited research has investigated the impact of the overlap between malnutrition and sarcopenia on mortality in this patient population. In this study, we examined the association of the overlap between malnutrition and sarcopenia with all-cause mortality in patients undergoing maintenance hemodialysis.

Method: The present prospective cohort study recruited outpatients on hemodialysis from three facilities in Japan. At the study baseline, data on patients’ characteristics including age, gender, body mass index, duration of dialysis, primary kidney diseases, 11 comorbid conditions, and laboratory parameters (including serum albumin level) were collected from medical records. In addition, muscle mass (skeletal muscle index [SMI]), muscle strength (handgrip strength), and physical performance (short physical performance battery [SPPB]) were measured by physical therapists. A comorbidity index was used to quantify the severity of comorbid illnesses, which was calculated based on primary kidney diseases and the 11 comorbidities. Malnutrition was identified based on geriatric nutritional risk index <98, which was calculated using the serum albumin level and body weight. Sarcopenia was diagnosed when patients had low muscle mass (SMI <7.0 kg/m² for males and <5.7 kg/m² for females) and low muscle strength (handgrip strength <28.0 kg for males and <18.0 kg for females) or low physical performance (SPPB <29), in accordance with the Asian Working Group for Sarcopenia 2019 criteria. After classifying the study participants into four groups based on the absence or presence of malnutrition and sarcopenia, the mortality risk was evaluated using the Kaplan-Meier method and Cox proportional hazard analysis. This study was approved by the Research Ethics Committee and conducted in accordance with the principles of the Declaration of Helsinki.

Results: A total of 379 patients on hemodialysis were included in the analysis. The mean age of the patients was 69.5±12.6 years, and 40.2% of the cohort being female. The mean duration of dialysis was 7.9±4.5 years. The most prevalent underlying kidney disease was diabetes mellitus. At baseline, the prevalence rates of malnutrition and sarcopenia were 32.7% and 28.2%, respectively. Over a mean follow-up period of 4.3 years, 23 patients died. The Kaplan-Meier analysis demonstrated a lower cumulative survival rate in patients with malnutrition and/or sarcopenia. After adjustment for the effect of age, gender, duration of dialysis, and comorbidity index, the hazard ratio in patients with both malnutrition and sarcopenia was significantly higher than in patients without both hazard ratio [HR] 5.78, 95% confidence interval [CI] 1.86-17.94). However, the hazard ratios in patients suffering from either malnutrition or sarcopenia alone were not significantly different (Table 1).

Conclusion: The present study has demonstrated the strong association of a state of co-occurrence between malnutrition and sarcopenia, which implies starvation and muscle wasting, with a poor prognosis in patients undergoing hemodialysis. The findings of this study have accentuated the significance of addressing both malnutrition and sarcopenia in routine clinical practice for patients undergoing maintenance hemodialysis.

#3160
IMPACT OF HEART FUNCTION ON ELDERLY INCIDENT HEMODIALYSIS PATIENTS
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Background and Aims: Cardiovascular disease (CVD) is the most common cause of death in patients on hemodialysis (HD). Indeed, left ventricular (LV) dysfunction, congestive heart failure and arrhythmia are independent predictors of poor survival and hospitalization in these patients. Among the patients who initiated HD, the proportions of the elderly patients aged >65 years are increasing worldwide. According to the Korean Renal Data System, the percentage of incident HD patients aged >65 years increased from 11% in 1990 to 53% in 2022. In addition, the prevalence of CVD increases with age. Therefore following these trends, investigating the impact of heart function on prognosis in elderly patients on HD is important for predicting prognosis and making appropriate treatment plans. This study aims to investigate the all-cause mortality in elderly incident HD patients according to heart function and presence of arrhythmia.

Method: 1,002 incident HD patients aged >70 years were recruited from a retrospective cohort of the Korean Society of Geriatric Nephrology. The primary outcome is all-cause mortality (6 months, overall) according to the LV function and presence of arrhythmia. To analyze, patients were divided into 6 groups according to the LV function (LV ejection fraction [LVEF])≥50%,
40≤LVEF<50%, LVEF<40%) and the presence of arrhythmia. The secondary outcome is all-cause mortality (6 months, overall) according to the LV function or presence of arrhythmia. To analyze, patients were divided into 3 groups according to the LV function and separately divided into 2 groups according to the presence of arrhythmia. Cox regression univariate and multivariate analyses was used.

**Results:** 1,002 patients were divided into 6 groups (LVEF≥50% without arrhythmia [N = 78; 75.6%], 40≤LVEF<50% without arrhythmia [N = 71, 7.1%], LVEF<40% without arrhythmia [N = 66, 6.6%], LVEF≥50% with arrhythmia [N = 124, 12.4%], 40≤LVEF<50% with arrhythmia [N = 15, 1.5%], LVEF<40% with arrhythmia [N = 19, 1.8%]). There were no differences of 6-month all-cause mortality among the groups. Compared with LVEF≥50% without arrhythmia group, 40≤LVEF<50% without arrhythmia (hazard ratio [HR], 1.59; 95% confidence interval [95% CI], 1.21-2.09; P = 0.001), LVEF<50% with arrhythmia (HR, 1.39; 95% CI, 1.12-1.74; P = 0.003) and LVEF<40% with arrhythmia groups (HR, 1.95; 95% CI, 1.19-3.17, P = 0.007) showed higher all-cause mortality of overall period. According to the LVEF groups, there were no differences of 6-month all-cause mortality among the groups. Compared with LVEF≥50% group, 40≤LVEF<50% group showed higher all-cause mortality of overall period (HR, 1.51; 95% CI, 1.18-1.94, P = 0.001). According to the arrhythmia groups, there were no differences of 6-month all-cause mortality between the groups. The presence of arrhythmia was associated with higher all-cause mortality of overall period (HR, 1.39; 95% CI, 1.15-1.69, P = 0.001).

**Conclusion:** Decreased heart function and presence of arrhythmia have negative impact on all-cause mortality of overall period, but not on 6-month all-cause mortality in elderly patients on incident HD. Therefore, evaluation of the heart function and detection of arrhythmia in elderly patients who start HD and providing the appropriate treatment to these patients would be helpful for improving the prognosis.

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**#3657**

**ASSOCIATION BETWEEN AGE, SARCOPENIA, AND MORTALITY IN PATIENTS UNDERGOING HEMODIALYSIS: A PROSPECTIVE COHORT STUDY**

Hiroto Imai, Ryota Matsuzawa, Shohai Yamamoto, Yuta Suzuki,
Manae Harada, Keigo Imamura, Shun Yoshikoshi, Daisuke Kakita,
Naoyuki Tsujimoto, Shiwori Osada, Kiyoshi Shimokado,
Atsuhiko Matsunaga and Akira Tamaki

Japan

**Background and Aims:** The mean age of Japanese patients undergoing hemodialysis at the end of 2018 was 68.75 years, demonstrating a 13-year increase since 1985. The healthcare management of the geriatric patients presents significant challenges, encompassing both clinical and societal aspects, as they often experience overlapping comorbidities while undergoing hemodialysis. A systematic review and meta-analysis published in 2022 reported that sarcopenia was associated with heightened mortality rates in patients undergoing dialysis therapy. However, only a limited number of studies have investigated this association among Asian populations, whose differences in body composition, nutritional status, and socio-economic background distinguish them from those in the United States and Europe. Notably, no studies have targeted the older demographic, who constitute the majority of Asian patients on hemodialysis and possess numerous risk factors for death. This study categorized Japanese patients undergoing hemodialysis by age, <75 and ≥75, and examined the impact of sarcopenia on mortality according to age.

**Method:** This multicenter prospective cohort study enrolled 404 outpatients undergoing hemodialysis from three facilities in Japan and followed them up for three years. At baseline, information on age, sex, dialysis vintage, body mass index, primary kidney diseases, comorbid conditions, and laboratory parameters (serum albumin, serum hemoglobin, and hematocrit) were collected from medical records. The geriatric nutritional risk index (GNRI) was calculated based on the patient’s serum albumin level and body weight. Sarcopenia was diagnosed in patients who had low muscle mass (skeletal muscle mass index <7.0 kg/m² for males and <5.7 kg/m² for females) and low muscle strength (handgrip strength <28.0 kg for males and <18 kg for females) or low physical performance (short physical performance battery score <9), according to the Asian Working Group for Sarcopenia 2019 criteria. The Kaplan-Meier method and Cox proportional hazard analysis were used to evaluate the independent association between sarcopenia and mortality after adjusting for baseline characteristics in patients aged <75 and ≥75 years.

**Results:** A total of 404 patients participated in this study, with a mean follow-up period of 30 months, during which 50 (12.4%) patients died. Participants had a mean age of 68.4 ± 12.6 years and 62.6% of them were male and the mean GNRI was 91.1 ± 21.2. Diabetes mellitus was the most prevalent underlying kidney disease among the study cohort (38.1%). The prevalence of sarcopenia in all patients, those under 75 years of age, and those 75 years and older was 37.6%, 22.7%, and 63.1%, respectively. Kaplan-Meier analyses indicated a higher mortality rate among patients with sarcopenia compared to those without. In the subgroup analysis for patients aged <75 years, sarcopenia was significantly associated with increased mortality risk after full adjustment (hazard ratio [HR], 2.56; 95% confidence interval [CI], 1.05–5.95). Conversely, in the subgroup of patients 75 years and older, sarcopenia was not significantly associated with all-cause mortality (HR, 0.69; 95% CI, 0.28–1.68), and only a low GNRI was independently associated with poor survival (HR, 0.98; 95% CI, 0.96–1.00).

**Conclusion:** This present study determined that the impact of sarcopenia on mortality among patients undergoing hemodialysis may be altered by their age. Specifically, among those aged 75 years and above, malnutrition was found to be a strong predictor of poor survival, rather than sarcopenia.

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**#3846**

**MALNUTRITION RISK IN HEMODIALYSIS PATIENTS AND SCREENING TOOLS PROGNOSIS: GNRI, CREATININE INDEX AND SPEW**

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1Diámetro Investimentos e Serviços, Lda., Medical Department, Sintra, Portugal, 2Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto FCNAUP, Porto, Portugal, 3Nova Medical School, Lisboa, Portugal, 4CINTESIS - Centro de Investigação em Tecnologias e Serviços de Saúde, Faculty of Medicine, University of Porto, Cintesis@RISE, MEDCIDS, Porto, Portugal, 5NOVA School of Science and Technology, CMA, Caparica, Portugal, 6Instituto Superior de Engenharia de Lisboa, ISEL, Lisboa, Portugal, 7Department of Estatística e Aplicação da Universidade de Lisboa, CEALI, Portugal, 8Hospital Santa Cruz, Serviço de Nefrologia, Carnaxide, Portugal, 9Hospital Beatriz Ângelo, Serviço de Nefrologia, Loures, Portugal, 10Faculty of Medicine, University of Lisbon, Centro de Cardiologia, Lisboa, Portugal, and 11Diámetro Corporate, Medical Department, Sweden

**Background and Aims:** Nutritional status clearly has a great impact on the prognosis of maintenance hemodialysis patients. Therefore, its management should be a priority and risk screening frequent and easily implemented, based on the biochemical and clinical routine parameters already available. Many tools fit these simple criteria, namely simple Protein Energy Wasting score (sPEW), Geriatric Nutritional Risk Index (GNRI) and Creatinine Index (Cr Index). These scores are associated with a high mortality and morbidity risk in hemodialysis (HD) patients. The objective of this study was to assess the performance of these tools regarding the estimation of all-cause mortality, in a 45-months follow-up of a large patient cohort.

**Method:** Historical cohort study of HD pts from 25 outpatient clinics. sPEW, GNRI and Cr Index were estimated. Kaplan-Meier estimator and univariable Cox regression models to analyze time until death were used. To compare survival curves the log-rank test or Tarone test were used, as appropriate. The level of significance α = .05 was considered. All data were analyzed using SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows. Armonk, NY, USA: IBM Corp).

**Results:** We analyzed 2322 pts, 59% males, 31.7% diabetic, with a median age of 70 years (P25 = 60, P75 = 79) followed up for a maximum of 45-month (P25 = 31; P75 = 45). All-cause mortality was observed in 778 pts (33.5%). To assess the mortality risk, the exposures GNRI and Cr Index, were discretized using quartiles.

**Table 1: Impact of sarcopenia on mortality in a Cox proportional hazards regression analysis.**

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenia versus non-sarcopenia</td>
<td>1.37</td>
<td>0.71–2.65</td>
<td>0.348</td>
</tr>
<tr>
<td>GNRI (per one-point decrease)</td>
<td>1.01</td>
<td>1.00–1.02</td>
<td>0.164</td>
</tr>
<tr>
<td>Age &lt;75 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenia versus non-sarcopenia</td>
<td>2.50</td>
<td>1.05–5.95</td>
<td>0.039</td>
</tr>
<tr>
<td>GNRI (per one-point decrease)</td>
<td>1.00</td>
<td>0.98–1.03</td>
<td>0.693</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarcopenia versus non-sarcopenia</td>
<td>0.69</td>
<td>0.28–1.68</td>
<td>0.414</td>
</tr>
<tr>
<td>GNRI (per one-point decrease)</td>
<td>1.02</td>
<td>1.00–1.04</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Adjusted for age, gender, dialysis vintage, hemoglobin, GNRI, and comorbid conditions.

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The median was 106.6 (P<sub>25</sub> = 99.4, P<sub>75</sub> = 114.2). The log-rank test results showed a significantly lower survival for patients in GNRI Q1 category (GNRI ≤ 99.4). A p-value < 0.001 was obtained when comparing patients in Q4, Q3 and Q2 with patients in Q1. The univariable Cox regression model showed that patients in Q1 had a 2-fold increased risk of death, when compared with Q4 (HR = 2.1, 95% CI: 1.7–2.6, p < 0.001).

**Creatinine Index**

The median was 12.648 (P<sub>25</sub> = 11.908, P<sub>75</sub> = 13.406). The log-rank test for the equality of survival functions for the different levels was considered statistically significant and showed a significantly lower survival for patients in CR Index Q1 category, when compared with the remaining categories (p < 0.001). The univariable Cox regression model showed that comparatively with Q4, patients in Q1 had a 5-fold increased risk of death (HR = 4.8, 95% CI: 3.7–6.0, p < 0.001), patients in Q2 a 3-fold increased risk of death (HR = 3.1, 95% CI: 2.4–3.9, p < 0.001), and patients in Q3 a 2-fold increased risk of death (HR = 1.9, 95% CI: 1.4 – 2.4, p < 0.001).

**sPEW**

The frequency of each score from 0 to 4 was 306, 380, 111, 1369 and 156, respectively. The log-rank test for the equality of survival functions corresponding to the different levels showed a significantly higher survival for patients with a sPEW score of 4 when compared with the remaining levels (p < 0.001). The univariable Cox regression model showed that comparatively with a score of 4, patients with a score of 0 had an 8-fold increased risk of death (HR = 7.7, 95% CI: 4.5–13.3, p < 0.001), score of 1 a 6-fold increase risk of death (HR = 5.6, 95% CI: 3.3–9.2, p < 0.001), score of 2 a 4-fold increase risk of death (HR = 4.1, 95% CI: 2.2–7.7, p < 0.001), and a score of 3, almost a 4-fold increased risk of death (HR = 3.7, 95% CI: 2.2–6.3, p < 0.001).

**Conclusion:** In this exploratory analysis, the three tools showed a significant association with mortality during follow-up. These tools, if adequately validated in future studies, may select patients for further intervention to modify the outcome.

**#4993**

**EFFECT OF ETELCALCETIDE TREATMENT ON ERYTHROPOIESIS-STIMULATING AGENTS (ESAS) REQUIREMENT IN HEMODIALYSIS PATIENTS: A SINGLE CENTER STUDY**

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HMC, Qatar

**Background and Aims:** Anemia is a common consequence of advanced chronic kidney disease (CKD). There are various causes of renal anemia like decreased production of and resistance to Erythropoietin, shortened survival of red blood cells and chronic blood loss. Secondary hyperparathyroidism is a potential cause of renal anemia in CKD patients due to direct effect on Erythropoietin synthesis, red cell survival and bone marrow fibrosis [1]. There are several reports of the beneficial effect of treatment of hyperparathyroidism on hemoglobin (Hb) levels. Etelecalcetide is a novel intravenous calcimimetic used for the treatment of secondary hyperparathyroidism in hemodialysis patients. However, there are very few reports of Etelecalcetide’s effect on anemia management in hemodialysis patients. We aimed to study the effect of Etelecalcetide on ESAs requirement in our hemodialysis cohort.

**Method:** This is a retrospective study in Al Wakra Hospital hemodialysis unit conducted on patients with uncontrolled secondary hyperparathyroidism who needed to be started on Etelecalcetide. Mean Hb and mean ESAs dose were calculated for a period of 6 months before and 6 months after starting Etelecalcetide, while iPTH levels were measured at the beginning and 6 months after starting Etelecalcetide. Inclusion criteria: hemodialysis patients who are on Etelecalcetide for at least 6 months. Exclusion criteria: Patients’ age < 12 years, hemodialysis duration < 12 months and patients with acute blood loss.

**Results:** Out of 94 hemodialysis patients, 26 (27.6%) were on Etelecalcetide. 2 patients were excluded, one for acute hematuria and the other for erosive gastritis. 24 patients were included (13 females and 11 males). Mean age of the patients was 58.7 years. 15 patients were on Darbepoetin, 8 on Erythropoietin and 1 patient was switched from Darbepoetin to Erythropoietin due to poor response. There was no significant difference in mean Hb levels for all the patients before and after starting Etelecalcetide (10.6 g/dl and 10.8 g/dl, respectively). Out of 24 patients, 19 had reduction while 5 had increase in ESAs dose requirement. In total, the mean reduction of ESAs dose for all the patients was 17.3%. There was a mean of 33.4% reduction in ESAs requirement for the 19 patients while a mean of 44% increase in the requirement for the 5 patients. Mean iPTH for the cohort at the time of starting Etelecalcetide and 6 months after was 1056 pg/ml and 473 pg/ml respectively. The mean reduction of iPTH for those who had decreased ESAs requirement was 58% while it was 38.8% for those who had increased ESA requirement.

**Conclusion:** This study showed that control of severe secondary hyperparathyroidism with Etelecalcetide was associated with reduction in ESAs requirement in hemodialysis patients. The more the control of hyperparathyroidism, the more the reduction of ESAs requirement. These findings were...
observed also in a one case report [2]. We believe that our study has one of the largest number of patients to show such an observation, however larger controlled studies are needed to confirm these preliminary findings in the improvement of anemia after treatment of hyperparathyroidism by Etelcalcetide.

REFERENCES


ASSOCIATION OF SERUM CALCIUM-TO-MAGNESIUM RATIO WITH CARDIOVASCULAR AND CEREBRAL VASCULAR DISEASES IN DIALYSIS PATIENTS.

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Background and Aims: Cardiovascular disease (CVD) and cerebral vascular accident (CVA) are the important complications and the leading causes of death in dialysis patients. High serum calcium (Ca) level promotes the clotting cascades and vascular calcification, which leads to CVD and CVA. Magnesium (Mg) is a well-known Ca blocker, inhibiting the formation of thrombin. An imbalance between serum Ca and Mg levels has been reported as an associated factor with CVD and mortality. This study investigated the associations of serum Ca-Mg ratio with CVD and CVA in dialysis patients.

Method: We conducted a cross-sectional analysis using baseline data from a multicenter prospective cohort for dialysis patients in South Korea. A total of 860 patients were divided into tertile groups according to serum Ca-Mg ratio levels. Patients with serum Ca-Mg ratio less than 3.28 were classified as the low group, and patients with serum Ca-Mg ratio more than 3.87 were classified as the high group, and the rest were classified as the middle group. Serum Ca level was calculated and applied as corrected Ca level considering serum albumin level. The associations of serum Ca-Mg ratio with prevalence of acute coronary syndrome (ACS), congestive heart failure, aortic artery calcification, and CVA were assessed.

Results: The average age of all patients was 59.1±12.1 years, and the average duration of dialysis was 7.9±5.9 years, and the duration of the low group was shorter than those of other groups. The high group had higher prevalence of peripheral vascular disease (P = 0.004). Serum albumin, phosphorus and Mg levels in the high group were lower than other groups (P < 0.001). The prevalence of ACS showed higher in the high group than in other groups (P = 0.017). The prevalence of cerebral infarction showed higher in the high group than the low group (P = 0.016). In multivariable logistic regression analysis, higher Ca-Mg ratio was independently associated with the prevalence of ACS (Odds ratio 1.321, 95% confidential interval 1.009-1.728, P = 0.043) and cerebral infarction (Odds ratio 1.392, 95% confidential interval 1.002-1.896, P = 0.036).

Conclusion: A high Ca-Mg ratio was associated with the development of ACS and cerebral infarction. If the optimal cut-off of Ca-Mg ratio is determined, it can be used as a predictive marker for ACS and cerebral infarction.
We prospectively enrolled the patients with ESRD undergoing hemodialysis using functional near-infrared spectroscopy (fNIRS), and analyzed the effect of hemodialysis on the functional brain connectivity.

Method: We prospectively enrolled the patients with ESRD undergoing hemodialysis for more than six months without any previous history of neurological or psychiatric disorders. The fNIRS data acquisition was made with a NIRSIT Lite device. Measurements were made three times in the resting state for each patient; before the start of hemodialysis (Pre-HD), one hour after the start of hemodialysis (Mid-HD), and after the end of hemodialysis (Post-HD). We processed and exported the entire data, and made a weighted connectivity matrix using a Pearson correlation analysis. From the connectivity matrix, we obtained the functional connectivity measures by applying a graph theoretical analysis (Fig. 1). We compared the differences of the functional connectivity measures according to hemodialysis in patients with ESRD.

Results: We included 34 patients with ESRD. Table 1 and Fig. 2 show the differences in functional brain connectivity according to hemodialysis. There were significant changes in the functional connectivity measures of the mean clustering coefficient, transitivity, and assortative coefficient in the comparisons between Pre-HD and Post-HD periods (0.353 vs. 0.399, p = 0.047; 0.523 vs. 0.600, p = 0.042; 0.043 vs. -0.012, p = 0.044; respectively). However, there were no changes in the connectivity measures of the mean clustering coefficient, transitivity, and assortative coefficient in the comparisons between Pre-HD and Mid-HD periods, and between Mid-HD and Post-HD periods. In addition, there were no significant differences in the connectivity measures of the average strength, global efficiency, and local efficiency in the comparisons among Pre-HD, Mid-HD, and Post-HD periods.

Conclusion: We demonstrate the significant effect of hemodialysis on the functional brain connectivity in patients with ESRD. The functional brain connectivity would change in a more efficient direction through hemodialysis.
Figure 1: The process of analyzing functional brain connectivity in patients using functional near-infrared spectroscopy.

Table 1: The changes of the measures of functional brain connectivity with hemodialysis in patients with end-stage renal disease.

<table>
<thead>
<tr>
<th>Network measures</th>
<th>Acquisition time</th>
<th>Values</th>
<th>Pairwise comparisons</th>
<th>Adjusted p-value</th>
<th>95% confidence interval</th>
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<tr>
<td>Average strength</td>
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<td>Global efficiency</td>
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<td>Pre-HD and Mid-HD</td>
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HD: hemodialysis
*Statistical significance

Figure 2: Changes in functional brain connectivity measures based on hemodialysis in patients. There were no differences in the average strength (A), global efficiency (B), and local efficiency (C) between the Pre–, Mid–, and Post–HD periods; however, significant changes were observed in the mean clustering coefficient (D), transitivity (E), and assortative coefficient (F) between the pre– and post–HD periods.
#3243
CANCER PATIENTS WITH END-STAGE KIDNEY DISEASE ON CHRONIC HEMODIALYSIS: CHANGING THE PARADIGM
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Background and Aims: In the last decade, new therapeutic regimens have dramatically improved the prognosis of cancer patients and changed the paradigm of a previously highly lethal disease, increasing the number of cancer patients with chronic kidney disease (CKD) who progress to end-stage kidney disease (ESKD). However decision-making regarding dialysis initiation in patients with cancer and ESKD remains however controversial. The aim of our study was to characterize the clinical course and evaluate survival outcomes of cancer patients on chronic hemodialysis (HD).

Method: We conducted a retrospective study of HD patients in a single oncology hospital unit between January 1991 and November 2022. Outpatients on HD for more than one month, who underwent dialysis after the diagnosis of cancer were included. Univariate and multivariate hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality were estimated using the Cox proportional hazards risk model.

Results: Two hundred and twelve patients were recruited. Mean age at HD initiation was 65.7±14.7 years. The most prevalent ESKD etiologies were cast nephropathy, chronic interstitial nephritis, and surgical removal of the kidney. The most common tumors were genitourinary, multiple myeloma (MM) and gastrointestinal corresponding to 80.6% of all cancers. There were 143 deaths among the HD patients.

Discussion: Our results highlight the importance of considering cancer patients for renal support therapies, including those with multiple tumors and metastatic disease. In fact, with the new treatments available, many patients have chronic oncological disease non-fatal in the short term. To the best of our knowledge, this is the largest study of cancer patients on chronic HD.

#3689
RELATIONSHIP BETWEEN STAPHYLOCOCCUS AUREUS NASAL CARRIAGE AND URAEMIC PRURITUS IN HEMODIALYSIS PATIENTS AND ITS INFLUENCE ON INFECTION
Hon-Yen Wu1,2,3,4, Ping-Hsiu Tsai1, Shih-Ping Hsu1, Chun-Hsing Liao1,2 and Mei-Ju Ko5

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Background and Aims: Uraemic pruritus is a common and distressing comorbid disease among patients undergoing haemodialysis (HD). The aetiology of uraemic pruritus is multifactorial and not fully understood. The role of skin microbiota in chronic inflammatory skin disease has long been discussed, but evidence regarding the relationship between uraemic pruritus and Staphylococcus aureus (SA) colonization is limited. The rate of SA nasal carriage in HD patients was more than double that of healthy individuals, and the phage type of SA infection was often the same as the type of SA carried in the HD patients' nares. SA colonization is associated with greater skin barrier disruption, which suggests a possibility to increase the risk of infection in patients with uraemic pruritus. This study aimed to assess the role of SA nasal carriage in uraemic pruritus, as well as the interplay among SA colonization, uraemic pruritus, and SA infection in HD patients.

Method: We conducted a prospective cohort study to enrol adult HD patients in the Far Eastern Memorial Hospital, a tertiary medical centre in Taiwan, in April 2019. Eligible patients should had received maintenance HD for more than three months. Patients were excluded if they had active infection or primary skin diseases. The intensity of uraemic pruritus was assessed using a visual analogue scale (VAS) from 0 to 10 (0 = no pruritus, 10 = the worst pruritus imaginable). Nasal swab culture was performed to examine the status of SA nasal carriage. Patients were followed until SA infection, death, or January 2020, whichever had occurred earlier. The definition of SA infection should fulfill both the clinical diagnosis and the results of microbiological culture. Multivariate linear regression models were used to assess the potential predictors for a higher pruritus intensity. Multivariate Cox proportional hazard models were used to analyse the risk of SA nasal carriage on SA infection among the HD patients.

Results: A total of 100 HD patients were enrolled, the mean age was 61.7 years and 69% were men. The mean dialysis vintage was 6.7 years. Among the participants, 55% had uraemic pruritus and the mean VAS score of pruritus intensity was 4.0. The prevalence of SA nasal carriage was higher in patients with uraemic pruritus than that in patients without uraemic pruritus (33% vs 13%, P = 0.024). The multivariate linear regression model showed that SA nasal carriage was an independent predictor of a higher VAS score of pruritus (parameter estimate, 1.18; 95% CI 0.05–2.30; P = 0.04) (Table 1). After follow-up for 10 months, there were four SA infection events in the pruritus patients and one event in the non-pruritus patients. The multivariate Cox proportional hazard model showed that patients with SA nasal carriage had a borderline higher risk for SA infection (adjusted hazard ratio, 50.9; 95% CI, 0.62-3689; P = 0.08) (Table 2).

Conclusion: SA nasal carriage is independently associated with uraemic pruritus, and is also an independent predictor for a higher pruritus intensity among HD patients. Moreover, SA colonization might predict SA infection in later follow-up period. This study provide evidence for future studies regarding the survey for SA colonization and application of nasal decolonization among HD patients with uraemic pruritus.
ROXADUSTAT-INDUCED HYPOTHYROIDISM: THE EFFECT OF ROXADUSTAT ON SUPPRESSION OF THYROID FUNCTION
Masato Ohsawa1, Tadashi Kuki1, Masahiro Nishihara1, Rento Ohsawa1 and Jin Oshikawa2

Background and Aims: There have been only two case reports of hypothyroidism in patients treated with roxadustat, a HIF-PH inhibitor as new renal anemia drug. However, there has yet been no studies to examine the effect of roxadustat on thyroid function.

Method: In this study, we retrospectively examined the effects of roxadustat on thyroid-stimulating hormone (TSH) in hemodialysis patients by two blood examinations, before and during treatment with roxadustat. We included patients who had TSH levels measured after at least two consecutive weeks of roxadustat treatment and before. We excluded patients with a history of taking other HIF-PH inhibitors before roxadustat. The period was from September 2021 to November 2022 in this interim analysis. A p value of \(<0.05\) was considered statistically significant. Analyses were performed using SPSS.

Results: 93 patients were included in this analysis. TSH levels significantly decreased after treatment with roxadustat. A total of 58.1% of patients had decreased TSH levels (2.23 ± 1.18 v.s. 1.81 ± 1.35, μIU/mL, p value = 0.040, Wilcoxon signed-rank test), and 18.3% of patients had a significant decrease below the normal range. Additionally, patients treated with thyroid hormone replacement therapy in primary hypothyroidism had a higher frequency (81.0%) of TSH decrease compared to patients without (p value = 0.013, Pearson's chi-square test).

Conclusion: This is the first study to examine that roxadustat has a suppressive effect on TSH secretion in hemodialysis patients. We also found that roxadustat-induced hypothyroidism is prevalent in the high frequency of TSH suppression, especially in primary hypothyroidism patients treated with thyroid hormone replacement therapy. Thyroid hormone receptor beta (THRβ), which is expressed in the hypothalamus and pituitary gland, plays an important role in regulating thyroid hormone through feedback mechanisms.

Yao et al. have reported that roxadustat has a similar structure to T3 and acts as a THRβ-selective ligand, particularly activating THRβ. Therefore, it is possible that roxadustat suppresses TSH secretion through negative feedback via THRβ. It is important to monitor thyroid function in patients receiving roxadustat. Roxadustat should be avoided in patients with primary hypothyroidism, since it is inferred that roxadustat-induced hypothyroidism cannot be improved by enhancement of thyroid hormone replacement therapy.

REFERENCES
#4969
AN ADEQUATE HYDRATION MANAGEMENT IMPROVES THE EFFICIENCY OF INTRADIALYTIC PHOSPHATE REMOVAL.

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Background and Aims: The excess of phosphate (P) is one of the major risk factors for death in patients undergoing hemodialysis (HD). Improving P removal efficiency should ameliorate their prognosis. We previously reported, increased urea nitrogen (UN) removal efficiency results in increased the removal efficiency of P from extracellular fluid (ECF), but did not improve that from intracellular fluid (ICF) (NDT, Vol 35, Sup3, P1401, 2020). We also reported that P removal from ICF accounted for in average about 44% of total intradialytic P removal. For improving total P removal efficiency, removal efficiency of P from ICF should be increased. As P is one of the major osmotic agents in ICF, water outflow from ICF will accompany P outflow. We explored correlation between intracellular P removal and intracellular water (ICW) reduction. And we also sought for the strategy which efficiently derive water from ICF in HD patients in order to increase intracellular P removal.

Method: Eighty-six patients undergoing 4-hour HD were enrolled this study. ICF, extracellular water (ECW) volume and body fat mass (BFM) in each patient were measured with biochemical impedance analysis method before and after HD session. Total body water (TBW) was calculated by ICW + ECW. The amount of intradialytic P removal from ICF and from ECF in each patient was calculated as previously reported (NDT, Vol 35, Sup3, P1401, 2020). The correlation between the amount of intradialytic P removal from ICF and the amount of ICW reduction was investigated. All patients were divided into three groups according to the amount of ICW reduction as high reduction (HR) group, middle reduction (MR) group and low reduction (LR) group. The amount of P removal from ICF was compared between these groups. ICF volume change (ΔICW%) was calculated as (preICW – postICW)/preICW in each patient. Where preICW = ICF volume at the starting of HD, postICW = ICF volume at the end of HD. Circulating plasma volume change (ΔCPV%) was calculated as (postTP – preTP)/postTP in each patient. Where postTP = serum total protein concentration (TP) at the end of HD, preTP = TP at the end of HD. Lean body mass (LBW) was calculated as BW – BFM. Body weight (BW) change (ΔBW%), LBW change (ΔLBW%) and TBW volume change (ΔTBW%) were calculated in the same way as ΔICW%.

To seek factors that effectively reduce ICW, the correlation with ΔICW% in ECW/TBW ratio, ΔCPV%, ΔCPV%/ΔBW% ratio, ΔCPV%/ΔLBW% ratio and ΔCPV%/ΔTBW% ratio was examined.

Results: The amount of intradialytic P removal from ICF positively correlated to the amount of ICW volume reduction (R = 0.279, y = 66.3x+2.85, p = 0.0076). It indicates an average of 66.3mg of P was removed from ICF per 1L of ICW reduction. In HR group, the amount of P removal from ICF was significantly larger than that in LR group (315.6 ± 117.8mg vs 538.2 ± 217.9mg, p = 0.019). ΔICW% negatively correlated to ΔECW% (R = 0.481, p = 0.000057). High ECW/TBW ratio indicates excess of ECW, which suggests having edema. ΔICW% positively correlated to ΔCPV% (R = 0.511, p = 0.0000051). Low ΔCPV% suggests insufficient of ultrafiltration. ΔICW% negatively correlated to ΔCPV%/ΔTBW% ratio (R = 0.421, p = 0.00011). High ΔCPV%/ΔTBW% ratio indicates insufficient plasma refill rate, which suggests overrate of ultrafiltration. But ΔICW% did not correlate to ΔCPV%/ΔBW% ratio (R = 0.184, p = 0.10) nor ΔCPV%/ΔLBW% ratio (R = 0.176, p = 0.12).

Conclusion: The amount of intradialytic P removal from ICF correlated to the amount of ICW reduction. For efficient reduction of ICW, low ECW/TBW ratio, high ΔCPV% and low ΔCPV%/ΔTBW% ratio were required. It was suggested that efficient P removal was achieved when non-edematous patients get ultrafiltration of appropriate rate and dose.

#4971
IMPACT OF RAMADAN FASTING ON NUTRITION, INFLAMMATION AND DIALYSIS ADEQUACY AMONG HEMODIALYSIS PATIENTS.

Eman Taher1, Mohamed Sobh1, Mohammed Kamal Nassar2 and Salwa El Wasif2

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Background and Aims: There is a paucity of data concerning safety of fasting in Ramadan in End stage kidney disease patients (ESKD) on haemodialysis (HD). The aim of the present study was to assess the possible effect of fasting on nutritional status (clinical, biochemical variables), inflammatory status and adequacy of haemodialysis. This observational study was carried out during 2019 when fasting duration was around 14 hours.

Method: Sixty-five patients suffered from ESKD who received regular HD for more than six months in dialysis unit, urology and nephrology center Mansoura university were included in this prospective observational study. Patients were categorized into three groups. 21 patients fasted all days of Ramadan, 25 patients fasted days other than session days and 19 patients never. We did not oblige our patient to fast. nutritional status was assessed clinically by Anthropometric measurements including body weight, BMI, triceps skin fold thickness (TSF) and estimation of protein catabolic rate (PCR) were measured, and laboratory by serum Albumin, cholesterol and fasting blood glucose. Neutrophils to lymphocytes ratio (NLR), Soluble receptor of advanced glycation end product(SRAGE) and human B-cell lymphoma/leukemia2 (BCL2) was measured as inflammatory markers, also dialysis adequacy was determined with urea reduction ratio (URR) and Kt/V. Assessment of all patients were carried out before and after Ramadan and was repeated 3 months after Ramadan in all patients.

Results: In 30 days fasting group: there was significant reductions (all P < 0.02), serum albumin, triceps skin fold thickness, Subjective global assessment score (SGA) for nutritional assessment also in inflammatory markers as neutrophils to lymphocytes ratio (NLR) and human Bcell lymphoma/leukemia2 (BCL2). But these were not accompanied by any significant change (all P > 0.05) in body mass index, serum cholesterol, fasting blood sugar (FBS), urea reduction ratio (URR), intradialytic weight gains (IDWG), Kt/V and human soluble receptor for advanced glycation end products (sRAGES). In the group Who was reported fasting in days other than HD session days: fasting led to significant reductions (all P < 0.05) only in serum albumin and triceps skin fold thickness. There were no significant changes in BMI, URR, Cholesterol, FBS, Kt/V, IDWG, SGA score, NLR, sRAGES and BCL2. In patients Who never fast at all: there was significant reduction (all P < 0.02) in triceps skin fold thickness, significant change in SGA score and also in sRAGES and BCL2.

Conclusion: There was no harmful effect for Muslim patients receiving regular HD who went to fast Ramadan in days other than HD session days. In the current study the fasting group has the benefit of both being fasting and non-significant changes in mostly all nutritional assessment points, inflammatory markers and the adequacy of HD.

#5608
THE INFLUENCE OF AMBULATORY BP ON THE ASSOCIATIONS OF SEX WITH CARDIOVASCULAR EVENTS AND MORTALITY IN DIALYSIS PATIENTS: A PROSPECTIVE COHORT STUDY

Pantelis Sarafidis, Marieta Theodorakopoulou, Fotini Iatridi, Areti Georgiou, Artemios Karagiannis, Eleni Karkamani, Alexandros Tsitsouridis, Danai Faitatzidou and Akaterini Papagianni

Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece

Background and Aims: Male patients with pre-dialysis CKD have worse ambulatory BP control than females and this is associated with higher mortality risk. Male hemodialysis patients have higher ambulatory BP levels compared to females. The aim of this study was to investigate the influence of ambulatory BP on the associations of sex with cardiovascular events and mortality in hemodialysis individuals. Male patients with pre-dialysis CKD have worse ambulatory BP control than females and this is associated with higher mortality risk. Male hemodialysis patients have higher ambulatory BP levels compared to females. The aim of this study was to investigate the influence of ambulatory BP on the associations of sex with cardiovascular events and mortality in hemodialysis individuals. Male patients with pre-dialysis CKD have worse ambulatory BP control than females and this is associated with higher mortality risk. Male hemodialysis patients have higher ambulatory BP levels compared to females. The aim of this study was to investigate the influence of ambulatory BP on the associations of sex with cardiovascular events and mortality in hemodialysis individuals.

Method: 129 male and 91 female hemodialysis patients with valid 48-hour ABPM were followed prospectively for 53.4±3.1 months. The primary endpoint was cardiovascular mortality; the secondary endpoint was a composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, resuscitation after cardiac arrest, hospitalization for heart failure, coronary or peripheral revascularization procedure.

Results: Cumulative-free from the primary endpoint was significantly lower for women (logrank-p = 0.032), while cumulative-free from the secondary endpoint did not differ significantly between the two groups (logrank-p = 0.644). The crude risk for cardiovascular mortality was significantly higher for women (HR = 1.613, 95% CI [1.037, 2.509]). The crude risk for the combined cardiovascular endpoint was not different between the two genders (HR = 0.918, 95% CI [0.638, 1.320]). After adjusting for other risk factors (age, diabetes, dialysis vintage, coronary disease) no significant differences in the risk for both the primary and the secondary endpoint were observed between women and men (primary: HR = 1.464 95% CI [0.929, 2.307]; secondary:0.866[95%CI[0.596,1.260])]. After further adjustment for 44-hour ambulatory BP the above relationships did not alter (primary: HR = 1.498, 95% CI [0.947, 2.368]; secondary: HR = 0.911, 95%CI [0.625, 1.327]).
Conclusion: In contrast to patients with pre-dialysis CKD, ambulatory BP adverse cardiovascular outcomes in hemodialysis patients.

**#6129**

**INTRADIALYTIC PARENTERAL NUTRITION IMPROVES PROTEIN STORES IN CHRONIC HEMODIALYSIS PATIENTS**

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1Doctor Peset University Hospital, Nephrology, València, Spain, 2University of Valencia, Medicine, València, Spain, 3Fisabio, València, Spain and 4Doctor Peset University Hospital, Pharmacy, València, Spain

**Background and Aims:** Intradialytic parenteral nutrition (IDPN) is a form of supplemental nutrition used to treat patients with malnutrition who receive hemodialysis (HD) and in which the oral feeding is not enough to cover basic caloric needs. Although this technique could improve biochemical markers of nutrition, information regarding its effect on body deposits is lacking. We evaluated the effect of IDPN on body composition parameters and nutritional status in prevalent HD patients.

**Method:** Retrospective observational study that included all prevalent hemodialysis patients who received NPID for more than 3 months at our Center from January 2018 to December 2022. All the patients received a concentrated 3-in-1 parenteral nutrition formula consisting of glucose solution, a lipid emulsion and an amino acid solution without electrolytes (OLIMEL N9⃝, Baxter). IDPN was infused at a constant rate not exceeding 300 ml/hour, via the venous drip chamber of HD monitor using infusion pump. Changes in lean tissue mass (LTM), intracellular water (ICW), and body cell mass (BCM) assessed by multifrequency bioimpedance spectroscopy (BIS) at baseline and at 3, 6, 9 and 12 months (primary outcomes) and other biochemical and anthropometric parameters (secondary outcomes) were used to assess the effect of NPID.

**Results:** Seventeen patients were included (women: 9, 53%; mean age: 68±15 y). After IDPN initiation, a gradual improvement in LTM, ICW and BCM was observed, reaching statistical significance at Month 3, 6, 9 and 12. Changes in fat inversely mirrored those of LTM (Table 1). Albumin levels and the normalized protein appearance increased, with a significant reduction in high-sensitive C-reactive protein and extracellular/intracellular body water ratio at month 9 and 12.

**Conclusion:** IDPN for 1-year was associated to increased muscle mass, supporting the hypothesis that this supplement nutrition could benefit nutritional status and revert protein-energy wasting in HD patients.

**Table 1: Effects of IDPN on body composition and nutrition.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (n = 17)</th>
<th>Month 3 (n = 17)</th>
<th>Month 6 (n = 11)</th>
<th>Month 9 (n = 9)</th>
<th>Month12 (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean Tissue Mass (kg)</td>
<td>25.1 ± 7.2</td>
<td>27.5 ± 7.0</td>
<td>26.4 ± 7.7</td>
<td>25.4 ± 6.8</td>
<td>27.1 ± 5.8</td>
</tr>
<tr>
<td>Body Cell Mass (kg)</td>
<td>12.3 ± 4.7</td>
<td>14.0 ± 4.6</td>
<td>13.2 ± 5.1</td>
<td>12.5 ± 4.9</td>
<td>13.6 ± 3.9</td>
</tr>
<tr>
<td>Fat (kg)</td>
<td>24.1± 8.8</td>
<td>21.6 ± 7.5</td>
<td>22.4 ± 9.8</td>
<td>22.8 ± 11.0</td>
<td>21.8 ± 9.4</td>
</tr>
<tr>
<td>Adipose Tissue Mass (kg)</td>
<td>32.8± 12.0</td>
<td>29.4 ± 10.1</td>
<td>30.5± 13.3</td>
<td>31.0 ± 15.0</td>
<td>29.7 ± 12.7</td>
</tr>
<tr>
<td>Total Body Water (L)</td>
<td>28.4 ± 5.8</td>
<td>29.4 ± 5.4</td>
<td>27.8 ± 5.1</td>
<td>26.6 ± 4.2</td>
<td>27.1 ± 4.4</td>
</tr>
<tr>
<td>Extracellular Body Water (L)</td>
<td>15.1 ± 3.1</td>
<td>15.3 ± 2.9</td>
<td>14.2 ± 2.6</td>
<td>13.4 ± 2.6</td>
<td>13.2 ± 2.2</td>
</tr>
<tr>
<td>Intracellular Body Water (L)</td>
<td>13.3 ± 3.0</td>
<td>14.0 ± 2.8</td>
<td>13.6 ± 3.0</td>
<td>13.2 ± 2.5</td>
<td>13.9 ± 2.5</td>
</tr>
<tr>
<td>Extracellular/Intracellular ratio</td>
<td>1.2 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>1.1 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>Overhydration (L)</td>
<td>2.9 ± 1.8</td>
<td>2.9 ± 1.9</td>
<td>2.0 ± 1.9</td>
<td>1.3 ± 1.6</td>
<td>0.8 ± 1.6</td>
</tr>
<tr>
<td>Relative OH (%)</td>
<td>18.7± 9.0</td>
<td>18.1 ± 11.2</td>
<td>13.3 ± 11.8</td>
<td>9.3 ± 11.8</td>
<td>6.3± 11.8</td>
</tr>
<tr>
<td>Phase angle at 50 KHz (degrees)</td>
<td>2.9 ± 0.8</td>
<td>2.9 ± 0.8</td>
<td>3.1 ± 0.7</td>
<td>3.0 ± 0.4</td>
<td>3.2 ± 0.4</td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>16.6± 8.3</td>
<td>17.8 ± 6.6</td>
<td>17.7 ± 4.6</td>
<td>19.4 ± 4.0</td>
<td>19.7± 4.9</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>2.8 ± 0.5</td>
<td>3.3 ± 0.5</td>
<td>3.4 ± 0.5</td>
<td>3.5 ± 0.5</td>
<td>3.6 ± 0.3</td>
</tr>
<tr>
<td>Transferrin (mg/dL)</td>
<td>131 ± 43</td>
<td>141 ± 37</td>
<td>148 ± 48</td>
<td>152 ± 34</td>
<td>141 ± 35</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>5.1 ± 1.5</td>
<td>5.6 ± 1.9</td>
<td>5.5 ± 2.1</td>
<td>6.6 ± 0.9</td>
<td>7.1 ± 1.5</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>128 ± 32</td>
<td>139 ± 37</td>
<td>142 ± 33</td>
<td>144 ± 37</td>
<td>138 ± 28</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>99 ± 52</td>
<td>101 ± 38</td>
<td>100 ± 48</td>
<td>99 ± 58</td>
<td>120 ± 91</td>
</tr>
<tr>
<td>nPNA (g/kg/d)</td>
<td>1.03 ± 0.40</td>
<td>1.06 ± 0.33</td>
<td>1.13 ± 0.45</td>
<td>1.13 ± 0.43</td>
<td>1.20 ± 0.14</td>
</tr>
<tr>
<td>hs-CRP (mg/dL)</td>
<td>83.0 (34.5-152.0)</td>
<td>37.0 (23.0-70.5)</td>
<td>30.0 (7.0-50.0)</td>
<td>27.0 (12.0-59.8)</td>
<td>24.0 (10.0-62.0)</td>
</tr>
<tr>
<td>Bicarbonate(mEq/L)</td>
<td>27.5 ± 3.0</td>
<td>26.0 ± 3.1</td>
<td>26.6±3.2</td>
<td>24.1 ± 1.9</td>
<td>24.3 ± 1.9</td>
</tr>
</tbody>
</table>

*p<0.05 Vs. baseline
#3255
BETA2 MICROGLOBULIN IS AN INDEPENDENT PARAMETER RELATED WITH DYSFUNCTION OF NATURAL KILLER CELL ACTIVITY IN HEMODIALYSIS PATIENTS
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1Gangnam Severance hospital, Yonsei University College of Medicine, Internal Medicine, Seoul, Rep. of South Korea, 2Yongin Severance hospital, Yonsei University College of Medicine, Internal Medicine, Yongin-si, Rep. of South Korea, 3CHA Bundang Medical Center, CHA University, Internal Medicine, Seongnam-si, Rep. of South Korea and 4Hanyang University Guri Hospital, Internal Medicine, Guri-si, Rep. of South Korea

Background and Aims: End-stage renal disease patients are characterized by immune dysfunction. Natural killer (NK) cells are lymphocytes of innate immune system that play a key role in an immune response towards viral infections and tumors. We aimed to analyze clinical factors related to the NK cell activity in chronic hemodialysis (HD) patients.

Method: Clinically stable 196 patients who were treated by HD for more than 3 months were enrolled from 4 outpatient HD clinics. NK cell activity was assessed using NK Vue assay (NKMAX, Sungnam, Korea) that uses serum of ex-vivo stimulated whole blood to detect interferon (IFN)-γ secreted from NK cells as an indicator of NK cell activity. All patients were stratified as abnormal (<250 pg/ml) and normal (≥250 pg/ml) groups according to NK cell activity.

Results: Mean age of the HD patients was 62.7 years [range 31 to 95 years] and mean HD duration was 49.2 months [range 3 to 221 months]. In total, 68 (35%) of HD patients showed abnormal NK cell activity. The abnormal NK cell activity group showed significantly increased age and shorter HD duration compared to the normal NK cell activity group (66.7 ± 11.9 vs. 60.6 ± 13.4 years, p = 0.001; 33.8 ± 33.0 vs. 57.5 ± 48.5 months, p<0.001, respectively).

The serum albumin and parathyroid hormone levels were significantly lower in the normal NK cell activity group (3.7 ± 0.4 vs. 3.9 ± 0.3 g/dL, p = 0.005 and 176 ± 153 vs. 240 ± 260 mg/50ml, respectively). In contrast, hemoglobin, blood urea nitrogen, urea reduction ratio, and C-reactive protein levels were comparable between the two groups. In multivariate regression analysis, old age, short dialysis duration, low serum albumin and high beta2 microglobulin levels were independent risk factors of abnormal NK cell activity in HD patients (adjusted odd ratio [AOR], 1.033; 95% confidence interval [CI], 1.005-1.062, p = 0.02; AOR, 0.981; 95% CI, 0.971-0.992; p<0.001, AOR, 0.395; 95% CI, 0.157-0.995; p = 0.049, and AOR, 1.042; 95% CI, 1.011-1.075; p = 0.008, respectively).

Conclusion: Our results suggest that young age and good nutrition as well as lower burden of middle molecule uremic toxin is associated with greater NK cell activity in HD patients.

#3312
EFFICACY OF TRANSCATHETER AORTIC VALVE IMPLANTATION FOR SEVERE AORTIC VALVE STENOSIS IN HEMODIALYSIS PATIENTS
Masahiro Nakagaki, Kenji Harada and Hidetoishi Kanai
Japan

Background and Aims: In Japan, of the >340,000 chronic dialysis patients, approximately 60% have lifestyle-related diseases including diabetes and nephrosclerosis. Two-thirds of maintenance dialysis patients (age, ≥65 years) often develop aortic stenosis (AS) and other serious and complex systemic cardiovascular disease complications associated with chronic kidney disease mineral and bone disorder (CKD-MBD). Furthermore, renal function loss and a prolonged state of renal failure are observed requiring renal replacement therapy (RRT). AS in dialysis patients progresses quickly, and the frequency of hospitalized treatment for heart failure increases with the worsening condition, leading to ADL deterioration, which may subsequently cause dialysis hypotension/interruption. At our hospital, of the 420 maintenance dialysis patients who died during hospitalization in 5 years before 2020 (420/1,637 ± 16%, 32 cases (8%) developed AS complications, which became their direct cause of death in 12 cases (3%), and aortic valve replacement (AVR) was performed in 5 cases (1%). Maintenance hemodialysis patients (HD) are at high risk group and have a poor prognosis for life. Previously, transcatheter aortic valve implantation (TAVI) was not indicated, but recently TAVI has been approved in Japan. Efficacy of TAVI for HD patients remains unclear, here we investigated several outcomes.

Method: A total of 123 maintenance dialysis patients with severe AS were included in 2019–2021. We examined TAVI group and AVR group for length of hospital stay, hospitalization costs, life expectancy, and rates of complications such as occurrence of arrhythmias.

Results: Over a 3-year period, we performed TAVI for 58 maintenance dialysis patients (mean age, 81 years); their median duration of hospitalization was 14 days for a median cost of 6,259,350 JPY. The mean age was older than that of 66 patients who underwent open-heart AVR during the same period (mean age, 73 years; 35 days for 7,192,570 JPY); therefore, the cost was less, and the rate of complications, including vital prognosis and arrhythmia, was not inferior in hospitalization period.

Conclusion: In conclusion, TAVI is effective for elderly maintenance dialysis patients with severe AS and has a positive health care economics, ADL maintenance.

#3579
AN INITIAL LOW-DOSE ETILOCALCETIDE APPROACH IS EFFECTIVE AND COST-SAVING IN HEMODIALYSIS PATIENTS WITH MODERATE SECONDARY HYPERPARATHYROIDISM
Andrea Carta1,2, Martina Tedesco1,2, Alice Guerini1,2, Federica Terni1,2, Corrado Camerini1, Stefano Possenti1, Paola Gaggia1, Federica Mesia1,2 and Federico Alberici1,2
1Spedali Civili di Brescia, Unità Operativa di Nefrologia, Brescia, Italy, 2Università degli Studi di Brescia - Facoltà di Medicina e Chirurgia, Dipartimento di Specialità Medico-Chirurgiche, Scienze Radiologiche e Sanità Pubblica, Brescia, Italy and 3Independent Researcher, Brescia, Italy

Background and Aims: Etelcalcetide (ETC) is an intravenous calcimimetic approved for the management of secondary hyperparathyroidism (SHPT) in hemodialysis (HD) patients, with benefits in terms of reduction of FGF23 levels and prevention of progression of left ventricular hypertrophy. The label recommendation is a starting dose of 5 mg after HD, to be titrated every 4 weeks according to parathyroid hormone (PTH) and calcium levels. However, it remains unclear what dosage is best to start with and, thus, how this treatment can be implemented in a real-life setting. The aim of this study was to assess the efficacy and cost-effectiveness of ETC started at lower doses than those suggested by the manufacturer in patients with moderate SHPT.

Methods: This is a retrospective observational study comparing two different initial ETC dosing strategies, a “Low-dose approach” (LD, ETC starting dose<10 mg/week) and a “Classic approach” (CL, ETC starting dose≥10 mg/week), in terms of effects on CKD-MBD related biomarkers and costs during the first year of prescription. The study was conducted on HD patients with basal PTH between 500 and 1500 ng/L, treated with ETC for at least 3 months between 2018 and 2022 at ASST Spedali Civili di Brescia. Monthly monitoring of serum calcium, phosphorus and PTH was performed in both groups for dose adjustment.

Table 1: Clinical features of patients in the LD and CL group, at baseline and last follow-up. Data are listed as median (IQR) for continuous variables and number (%) for categorical variables.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LD (n = 24)</th>
<th>CL (n = 29)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>11 (46%)</td>
<td>17 (59%)</td>
<td>0.353</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70 (50–78)</td>
<td>63 (52–72)</td>
<td>0.300</td>
</tr>
<tr>
<td>HD vintage (years)</td>
<td>5 (2–8)</td>
<td>5 (3–6)</td>
<td>0.552</td>
</tr>
<tr>
<td>HD modality</td>
<td></td>
<td></td>
<td>0.328</td>
</tr>
<tr>
<td>HDI</td>
<td>14</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>9.0 (8.6–9.6)</td>
<td>9.2 (9.0–9.7)</td>
<td>0.209</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>5.6 (4.4–6.4)</td>
<td>5.5 (4.8–7.4)</td>
<td>0.693</td>
</tr>
<tr>
<td>PTH (ng/L)</td>
<td>633 (601–813)</td>
<td>769 (630–931)</td>
<td>0.980</td>
</tr>
<tr>
<td>Initial dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETC (mg/w)</td>
<td>7.5 (5–7.5)</td>
<td>15 (15–15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Paracalcit (mg/c)</td>
<td>0 (0–10)</td>
<td>0 (0–5)</td>
<td>0.192</td>
</tr>
<tr>
<td>Follow-up (weeks)</td>
<td>52 (34–52)</td>
<td>52 (52–52)</td>
<td>0.315</td>
</tr>
<tr>
<td>End of follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>8.7 (8.4–8.8)</td>
<td>8.6 (8.2–9.1)</td>
<td>0.668</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>4.6 (3.7–6.9)</td>
<td>4.7 (4.2–6.2)</td>
<td>0.775</td>
</tr>
<tr>
<td>PTH (ng/L)</td>
<td>282 (207–332)</td>
<td>294 (151–382)</td>
<td>0.825</td>
</tr>
<tr>
<td>Cause of ETC discontinuation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>Gastro-intestinal intolerance</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>PTH over-suppression</td>
<td>1 (4%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
</tbody>
</table>
Results: Overall, 53 patients were identified, 24 in the LD and 29 in the CL group. Both groups showed similar baseline characteristics (Table 1). Median follow-up was 52 weeks, during which 4 patients (one in the LD and three in the CL group) discontinued ETC (Table 1). At the end of follow-up, 92% of patients in the LD and 90% in the CL group achieved a decrease in PTH ≥ 30% compared to baseline, with median PTH levels of 282 (207 - 332) and 294 (151 – 382) ng/l, respectively (p = 0.825). Other CKD-MBD biochemical parameters were comparable between the two groups at all timepoints (Figure 1). The median of average ETC weekly doses per patient was 7.6 (6.2–10.2) mg in the LD and 10.6 (9.7 – 15) mg in the CL group (p < 0.001). During follow-up, the median ETC dose remained stable in the LD group, while partially decreasing in the CL group (Figure 1). Use of paricalcitol was comparable in both groups.

At cost analysis, the median of average ETC weekly costs per patient was €36.6 (29.6–50.0) in the LD and €50.5 (46.4–71.7) in the CL group (p < 0.001). This translates into an average yearly cost per patient of €1909 and €2635 using the LD and CL approach, respectively, with a saving of €726 per patient-year in favour of the LD strategy.

Conclusion: In this retrospective study in HD patients with moderate sHPT, we showed that starting ETC at a lower dose than the one suggested by the manufacturer is as effective as the classic approach in terms of control of CKD-MBD parameters, with a significant reduction in treatment costs. Future prospective studies will be needed to validate the results in bigger cohorts, test whether these benefits can extend beyond the first year of treatment and assess the effects on FGF23 levels and other relevant clinical outcomes.

#3927
AN ANOREXIGENIC HORMONE IN PEDIATRIC CKD PATIENTS
Dina E. Sallam
Faculty of Medicine, Ain Shams University, Pediatric Nephrology, Cairo, Egypt

Background and Aims: Chronic kidney disease (CKD) is a major health problem associated with faltering growth, which is a complex process, where anorexia, inadequate oral intake in addition to disturbed body metabolism play a significant role. Leptin, the anorexigenic hormone that’s secreted by fat tissue, and affect appetite, & hence, aids to weigh loss & faltering growth. The present study evaluated serum leptin level, & its relation to growth parameters in pediatric patients with different stages of CKD.

Method: A cross-sectional study that was conducted on 87 subjects, who were divided equally into groups; CKD stage 5 on regular hemodialysis (CKD5d), & CKD stage 2–4, & age & gender matched controls. Patient with diabetes, infected with hepatitis C virus, & on growth hormone therapies were excluded. Full history taking, assessment of growth parameters using gender & age specific Z-scores of heights, weight & body mass index were done. Fasting serum leptin, calcium, phosphorus, PTH, albumin, total proteins, iron & hemoglobin were measured.

Results: Our patients had significantly lower growth parameters compared to controls. Hypocalcemia, high PTH, iron deficiency anemia & hypoalbuminemia were significant in CKD2-4 groups compared to other groups. Serum leptin was abnormally high in 12.6% of CKD patients. The median leptin level was comparable between the groups (p = 0.20). Serum leptin hadn’t changed significantly as regards gender, BMI Z-scores, diagnoses, or CKD stage (p = 1.00, 0.379, 0.542, 0.171 respectively). A negative correlation was found between leptin level & CKD duration (r = -0.276, P = 0.036), otherwise, no correlations were found with clinical & laboratory variables.

Conclusion: Leptin level was not affected by CKD stage & not a useful marker for growth in pediatric CKD patients. Large studies on relationship between leptin & growth is needed.

#4237
EFFICACY AND TOLERABILITY OF DIRECT-ACTING ANTIVIRALS IN HEMODIALYSIS PATIENTS WITH CHRONIC HEPATITIS C
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Background and Aims: Hepatitis C virus (HCV) infection is common in hemodialysis (HD) patients and is associated with increased morbidity and mortality. In recent years major progress in the treatment of HCV infection has been made with the entry into use of direct-acting antivirals (DAAs), which target viral proteins, leading to increases in sustained virological response (SVR) and a marked decrease in side effects. The aim of the study was to
Evaluate the efficacy and frequency of side-effects of DAA therapy in HD patients with HCV infection.

Method: The multicentric prospective cohort study included 42 HD patients with HCV infection over the last two years. DAs were administered according to HCV genotype and drug interactions considering guidelines for a period of 12 weeks (for HCV genotype 1: Elbasvir/Grazoprevir or Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir, and for HCV genotype 4: Elbasvir/Grazoprevir or Ombitasvir/Paritaprevir/Ritonavir). The following clinical parameters were measured: 0, 4, 8, 12, and 24 (12 weeks after the completion of treatment with DAA) were analyzed: presence of side effects, PCR HCV titer (ref. range: <12 IU/mL negative), hemoglobin (Hgb-g/L), eotinin dose (IU/kg/week), alanine aminotransferase level (ALT-U/L), and gamma-glutamyl transferase level (GGT-U/L). Before treatment with DAA liver fibrosis score (F0-4) was defined by Fibroscan and the patients with liver stiffness over 12 kPa (Fibrosis score F4) were considered cirrhotic, but only patients with compensated cirrhosis (Child-Pugh score class A) were treated. For statistical analysis chi-square test and combined analysis of variance for repeated measures were performed by IBM SPSS softser. PCR HCV titer was analyzed with logarithmic transformation of data.

Results: Over the observed period 42 HD patients with HCV infection (25M and 17F) with the average age 56.78±11.6 years and average HD vintage 159±75 months were included in the study. Twenty-six patients (61.9%) were with HCV genotype 1 and 16 patients (38.1%) with HCV genotype 4. Ten patients (23.8%) were with compensated cirrhosis (F4 fibrosis score by Fibroscan). Three patients (7.1%) had mild gastrointestinal side effects and only one patient (2.4%) discontinued the therapy during the first week due to intolerance to the treatment. All 41 patients (100%) who completed 12 weeks of DAA therapy were PCR HCV negative at 4 weeks of treatment and achieved rapid virological response (RVR) and 12 weeks after the completion of treatment and achieved sustained virological response (SVR12) that was statistically significant (p<0.001). In regard to PCR HCV titer before DAA therapy there was no statistically significant difference among HD patients according to cirrhotic status and HCV genotype. There was no statistically significant change of hemoglobin level and eotinin dose in HD patients during the DAA therapy. The ALT and GGT levels statistically significantly decreased at weeks 12 and 24 compared to week 0 in all treated patients with DAA (ALT week0 = 35.2±21.7; ALTweek12 = 21.8±16.2; ALTweek24 = 23.5±13.1; p<0.001 and GGT week0 = 53.3±67; GGT week12 = 18.6±6.6; GGT week24 = 19.4±11.5; p = 0.042 respectively). The therapy with DAA was equally effective in patients with compensated cirrhosis and in patients without cirrhosis and there was statistically significant decrease of ALT and GGT levels in both groups of patients (p = 0.002 and p<0.05 respectively). In regard to HCV genotype DAA were equally effective in patients with HCV genotype 1 and in patients with HCV genotype 4 and ALT and GGT levels statistically significantly decreased in both groups of patients (p<0.001 and p<0.05 respectively).

Conclusion: The therapy with DAA in HD patients with HCV infection was extremely effective and SVR12 was achieved in 100% of treated patients. The administered DAA were equally effective in patients with compensated cirrhosis and in patients without cirrhosis, and in patients with HCV genotype 1 and HCV genotype 4. The therapy with DAA was well tolerated, 7.1% of patients had mild side effects and 2.4% of patients discontinued the therapy due to intolerance.

Method: 12 stable patients on HD were included, with a minimum time on HD of 3 months. Each patient underwent 4 random HD sessions in which only the dialysis membrane and/or the modality were changed. They underwent an HD session with a high-flux polyethylene membrane, another session with this same filter in OL-HDF, another with MCO membrane, and another with HFR-H. All sessions were held in a short period. In all of them, pre- and post-dialysis blood samples were taken to assess the clearance of both conventional urmeric toxins and protein-bound toxins (indoxyl-sulfate and p-cresol), as well as molecules associated with the microinflammation process (proinflammatory monocytes: CD14+ /CD16++ and proinflammatory cytokines).

Results: When evaluating the effect of the different HD techniques on the percentage of proinflammatory monocytes, a relevant, although not significant, decrease was observed in the OL-HDF and HFR-H techniques. Likewise, when evaluating the profile of markers of inflammatory activity, such as IL-12B, IL-17C, CD14 or TNFRSF19, an important decrease was observed after the dialysis session in HFR-H compared to the rest of the techniques analyzed.

Conclusion: After analyzing the results of our study, the HD technique that combines convection + adsorption + diffusion (with a novelty high permeability filter), HFR-H, is the only one that has shown significantly greater clearance of proinflammatory cytokines, as well as a greater elimination of activated monocytes and protein-bound toxins, although without reaching statistical significance. These results, although preliminary, are promising and open up a new line of research to improve CVD in HD patients.

GUT MICROBE-DERIVED UREMIC TOXIN TRIMETHYLAMINE N-OXIDE CONTRIBUTES TO CARDIAC REMODELING IN PATIENTS ON HEMODIALYSIS

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Background and Aims: It is well established that cardiovascular pathology is the leading cause of increased morbidity and mortality in chronic kidney disease patients, especially in the terminal stage. This is explained by high prevalence of both traditional and non-traditional cardiovascular risk factors, among which inflammation, intestinal dysbiosis and microbe-derived uremic toxins such as indoxyl sulfate, p-cresyl sulfate, trimethylamine-N-oxide (TMAO) are recently considered the main role. However, the potential underlying mechanisms of these findings have not been fully elucidated. Here we aimed to investigate the association of serum TMAO with echocardiographic parameters of cardiac remodeling in patients receiving hemodialysis treatment.

Method: One hundred and forty (85M, 55F) clinically stable patients on dialysis were studied. The median (interquartile range) age was 56.5 (46.6-50.5) years, median duration of dialysis treatment – 48 (14.5-97) months, 39 (27.9%) were diabetic, 109 (77.9%) had high blood pressure, 39 (27.9%) – previous history of ischemic heart disease, including 8 (5.7%) suffered a myocardial infarction. All patients underwent transthoracic echocardiography (General Electric Vivid E95 device) with the registration of standard parameters. The determination of TMAO in serum was performed by LC/MS using a Shimadzu-8060 system combined with a Shimadzu LC-20AD liquid chromatograph. Statistical analysis was performed with STATISTICA 14.0 program. Non-parametric Spearman's rank correlation method was used to evaluate the associations between serum TMAO level and echocardiographic parameters. Value of p<0.05 was considered statistically significant in all analyses.

Results: Median serum TMAO was 524 (3588-8701) ng/mL. Echocardiography data: end-systolic left ventricular (LV) size is 38.2±0.6 mm, end-systolic LV volume – 62.0±4.4 ml, end-diastolic LV size – 55.8±1.3 mm, end-diastolic LV volume – 111.5±19.7 ml, ejection fraction (according to Simpson method) – 53.2±7.2%, shortening fraction – 28.9±4.4%, inter-ventricular septum thickness – 11.6±0.2 mm, left atrial wall thickness – 11.9±0.1 mm, LV mass index – 142.8±6.4 g/m², LV mass – 298.6±8.8 g, relative wall thickness – 0.43±0.3, number of patients with LV remodeling or hypertrophy – 98 (70%). LV diastolic functional parameters (n = 113): E = 0.69±0.2 m/s, A = 0.79±0.2 m/s, E/A (early (E) to late (A) ventricular filling ratio) – 0.89±0.2, deceleration time (DT) – 211±52 ms, number of patients with diastolic dysfunction – 104 (74.3%). Statistically significant correlation was found between TMAO concentration and end-diastolic LV volume (r = 0.315; p = 0.028), LV mass (r = 0.409; p = 0.011) and DT (r = 0.272; p = 0.041). TMAO levels in individuals with LV myocardial hypertrophy and diastolic dysfunction was significantly higher than without these abnormalities (Mann–Whitney U-test p = 0.037 and p = 0.043, correspondingly).

Conclusion: Our results suggest that elevated TMAO may contribute to cardiac remodeling in hemodialysis patients through the myocardial fibrosis.
and hypertrophy. The pathophysiological mechanisms of TMAO must be investigated further for a better understanding of its role in cardiovascular disease progression and to develop therapeutic interventions against uremic toxicity.

#4171
DIALYSIS WITHOUT SOCKS: DETECTION OF ULCERS AND AMPUTATIONS IN HEMODIALYSIS
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Spain
Background and Aims: Dialysis patients are at high risk of ischemia and foot ulcers (14.4%) that frequently precede severe complications, including amputations (5.9%), hospitalizations, and mortality. Critical ischemia in this location accounts for 20% of the annual causes of death in hemodialysis, produces pain that is difficult to control and greatly reduces the quality of life. The aim of this work was to analyze the prevalence and factors associated with amputations in hemodialysis patients, and to assess the evolution after amputation.
Method: Carrying out a survey by email sent by the SEN (Spanish Society of Nephrology) and SOMANE (Madrid Society of Nephrology). Retrospective, cross-sectional, multicenter study. The survey sent to all hemodialysis units nationwide. Answered by 47 Centers. The exclusion criteria were oncological-traumatic amputations.
Results: • 50% of the Units have more than 70 patients
• 40% diabetics
• In most Units only 5% of dialysis patients have ulcers
• 70% of the centers answer that 5% have minor amputations and 5% have more serious amputations
• 63% of the centers answer that 5% of the patients have more than one amputation
• Risk factors for amputation: > 60 years, male, diabetes, smoking, hyperphosphatemia, malnutrition, ischemic heart disease
• In most Units <10% of amputees have been prosthettized
• Annual mortality in patients with chronic ischemia is 20%.
• Most of the Units use some diagnostic measure to screen for ulcers and/or chronic ischemia of lower limbs.
Conclusion: • Most dialysis units have patients with ulcers in the lower limbs that precede amputations, mortality and dependency.
• Having amputee patients in the Unit entails reorganization of work and an effort of human and material resources.

Figure 1:

#6201
CHANGES ON LEFT VENTRICULAR FUNCTION AND CHARACTERISTICS ACCORDING TO THE DEGREE OF INTERDIALYTIC WEIGHT GAIN IN MAINTENANCE HEMODIALYSIS PATIENTS
Vasileios Anastasiou1, Maria Eleni Alexandrou2, Vasileios Kamperidis3, Stylianos Daios3, Konstantinos Tsilonis4, Marieta Theodorakopoulou2, Dimitrios Mousidis5, Foteini Iatriki5, George Giannakoulas1, Antonios Ziakas1 and Pantelis Sarafidis1
1Aristotle University of Thessaloniki, First Department of Cardiology, AHEPA Hospital, Thessaloniki, Greece and 2Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece
Background and Aims: Pronounced pulmonary circulation overloading has been observed in hemodialysis patients with higher fluid intake over the long interdialytic interval. This study aimed to evaluate the impact of the degree of fluid accumulation on left ventricular (LV) systolic and diastolic function and sizing characteristics.
Method: For the present analysis, 41 patients receiving maintenance hemodialysis thrice-weekly were divided by the recommended threshold of interdialytic-weight-gain corrected for dry weight (IDWG%) into a higher (> 4.5%) and a lower (< 4.5%) IDWG% group. All participants underwent 4 echocardiographic assessments at the start and the end of the 3-day and the 2-day interdialytic interval in a cross over design.
Results: Over the 3-day interval, significant increments in stroke volume (SV) were observed for both groups, but were more prominent in the higher IDWG% group (> 4.5%) (18.63±22.84% vs. < 4.5% 12.6±14.48mmHg, p = 0.04). Similarly, a greater increase in cardiac output was evidenced in patients with higher IDWG% over the 2-day interval (> 4.5% 1.31±1.38 vs. < 4.5% 0.36±2.08/l/m2, p = 0.012). With regards to diastolic function, a significant increase in E/A and E/E'm ratios was observed over the 3-day interval, but significant between-group differences in interdialytic changes were detected only for the E/A ratio (IDWG%> 4.5% 0.35±0.29 vs. < 4.5% 0.06±0.44, p = 0.035). Left atrial dimensions and LV mass were enlarged to a similar extent in both study-groups during both intervals.
Conclusion: Patients exceeding the recommended threshold of interdialytic fluid accumulation experience higher increases in SV and deterioration of preload-dependent indexes of diastolic function, particularly during the 3-day interval.
THE APOPROTEIN E (APOE) POLYMORPHISM AND PROPROTEIN CONVERTASE SUBTILISIN KEXIN 9 (PCSK9) IN HEMODIALYSIS (HD) PATIENTS

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Background and Aims: The apoE polymorphism and PCSK9 play an important role in lipid metabolism in healthy subjects, however, its role in HD patients remains unclear. We investigated the apoE polymorphism and PCSK9 as well as a lipid profile to clarify the impact of these factors on prognosis in HD patients. We also examined the association of cardiovascular (CVD) events in dead HD patients and clinical features.

Method: HD patients (n = 296, m/f; 207/89, DM; 152, age; 69.8±12.1, HD duration; 68.7±72.0 months) were subjected to this study. Written informed consent was obtained from each patient. Of these patients 85 subjects (m/f; 61/24, DM; 54, HD duration; 98.6±53.5 months) died during this study (from June 2011 to December 2022). Blood samples were collected to analyze the apoE genotypes by the invader method, serum concentrations of PCSK9-heterodimers and PCSK9-free fragments were measured using ELISA (BML Co. Ltd., Tokyo, Japan) and serum concentrations of apoA1, apoA2, apoB, apoC2, apoC3 and apoE were estimated using turbidimetric immunoassay. For the death cases we used multivariable logistic regression to control for the potentially confounding roles of type 2 diabetes mellitus (DM), apoE genotypes, and serum concentrations of PCSK9-heterodimers, PCSK9-free segments, apoA1, apoA2, apoB, apoC2, apoC3 and apoE. Survival probabilities in dead HD patients with CVD events according to the apoE genotypes were analyzed using the Kaplan-Meier curves. A p value less than 0.05 was considered statistically significant.

Results: The apoE allele frequencies in HD patients (n = 296) were ε2; 0.044, ε3; 0.870 and ε4; 0.086, whereas those in Japanese healthy controls were ε2; 0.036, ε3; 0.848 and ε4; 0.116 (Eto M., et al. Clin Genet 30:422-427, 1986.), demonstrating the ε2 frequency in HD patients had a trend to be higher than that in Japanese healthy controls (p = 0.096). The serum concentrations of PCSK9-heterodimers and PCSK9-free fragments in female HD patients (n = 89, 227.0±88.0 ng/ml and 41.9±19.1 ng/ml, respectively) were significantly higher than those in male HD patients (n = 207, 195.9±70.3 ng/ml, p = 0.001, and 35.8±15.3 ng/ml, p<0.004, respectively). The serum concentrations of PCSK9-heterodimers in HD patients with DM (n = 152); 213.8±77.6 ng/ml showed a trend to be higher than those in HD patients without DM (n = 144); 196.3±76.1 ng/ml (p = 0.05). The multivariable logistic regression analysis demonstrated the serum concentration of apoA1 and apoE polymorphism showed statistically significant impact on CVD events in dead HD patients (Table 1). The Kaplan-Meier analysis revealed the apoE polymorphism had a significant impact on the survival probability in dead HD patients with CVD events (Figure 1).

Conclusion: Recent studies reported the association between apoE2 and renal insufficiency in Japanese type2 DM. ApoE2 may be one of the attributable factors that lead to the end stage kidney disease. PCSK9-heterodimers bind to LDL cholesterol receptors (LDLr) and prevent LDLr from shuttling back to the surface and instead target it for degradation, however, PCSK9-free segments have weaker effects to bind to LDLr. Significance of higher serum concentrations of PCSK9-heterodimers and PCSK9-free fragments in female HD patients than male HD patients depends on future investigation. ApoE2 and the serum concentration of apoA1 contribute to CVD events. The prognosis of the HD patients with apoE2 or apoE4 were poorer than that with apoE3/3. The apoE polymorphism and PCSK9 may be key factors in lipid metabolism as well as prognosis of HD patients.

Table 1: Multivariable logistic regression analysis on predictors of cardiovascular events.

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Odds Ratio (95%CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>0.41 (0.10-1.52)</td>
<td>0.1860</td>
</tr>
<tr>
<td>apoE4/3/2</td>
<td>0.17 (0.02-0.95)</td>
<td>0.0465*</td>
</tr>
<tr>
<td>PCSK9-heterodimers</td>
<td>0.99 (0.98-1.00)</td>
<td>0.3759</td>
</tr>
<tr>
<td>PCSK9-free fragments</td>
<td>1.02 (0.98-1.08)</td>
<td>0.2294</td>
</tr>
<tr>
<td>apoA1</td>
<td>1.04 (1.01-1.08)</td>
<td>0.0178*</td>
</tr>
<tr>
<td>apoA2</td>
<td>0.96 (0.76-1.20)</td>
<td>0.7696</td>
</tr>
<tr>
<td>apoB</td>
<td>1.02 (0.98-1.07)</td>
<td>0.1693</td>
</tr>
<tr>
<td>apoC2</td>
<td>0.67 (0.36-1.18)</td>
<td>0.1789</td>
</tr>
<tr>
<td>apoC3</td>
<td>0.93 (0.68-1.23)</td>
<td>0.6233</td>
</tr>
<tr>
<td>apoE</td>
<td>0.86 (0.42-1.75)</td>
<td>0.6932</td>
</tr>
</tbody>
</table>

Figure 1: HD durations in dead HD patients with apoE2+ and apoE4+ were shorter than those in patients with apoE3/3 (p = 0.0268).
ASSOCIATION OF LOW BLOOD SELENIUM CONCENTRATIONS WITH POOR MUSCLE MASS AND STRENGTH IN JAPANESE HEMODIALYSIS PATIENTS

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Background and Aims: Trace elements play an important role in muscle function and metabolism. Little information is available of a role of trace elements for sarcopenia (i.e. low muscle mass and strength) in patients on hemodialysis (HD). We aimed to investigate association between blood levels of trace elements and nutritional status or sarcopenia in HD patients.

Method: This cross-sectional study including patients undergoing HD at our center was conducted in June 2022. Clinical/demographic data and blood samples were collected before HD sessions at start of the week. Blood levels of zinc (Zn), copper (Cu), selenium (Se), and manganese (Mn), serum levels of creatinine (Cr), total cholesterol (Tch) and albumin (Alb) and body mass index (BMI) were measured. Handgrip strength, gait speed and muscle mass (skeletal muscle index: SMI) measured using dual-energy x-ray absorptiometry were analyzed. Sarcopenia was assessed by Asian Working Group for Sarcopenia (AWGS) and nutritional status by the Nutritional Risk Japanese-Hemodialysis (NRI-JH), which was calculated based on serum Cr, Tch, Alb and BMI (PLoS One. 2019, 14(3):e0214524). Pearson’s correlation coefficient test, multivariate logistic regression analyses were performed to evaluate the relationship between trace elements and nutritional indicators.

Results: Eighty-two patients (56 males and 26 females) were included, with a median dialysis vintage of 9.1±7.1 years and an average age of 68.7±12.2 years. Severe malnourished patients as defined by the NRI-JH and sarcopenia defined by AWGS accounted for 6.0% and 37.8% of enrolled patients, respectively. In all patients, the mean levels of Zn, Cu, Se, and Mn (in μg/dL) were 65.8±11.3, 84.1±22.2, 9.2±1.5 and 1.2±0.6, respectively. The levels of Zn, Cu, Se and Mn were lower than normal levels in 72 cases (87.8%), 18 cases (22%), 57 cases (69.5%), and 13 cases (15.9%), respectively. There was an inverse correlation were lower than normal levels in 72 cases (87.8%), 18 cases (22%), 57 cases (69.5%), and 13 cases (15.9%), respectively. There was an inverse correlation between the levels of Se and age (r = -0.298, p = 0.003) but not HD vintage. No significant correlation was found between the NRI-JH scores and blood levels of trace elements in all patients. Blood trace elements have been shown to be affected by gender. Thus, we next examined whether blood levels of trace elements and the relationship between blood trace elements and SMI and strength are different between male and female HD patients.

The levels of Zn and Mn did not differ between males and females. The levels of Cu were lower in males (79.8±19.3 μg/dL) than females (93.0±25.4 μg/dL, p = 0.025). In contrast, the levels of Se were higher in males (9.5±1.5 μg/dL) than females (8.6±1.2 μg/dL, p = 0.0017). The multivariate logistic regression showed that higher blood levels of Zn and Se and lower Mn levels were independently associated with grip strength (p < 0.01) but not gait speed in males. There was a significant positive correlation between Se and SMI (r = 0.305, p = 0.02) but not gait speed in males. In females, grip strength (r = 0.39, p = 0.048) and gait speed (r = 0.66, p < 0.001) were independently associated with the Se levels but not Zn, Cu and Mn. However, there was no association between SMI and blood levels of Se, Zn and Mn in females.

Conclusion: Blood levels of Se were independently associated with grip strength and SMI in male HD patients. In female HD patients, the levels of Se were positively correlated with grip power and gait speed. Se may be implicated in muscle function and metabolism in HD patients.

TIMING OF ATRIAL FIBRILLATION OCCURRENCE IN HEMODIALYSIS PATIENTS WITH CARDIAC IMPLANTABLE ELECTRICAL DEVICES

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Background and Aims: Hemodialysis (HD) patients has the high prevalence of atrial fibrillation (AF), and the procedure of HD itself might be related to risk factors for the onset of AF. On the other hand, cardiac implantable electronic devices (CIEDs), such as pacemaker, implantable cardioverter-defibrillators (ICD) and cardiac resynchronization therapy (CRT) have the function for arrhythmia detection. However, in HD patients with CIEDs, there are no studies that observe AF over long periods of time. The aim of this study is to investigate AF onset and duration of HD patients with AF, using the AF detection and memory function of CIEDs.

Method: Consecutive HD patients who were newly implanted with CIEDs between January 2008 and December 2021 were retrospectively analyzed in this study. Patients with chronic AF, with leadless pacemaker and without post-implantation follow-up were excluded from this study. Subclinical AF was defined from previous studies as atrial tachyarrhythmia lasting more than 6 minutes in memories of devices. The primary endpoint of this study was the subclinical AF within one year after CIESDs implantation. HD week was defined as follows according to HD schedule, HD1: Monday or Tuesday; HD1+1: Tuesday or Wednesday; HD2 Wednesday or Thursday; HD2+1 Thursday or Friday; HD3 Friday or Saturday; HD3+1 as Saturday or Sunday; and HD3+2 Sunday or Monday. We examined the association between onset and duration of AF and HD.

Results: Fifty-four HD patients who had been implanted with CIEDs (pacemaker: 37, ICD: 6, CRT: 11) were enrolled in the study. During a mean follow-up period of 352 ± 36 days, in 26 of 54 (48.1%) patients, 124 subclinical AF events (1-8 events / patient) were detected with CIEDs. History of clinical AF (46.2% vs 7.1%, p = 0.003) and sick sinus syndrome (53.8% vs 10.7%, p = 0.005) were significantly higher in HD patients with than without subclinical AF. The frequency of subclinical AF onset on HD day was approximately twice higher than on non-HD day (83 episodes [27.7 episodes/day] vs 41 episodes [10.3 episodes/day]), and subclinical AF onset on HD1 day was most frequent among a week (Figure 1a). Limited to HD day, subclinical AF events were observed more frequently especially during HD (30/86 events: 34.9%) and five hours after HD (28/86 events: 32.6%) (Fig. 1-b). Subclinical AF duration was significantly longer during HD compared to non-HD time (216 [90, 1066] min vs 96 [30, 418] min, p = 0.008).

Conclusion: In HD patients, subclinical AF occurred more frequently on HD day, especially during HD and several hours after HD. Careful observation during and after HD might help early diagnosis of clinical AF.
Background and Aims: In contrast to portable whole-body bioimpedance, which estimates fluid status at a single point in time, thoracic bioimpedance applied by a wearable device could enable continuous measurements. However, clinical experience with thoracic bioimpedance in patients in dialysis is still limited. The aim of this study is to test the reproducibility of whole-body and thoracic bioimpedance measurements and to compare their association with hemodynamic changes during hemodialysis.

Method: In total, 54 patients were included in this cross-sectional observational study. Whole-body resistance at 5kHz, thoracic resistance at 8kHz, systolic blood pressure and ultrafiltration volume were measured. All measurements were taken at pre- and end-dialysis during two consecutive sessions. Data were approached by mixed-modelling and Spearman correlation analysis.
Figure 1: Subject-specific plot showing the pre-to-end changes in whole-body (A) and thoracic (B) bioimpedance for session 1 and 2, representing the intraclass correlation (ICC).

Table 1: Spearman correlation coefficient between hemodynamic parameters (ultrafiltration volume and pre-to-end dialysis changes in blood pressure) and changes in the resistance component of whole-body and thoracic bioimpedance. All p-values were < .001.

<table>
<thead>
<tr>
<th></th>
<th>Session 1</th>
<th></th>
<th>Session 2</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Δ whole-body</td>
<td>Δ thoracic</td>
<td>Δ whole-body</td>
<td>Δ thoracic</td>
</tr>
</tbody>
</table>

Results: Intraclass correlation of pre- to end-dialysis changes in whole-body and thoracic resistance between the first and second session was .71 [.58 – .8] and .72 [.6 – .81] respectively (Fig. 1). The correlation between ultrafiltration volume and relative whole-body and thoracic resistance was respectively .94 [.91 – .96], p < .001 and .76 [.66 – .83], p < .001 in the first session and .95 [.93 – .97], p < .001 and .75 [.65 – .82], p < .001 in the second session (Table 1). Changes in systolic blood pressure negatively correlated to both bioimpedance techniques (whole-body resistance in the first session: -.37 [-.19 – -.53], p < .001; in the second session: -.37 [-.19 – -.53], p < .001; thoracic resistance in the first session -.45 [-.28 – -.59], p < .001; in the second session -.39 [-.22 – -.54], p < .001) (Table 1).

Conclusion: Bioimpedance signals from both devices were moderately reproducible between two dialysis sessions. Whereas the relation between changes in ultrafiltration volume and relative whole-body and thoracic blood pressure was at least comparable for thoracic measurements. Thoracic bioimpedance measurements by a wearable device may serve as an interesting alternative to whole-body measurements for continuous hemodynamic monitoring during hemodialysis.

#4358

INCREASED RV PRESSURE AS A PREDICTOR OF ACUTE DECOMPENSATED HF IN ESRD PATIENTS ON MAINTENANCE HD
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Background and Aims: Many patients with end-stage renal disease (ESRD) on hemodialysis (HD) have reduced vascular compliance and are likely to develop heart failure (HF). This study aimed to determine the factors associated with acute decompensation events among ESRD patients undergoing HD.

Methods: We retrospectively investigated ESRD patients on HD using a medical record review. We divided the patients into those admitted to hospital due to acute decompensated heart failure (ADHF) and those who were not. We compared the medical histories, electrocardiograms, and echocardiographic and laboratory data between the two groups. The cut-off value of the TR jet velocity for predicting an ADHF with corresponding sensitivity and specificity was estimated using a receiving operator characteristic (ROC) curve analysis. A p value < 0.05 was considered to indicate statistical significance.

Results: Of the 188 ESRD patients on HD, 87 were excluded, and 101 were enrolled (mean age: 63.7 years; 52.1% male). Thirty patients (29.7%) were admitted due to ADHF. These patients exhibited similar left ventricular ejection fraction (LVEF), left ventricular (LV) mass index, and E/E′ values compared to the non-ADHF group. However, the ADHF group exhibited significantly higher tricuspid regurgitation (TR) jet velocity (2.9±0.6 vs. 2.5±0.4 m/s; p = 0.004) and right ventricular systolic pressure (RVSP) (43.5±17.2 vs. 34.2±9.9 mmHg; p = 0.009) than the non-ADHF group, respectively. A multivariate logistic regression analysis demonstrated that the TR jet velocity (odds ratio, 8.356; 95% confidence interval, 1.806–38.658; p = 0.007) was an independent predictor of ADHF after adjusting for age and sex, while the LVEF and E/E′ were not.
Conclusions: Our data showed that an increased TR jet velocity was an independent predictor of ADHF events in ESRD patients on HD, but the LVEF and E/E' were not.

#5042
ASSOCIATIONS BETWEEN SARCOPENIA, CARDIOVASCULAR HEALTH AND HABITUAL PHYSICAL ACTIVITY IN PATIENTS ON HAEMODIALYSIS
Noemi Vadaszy1, Sherna Adenwalla2, Roseanne E Billany3, Daniel March2, Hannah Young3, Alice Smith1, Matthew Graham-Brown2,4 and James Burton2,4
1University of Leicester, Leicester Kidney Lifestyle Team, Department of Population Health Sciences, Leicester, United Kingdom, 2University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom, 3University of Leicester, Department of Population Health Sciences, Leicester, United Kingdom and 4University Hospitals Leicester, John Walls Renal Unit, Leicester, United Kingdom

Background and Aims: Patients with end-stage kidney disease (ESKD) show skeletal muscle abnormalities such as sarcopenia (presence of low muscle mass, strength, and physical performance). Severe sarcopenia and its components are associated with poor clinical outcomes, decreased quality of life (QoL), and mortality. The direction of the relationships between sarcopenia and cardiovascular disease are less clear as are the impact of exercise interventions in patients with severe sarcopenia.

Method: This is a post-hoc analysis of the CYCLE-HD study, which was a randomised controlled trial assessing the effects of a 6-month structured intradialytic cycling intervention on cardiovascular health in those on haemodialysis. Presence of sarcopenia was established using the European Working Group of Sarcopenia in Older People (EWGSOP) definition. A cut off of <17.5 kg/m² in men and <14.5 kg/m² in women were used for fat free mass to establish muscle quantity using bioimpedance. The cut off of 15 seconds on the sit to stand 5 tests was used to establish muscle strength and a score of ≤8 on the short physical performance battery was used to assess physical performance. If all three criteria were met, severe sarcopenia was confirmed. Accelerometry assessed habitual physical activity (PA) and the general practice physical activity questionnaire assessed self-reported PA.

Results: 130 patients (57 [±15] years, 95 [73.08%] male) were included in the analysis of whom 65 patients underwent the intradialytic cycling intervention. 31 (23.85%) patients had severe sarcopenia. 107 (82.31%) had low muscle mass, 92 (70.77%) had low strength, and 48 (36.92%) had low physical performance. Severe sarcopenia was a significant predictor for self-reported PA status (p = .042, PseudoR² = 0.043) at baseline but not for any other outcomes. However, low muscle mass was a significant predictor for LV mass (p = .014, R² = 0.04, β = -6.76). Low muscle strength was a significant predictor for higher pulse wave velocity (p = .010, R² = 0.056, B = 2.57) and global native T1 (p = .001, R² = 0.091, B = 26.79). Low fat mass (p = .005, R² = 0.07, B = -2198.63) and physical performance were significant predictors for mean steps (p < .001, R² = 0.12, B = -209.16). Baseline severe sarcopenia or its components were not predictors for cardiovascular or habitual PA changes following intradialytic exercise.

Conclusion: Severe sarcopenia was present in nearly quarter of the participants, but the majority showed at least one muscle health related abnormality (low muscle mass, strength or physical performance). These markers of sarcopenia showed associations with habitual PA and structural markers of cardiovascular disease. However, the presence of sarcopenia may not limit the benefits offered by intradialytic exercise. Patients with sarcopenic traits should be encouraged to participate in appropriate interventions to improve health and wellbeing.

#3355
GERIATRIC NUTRITIONAL RISK INDEX AND EARLY MORTALITY IN INCIDENT HEMODIALYSIS PATIENTS
Ajin Cho1, Ji Hyeon Park2, Do Hyoung Kim1 and Hyun Kyung Kim1
1846
Background and Aims: The nutrition status at initiation of hemodialysis (HD) might be associated with early mortality in patients undergoing HD. The Geriatric Nutritional Risk Index (GNRI) is a simple and useful nutritional screening method, and this study aimed to investigate the association between the initial GNRI and mortality in incident patients in the first year after initiation of HD.

Method: A nationwide retrospective cohort study was conducted based on the Korean Renal Data System database. Patients who underwent HD from January 2016 to December 2019 and were eligible for GNRI screening were included. They were followed up until the end of 2020 or study departure. Patients were compared by GNRI quartiles. The primary outcome was all-cause mortality, and a Cox proportional hazard model was used to analyze the association between GNRI and mortality. Accuracy comparison of the models including GNRI or body mass index (BMI) were analyzed by Receiver-operating characteristic curves, and the differences were tested by the DeLong test.

Results: A total of 10,545 patients were included, and the mean age was 63.9 ± 3.7 years. Patients with GNRI < 91.4 at the initiation of HD were older, were more often female, and a lower proportion of them had arteriovenous fistula for vascular access. A high GNRI value at the initiation of HD was associated with low all-cause mortality (hazard ratio (HR) 0.93; 95% confidence interval (95%CI) 0.92–0.94; p < 0.001). The group with GNRI < 91.4 (Quartile 1) showed the lowest survival in the first year after HD initiation (p < 0.001). Quartile 1 and Quartile 2 (91.4 – 96.8) showed a significantly increased all-cause mortality (HR 3.64; 95%CI 2.60 – 5.10; p < 0.001 for Quartile 1 and HR 1.55; 95% CI 1.09 – 2.22; p = 0.015 for Quartile 2) in comparison with Quartile 4 (101.4 – 129.6). Risk of cardiovascular mortality was high in the Quartile 1 (vs. Quartile 4; HR 3.16; 95%CI 1.94 – 5.13; p < 0.001). In addition, Area Under the ROC Curve (AUC) values for all-cause mortality were 79.1 (95%CI 77.1–81.2) and 75.9 (95%CI 73.8–78.1) for GNRI and BMI, respectively, and the differences of AUCs were significant (p < 0.001).

Conclusion: This study demonstrates that low GNRI levels are associated with all-cause and cardiovascular mortality in HD patients during the early ESRD period. These findings suggest that GNRI is a significant predictor of mortality in these patients.

#3388

ASSOCIATIONS BETWEEN PHYSICAL ACTIVITY, PHYSICAL FUNCTION AND BONE METABOLISM MARKERS IN HAEMODIALYSIS PATIENTS: A PRELIMINARY CROSS-SECTIONAL STUDY

Diogo Vaz Leal1, Daniela Cardoso1, Pedro Martins1,2, Manuel Anibal A. Ferreira1,2, Luke Baker3, Alice Smith4 and João Viana1

1CIDESD - Centro de Investigação em Desporto, Saúde e Desenvolvimento Humano, University of Maia, Maia, Portugal, 2NephroCare Portugal SA, Lisboa, Portugal, 3Nova Medical School, Lisboa, Portugal and 4Leicester Kidney Lifestyle Team, Department of Health Sciences, University of Leicester, Leicester, United Kingdom

Background and Aims: Chronic kidney disease (CKD) patients suffering from end-stage renal disease often undergo dialysis treatment. Haemodialysis (HD) patients spend most of their time in sedentary behaviour, having therefore poor physical function, as well as frequently develop mineral and bone disorders due to disease-induced systemic alterations such as abnormally high bone resorption rates exceeding bone formation. In healthy individuals, there is considerable evidence highlighting the associations between physical activity (PA), physical function (PF), and bone health. In HD patients, however, evidence on the association between these variables is still scarce. Therefore, the present preliminary study seeks to characterise HD patients in terms of their PA and PF and to identify any associations between these and markers of bone metabolism.

Method: A cross-sectional design study recruited 88 adult HD patients (males: 68%, age: 66±14 years, dialysis vintage: 42.5± months) from three clinics in Portugal. Resting blood samples were collected from the patients’ fistula at the start of the second dialysis session of the week. Plasma levels of the bone markers tartrate-resistant acid phosphatase 5b (TRAP-5b) (IDS, Tyne and Wear, UK), and sclerostin (SOST) and receptor activator of nuclear factor kappa-B ligand (RANKL) (Biomedica Immunoassays, Vienna, Austria) were measured by commercially-available enzyme-linked immunosorbent assays (ELISA), and osteocalcin (OCN) (Biogen, Madrid, Spain) and osteoprotegerin (OPG) (R&D Systems, Abingdon, UK) via DuoSet ELISA kits. PF was assessed by completing the Sit to Stand 60 (STS60), the STSS, the Incremental Shuttle Walk Test (ISWT), the Timed Up and Go (TUG), and handgrip strength (HGS). All participants wore tri-axial accelerometers continuously for a week to estimate PA levels.

Results: Accelerometers were worn for an average 13±2h/day and data showed that 81±11% of the time was spent in sedentary behaviour, and 18±10% in light PA. Associations between PA, PF and markers of bone metabolism are described in Table 1. Weekly sedentary time was associated with reduced agility (TUG), muscle endurance (STS60, ISWT), and muscle power and strength (STSS), whereas light PA levels were associated with an increment in overall PF. Also, light PA levels were associated with decreased TRAP-5b and OPG, but elevated circulating OCN, supporting a potential modulatory effect of PA on bone turnover. Decreased overall PF were associated with increased concentrations of OPG, with muscle endurance and strength associated with increased circulating TRAP-5b.

Conclusion: Our data suggests that sedentarism may be responsible for a reduced PF, which in turn was associated with increased inhibition of osteoclastogenesis via OPG activity. Yet, a rather small increase in PA levels may lead to PF gains and could be a trigger for OCN activity and TRAP-5b inhibition. Therefore, increasing PA levels may modulate bone metabolism through mechanisms that favor bone formation.
Table 1: Factors associated with sarcopenia.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.094</td>
<td>1.061-1.127</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>3.44</td>
<td>1.438-8.227</td>
<td>0.005</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.701</td>
<td>0.596-0.823</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>1.09</td>
<td>1.017-1.169</td>
<td>0.015</td>
</tr>
<tr>
<td>Magnesium (mmol/L)</td>
<td>0.06</td>
<td>0.004-0.9</td>
<td>0.042</td>
</tr>
<tr>
<td>Phosphorus (mmol/L)</td>
<td>-</td>
<td>-</td>
<td>0.656</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>-</td>
<td>-</td>
<td>0.987</td>
</tr>
<tr>
<td>Fracture history</td>
<td>-</td>
<td>-</td>
<td>0.251</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.756</td>
<td>1.416-9.963</td>
<td>0.008</td>
</tr>
<tr>
<td>Dialysis vintage (years)</td>
<td>-</td>
<td>-</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 2: Cox regression models for mortality according to osteosarcopenia.

<table>
<thead>
<tr>
<th>Model</th>
<th>COX regression analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>HR</td>
</tr>
<tr>
<td>1</td>
<td>OP alone</td>
</tr>
<tr>
<td></td>
<td>SP alone</td>
</tr>
<tr>
<td></td>
<td>OS</td>
</tr>
<tr>
<td>2</td>
<td>OP alone</td>
</tr>
<tr>
<td></td>
<td>SP alone</td>
</tr>
<tr>
<td></td>
<td>OS</td>
</tr>
</tbody>
</table>

OSTEOASARCOPENIA AMONG PATIENTS UNDERGOING HEMODIALYSIS IS RELATED WITH MORTALITY

Ting Xiang, Li Zhou and Ping Fu
West China Hospital, Sichuan University, Kidney Research Institute, Division of Nephrology, chengdu, P.R.China

Background and Aims: Sarcopenia and osteoporosis are closely interconnected and associated with adverse health outcomes. Osteosarcopenia means the concurrent presence of the two conditions and has rarely been reported in hemodialysis patients. Whether hemodialysis patients with osteosarcopenia are at greater risk of mortality than those with either condition alone remains unknown. The aim of this study was to explore the prevalence of sarcopenia and its association with osteoporosis and to determine its impact on survival risk in hemodialysis patients.

Method: A total of 209 adults undergoing hemodialysis were enrolled from the dialysis center in the West China Hospital of Sichuan University. Muscle mass, handgrip strength, bone mineral density (BMD), and biochemical parameters were assessed. All deaths were recorded during a follow-up of 34.8 ± 13.8 months.

Results: Seventy-eight patients were diagnosed with sarcopenia with a prevalence of 37.3%. After adjustment for potential confounders, age (OR = 1.094, P <0.001), female (OR = 3.44, P = 0.005), diabetes (OR = 3.756, P = 0.008), CRP (OR = 1.09, P = 0.015), serum magnesium (OR = 0.06, P = 0.042) and BMI (OR = 0.701, P <0.001) were independently associated with sarcopenia (Table 1). Among the 209 patients, 103 patients completed the BMD assessment. The prevalence of osteosarcopenia was 22.3%, while 20.4% of participants had sarcopenia alone and 12.6% had osteoporosis alone. The respective proportions of patients who died were 10.9% for nonsarcopenia/nonosteoporosis, 15.4% for osteoporosis alone, 47.6% for sarcopenia alone, and 47.8% for osteosarcopenia. Cox regression analysis showed that osteosarcopenia was independently associated with all-cause mortality (HR = 3.541, 95% CI: 1.035-12.117), while osteoporosis alone and sarcopenia alone were not (Table 2).

Conclusion: Patients undergoing hemodialysis had a high incidence of sarcopenia and osteosarcopenia, muscle mass and strength showed a significant association with BMD, and osteosarcopenia might have a powerful impact on mortality in those patients.

INCIDENCE AND TYPES OF GASTROINTESTINAL BLEEDING EPISODES IN DIALYSIS

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1 Fresenius Medical Care, Global Medical Office, Waltham, United States of America, 2 Fresenius Medical Care, Global Medical Office, Bad Homburg, Germany, 3 Fresenius Medical Care AG & Co. KGaA, Global Medical Office, Bad Homburg, Germany, 4 University College London, London, United Kingdom, 5 Karolinska University Hospital, Dept of Renal Medicine, Stockholm, Sweden and 6 University Hospital RWTH Aachen, Division of Nephrology and Clinical Immunology, Aachen, Germany

Background and Aims: Gastrointestinal bleeding (GIB) has been suggested to be the most frequent cause of bleeding events in the dialysis population [1]. Despite this, there are scarce reports showing GIB incidence in large cohorts and the occurrence of specific GIB types is unknown. We used data on a nationally representative sample of dialysis patients treated at an integrated...
Gastrointestinal bleeding episode types and incidence rates in dialysis.

<table>
<thead>
<tr>
<th>GIB Type</th>
<th>GIB Subtype</th>
<th>GIB Comorbidity (n = 12350 patients)</th>
<th>GIB Hospitalization (n = 25315 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Observation</td>
<td>Incidence p1000py</td>
</tr>
<tr>
<td>Upper</td>
<td>Esophageal varices, ulcers, perforation, &amp; hemorrhage</td>
<td>715</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Gastric, duodenal, peptic, or gastrojejunal ulcers/perforation</td>
<td>2919</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>Gastritis &amp; duodenitis with hemorrhage</td>
<td>2859</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>Angiodysplasia of stomach &amp; duodenum with hemorrhage</td>
<td>199</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Hematemesis</td>
<td>509</td>
<td>0.4</td>
</tr>
<tr>
<td>Lower</td>
<td>Perforation of intestine</td>
<td>133</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Hemorrhage of rectum &amp; anus</td>
<td>687</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Diverticulosis &amp; diverticulitis of colon with hemorrhage</td>
<td>260</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Diverticulosis &amp; diverticulitis of small intestine with hemorrhage</td>
<td>226</td>
<td>0.2</td>
</tr>
<tr>
<td>Unspecified</td>
<td>Hemoperitoneum, melena, unspecified GI hemorrhage</td>
<td>9095</td>
<td>6.9</td>
</tr>
</tbody>
</table>

REFERENCES


#3662 FREQUENCY OF INR TESTING IN HEMODIALYSIS PATIENTS ON VITAMIN K ANTAGONISTS: A RETROSPECTIVE STUDY

Mabel Aoun, Juliette Baleynaud, Beatrice Champiaux-Dechamps, Marion Gritti, Lionel Le Mouellic and Gabrielle Duneau

AUB Santé, Nephrology, Lorient, France

Background and Aims: Despite the rising of direct oral anticoagulant agents’ use in the general population, vitamin K antagonists (VKA) are still used in hemodialysis (HD) French patients with atrial fibrillation. These HD patients on VKA have also poor levels of time in therapeutic range. It is recommended generally to follow patients with monthly INR, however there is lack of such evidence in HD. This study aims to analyze the frequency of INR testing needed in HD patients.

Method: This is a retrospective study of all patients treated with VKA in three French dialysis units between 1st January and 31st December 2022. Patients are followed with weekly INR. Variables collected included over twelve months the number of INR tests, their percentage within target, above target and below target, and number of VKA dose adjustment. Bleedings, transfusions, thrombotic events and antibiotic use were recorded. Linear regression analysis evaluated factors associated with number of VKA dose adjustment per year. This study was conducted in concordance with the Declaration of Helsinki 1975.

Results: Out of 160 HD patients, 45 (28.1%) were on VKA for paroxysmal or chronic atrial fibrillation. Their characteristics are summarized in Table 1. A total of 2609 INR tests were performed over a year with a mean of 57.9±18.8 per patient. The median number of VKA dose adjustment per year was 11 (8, 13). A significant correlation was found between the number of antibiotics and number of VKA dose adjustment (Spearman Rho = 0.360, p = 0.015). In univariate regression analysis, factors associated with higher numbers of dose adjustment were diabetes, sevelamer and blood flow (Table 2). Bleeding was not significantly different between those with high versus low VKA dose adjustment.

Conclusion: In this study, 22% of tests led to VKA dose adjustment. Patients with diabetes, on sevelamer, treated with antibiotics and with lower serum albumin needed frequent INR testing more than once monthly. These results could be helpful in contexts with limited resources.
Table 1: General characteristics of patients.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total N = 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>77.3±10.4</td>
</tr>
<tr>
<td>Gender (M/F), n(%)</td>
<td>30/15 (66.7/33.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dialysis parameters</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Dialysis vintage, months</td>
<td>42.5 (25.5, 70)</td>
</tr>
<tr>
<td>Catheter/Fistula, n(%)</td>
<td>7/38 (15.6/84.4)</td>
</tr>
<tr>
<td>Dry weight</td>
<td>76 ±17.8</td>
</tr>
<tr>
<td>Blood flow</td>
<td>350 (350, 350)</td>
</tr>
<tr>
<td>Dialysate flow</td>
<td>546.7 ±50.5</td>
</tr>
<tr>
<td>In dialysis Heparin/LMWH, n(%)</td>
<td>30/15 (66.7/33.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes, n(%)</td>
<td>16 (35.6)</td>
</tr>
<tr>
<td>Hypertension, n(%)</td>
<td>41 (91.1)</td>
</tr>
<tr>
<td>Current smoking status, n(%)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Dyslipidemia, n(%)</td>
<td>39 (86.7)</td>
</tr>
<tr>
<td>Coronary artery disease, n(%)</td>
<td>19 (42.2)</td>
</tr>
<tr>
<td>LVEF, Median (IQR)</td>
<td>60 (58.5, 65)</td>
</tr>
<tr>
<td>Cancer, n(%)</td>
<td>20 (44.4)</td>
</tr>
<tr>
<td>Colectomy, n(%)</td>
<td>10 (22.2)</td>
</tr>
<tr>
<td>Serum albumin over one year, g/L</td>
<td>35.3±4.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medications</th>
<th></th>
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<tr>
<td>Sevelamer, n(%)</td>
<td>15 (33.3)</td>
</tr>
<tr>
<td>Kayexalate, n(%)</td>
<td>21 (46.7)</td>
</tr>
<tr>
<td>Laxatives, n(%)</td>
<td>17 (37.8)</td>
</tr>
<tr>
<td>PPI, n(%)</td>
<td>30 (66.7)</td>
</tr>
<tr>
<td>Antiplatelets, n(%)</td>
<td>11 (24.4)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Events</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular access stenosis or thrombosis, n(%)</td>
<td>12 (26.7)</td>
</tr>
<tr>
<td>Bleeding, n(%)</td>
<td>16 (35.6)</td>
</tr>
<tr>
<td>Transfusion for bleeding, n(%)</td>
<td>12 (26.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VKA use and INR testing</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Warfarin/Fluidione, n(%)</td>
<td>36/9 (80/20)</td>
</tr>
<tr>
<td>Months on VKA</td>
<td>45 (24, 81)</td>
</tr>
<tr>
<td>Number of INR testing per year</td>
<td>57.9 ±18.6</td>
</tr>
<tr>
<td>Percentage of INR within target</td>
<td>58.2 ±16</td>
</tr>
<tr>
<td>Percentage of INR above target</td>
<td>13.8 ±7.6</td>
</tr>
<tr>
<td>Percentage of INR below target</td>
<td>27.8 ±13.7</td>
</tr>
<tr>
<td>Number of adjustments of VKA dose per year</td>
<td>11 (8, 13)</td>
</tr>
<tr>
<td>Percentage of INRs tests used for dose adjustment</td>
<td>4.2 ±2.7</td>
</tr>
<tr>
<td>Months without VKA dose adjustment</td>
<td>36.7 ±22.5</td>
</tr>
<tr>
<td>Percentage of months without dose adjustment</td>
<td>11.8 ±11</td>
</tr>
</tbody>
</table>

Continuous variables with normal distribution are reported as mean±SD and those skewed as median (IQR).

Table 2: Linear regression analysis of factors associated with number of VKA dose adjustment.

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Unstandardized coefficient B</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>-0.193</td>
<td>-0.441, 0.055</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6.662</td>
<td>1.562, 11.761</td>
</tr>
<tr>
<td>Blood flow</td>
<td>0.062</td>
<td>-0.025, 0.149</td>
</tr>
<tr>
<td>Dialysate flow</td>
<td>0.061</td>
<td>0.012, 0.110</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>-0.491</td>
<td>-1.090, 0.108</td>
</tr>
<tr>
<td>Sevelamer</td>
<td>6.033</td>
<td>0.771, 11.296</td>
</tr>
<tr>
<td>Number of antibiotics per year</td>
<td>2.043</td>
<td>-0.703, 4.789</td>
</tr>
</tbody>
</table>

#4130

**CHA2DS2-VASc score as a predictor of cardiovascular morbidity and mortality and all-cause mortality in patients undergoing chronic hemodialysis**

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**Background and Aims:** End stage kidney disease (ESKD) is a well-recognized risk factor for cardiovascular and all-cause mortality. The recognition of high-risk patients could lead to a different approach and better treatment of the patients undergoing chronic hemodialysis. The CHA2DS2-VASc score was originally used to predict the annual cerebral infarction in patients with atrial fibrillation. However, it is also a useful predictor of outcome in other cardiovascular conditions, independent of atrial fibrillation. The aim of this study was to assess whether CHA2DS2-VASc score may be used as a risk stratification tool for ESKD patients undergoing chronic hemodialysis.

**Method:** We performed a single-centre retrospective study of 201 adult patients undergoing chronic hemodialysis in our institution from January
2020 to December 2022 with a follow up period of at least 12 months. CHA2DS2-VASc score was calculated for each patient according to the data from January 1st 2020 or at the moment of haemodialysis initiation, if the date of the first dialysis was after that date. Patients were followed until January 1st 2023, or until their death or kidney transplantation. Demographic, clinical and laboratory parameters, as well as used medications, were analyzed. Occurrences of myocardial infarction, stroke, revascularization procedure, new hospitalization for heart failure, cardiovascular death, or all-cause mortality were recorded for each patient. Patients were divided into three groups according to their CHA2DS2-VASc score: low (0-2), intermediate (3), high (≥4).

Results: The group with a low CHA2DS2-VASc score (0-2)-group I included 80 (39.8%) patients, the group with an intermediate score (3)-group II included 62 (30.8%) patients, and the group with a high score (≥4)-group III included 59 (29.4%) patients. Mean follow-up time was 918 ± 317 days. Patients in the group with higher CHA2DS2-VASc scores (group III) were predominantly females (group III 62.7% vs group II 45.2% vs group I 23.8%; p < 0.01) and older (group III 74.9±7.4 years vs group II 68.7±7.6 years vs group I 55.2±11.3 years; p < 0.01). They also had a higher prevalence of diabetes mellitus (group III 61.0% vs group II 45.2% vs group I 21.3%; p < 0.01) and vascular disease (group III 30.5% vs group II 12.9% vs group I 3.8%; p < 0.01). Major adverse cardiovascular events (MACE) were significantly more prevalent in patients with higher CHA2DS2-VASc scores (p < 0.01) (Fig. 1). All-cause mortality was significantly higher in group II and group III, compared to the group I (p<0.05) (Fig. 1). The patients in the group II and group III had a significantly higher risk of all-cause mortality and cardiovascular mortality than the patients in the group I (p<0.05) (Fig. 2). Using a group I as a reference, group II and group III had a higher risk of all-cause mortality (HR 1.92, 95% CI 1.01-3.66, p<0.05 and HR 2.47, 95% CI 1.32- 4.63, p<0.01, respectively) and cardiovascular mortality (HR 3.56, 95% CI 1.18-9.53, p<0.05 and HR 6.58, 95% CI 2.48-17.46, p<0.001, respectively). Each one-point increase in CHA2DS2-VASc score was associated with a two-fold increased risk of MACE and a 47% increased risk of all-cause mortality.

Conclusion: The CHA2DS2-VASc score is a simple, easy-to-calculate tool that can be used to identify high-risk ESKD patients enduring chronic hemodialysis. Clinical utilization of the CHA2DS2-VASc score in risk stratification of these patients could intensify patient care and lead to better outcomes by reducing cardiovascular morbidity and mortality and all-cause mortality.

#4279
ATTENTION AND EMOTIONAL COGNITIVE DEFICITS IN HEMODIALYSIS PATIENTS WITH NORMAL NEUROCOGNITIVE SCREENING TEST RESULTS: AN EGYPTIAN TRIPLE CENTER STUDY
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Background and Aims: Cognitive impairment (CI) is common in hemodialysis (HD) patients. St. Louis University Mental Status (SLUMS) examination is a traditional cognitive assessment method that relies on a pen-and-paper format. SLUMS test is known to be one of the most sensitive tests to detect early CI. Its questions cover many functions, including memory, attention, orientation, and overall executive function. This study aimed to compare its results with computerized neurocognitive battery assessment for attention and emotional orientation functions.

Method: One hundred twenty HD patients from three different in-hospital HD centers in Dakhla governorate, Egypt, were subjected to the 10-minute Arabic-validated version of the SLUMS test for early CI. Its questions cover many functions, including memory, attention, orientation, and overall executive function. This study aimed to compare its results with computerized neurocognitive battery assessment for attention and emotional orientation functions.

Results: Of the 120 SLUMS-tested patients, 50 patients (41.6%) had no CI, 43 with mild to moderate CI (36%), and 27 with severe CI (22.4%). The classified 50 HD patients with no CI results within the computerized neurocognitive battery assessment revealed significantly reduced scores than
matched healthy controls in the number of true positive answers of continuous number performance test for attention (90.46±26.61 vs. 109.15±14.56, respectively, p < 0.001), emotion recognition correct answers (29.44±5.54 vs. 31.41±4.65, respectively, p 0.02), emotional recognition response times by m.seconds (3482.76±2907.62 vs. 2907.62±732.98, respectively, p < 0.001), and correct answers of emotion differentiation test (19.82±5.88 vs. 23.77±3.63, respectively, p <0.001). HD patients' age was the only clinical correlate to emotional recognition and differentiation accurateness (rho = 0.442, p <0.001 and rho = 0.3, p 0.02, respectively).

**Conclusion:** Early detection of CI in HD patients is an important target to improve the patient's quality of life and functionality. The complete dependence on the known simple screening assessment may miss a significant portion of the early-affected personnel.

#4655

**IMPACT OF MAGNESIUM ASPARATE AND L-CARNITINE ON INFLAMMATION, INSULIN RESISTANCE AND ATHEROSCLEROSIS PROGRESSION IN DIABETIC HEMODIALYSIS PATIENTS**

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**Background and Aims:** The development of new pathogenetic treatment programs to reduce cardiovascular risk in diabetic patients with end-stage kidney disease is an important task of modern nephrology. In these conditions, considering the essential role of magnesium and L-carnitine deficiency in the mechanisms (via endothelial and metabolic disorders) of cardiovascular diseases, we evaluated the effect of the combined use of magnesium aspartate and L-carnitine on inflammation, insulin resistance and the atherosclerosis progression of carotid arteries in type 2 diabetic hemodialysis (HD) patients.

**Method:** 42 type 2 diabetic HD patients were included in this prospective cohort study (male, 26; age, 59.5±0.7 years; HD duration, 31.2±4.6 month; diabetes mellitus duration, 174.6±7.8 month). Depending on the treatment programme, patients were divided into two groups: the 1st (main) group (n = 22) in addition to basic treatment (hypoglycemic, antihypertensive therapy, correction of anemia, hyperparathyroidism, hyperphosphatemia) was treated by combination of magnesium aspartate (0.5 g/day orally) and L-carnitine (1 g/day parenterally after each HD session (three times weekly); the 2nd (comparison) group (n = 20) was only on the standard therapy. Complex treatment lasted 12-months; administration of L-carnitine was performed continuously throughout the year, while magnesium aspartate – by three 2-months’ courses per year. Serum content of tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP) and fibrinogen as inflammatory biomarkers were determined. The homoeostasis model of assessment-insulin resistance (HOMA-IR) as an index of insulin resistance was estimated. Common carotid artery intima-media thickness (CCA IMT) as an index of the atherosclerosis severity was measured by ultrasound. Data are expressed as means ± SEM. Wilcoxon T-test was used for comparison of the dependent variables, Mann-Whitney U-test – for independent ones.

**Results:** In diabetic HD patients undergoing complex treatment with a combination of magnesium aspartate and L-carnitine after 12 months of observation CCA IMT did not change (0.88 ± 0.05 vs. 0.88 ± 0.05 mm; Z = 0.09, p = 0.925), while a significant increase (by 9.1%) in the CCA IMT was determined in subjects, who were on basic therapy (0.98 ± 0.04 vs. 1.07 ± 0.04 mm; Z = 2.27, p = 0.023). In addition, after 12 months of treatment, the indicated index between 1st and 2nd groups differed (p = 0.006). By the end of follow-up, the TNF-α, CRP and fibrinogen contents in patients who were on modified therapy were 44.7, 56.4 and 78.2% from baseline, a similar indices in patients receiving standard treatment – 70.7, 77.3 and 88.8% respectively, and after one year the main group and the comparison group on the serum concentrations of TNF-α (p = 0.089), CRP (p = 0.030) and fibrinogen (p = 0.026) differed. Magnesium aspartate and L-carnitine supplementation significantly improve HOMA-IR, and after 12 months of observation, the indicated index in the 2nd group exceeded (p = 0.003) that in the 1st one (Table 1).

**Conclusion:** (1) The combined use of magnesium aspartate and L-carnitine, in addition to the basic 12-month treatment, prevents the atherosclerosis progression of CCA, provides an effective reduction of the activity of chronic inflammation, improves insulin resistance in type 2 diabetic HD patients. (2) Long-term modified treatment may reduce the cardiovascular risk in these subjects.

**Table 1: Indices of chronic inflammation and insulin resistance in type 2 diabetic HD patients on the background of different treatment programs.**

<table>
<thead>
<tr>
<th>Index</th>
<th>Main group (n = 22)</th>
<th>Comparison group (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>TNF-α, ng/L</td>
<td>14.08 ± 1.77</td>
<td>6.29 ± 0.58</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>9.16 ± 1.49</td>
<td>5.17 ± 0.77</td>
</tr>
<tr>
<td>Fibrinogen, g/L</td>
<td>5.19 ± 0.27</td>
<td>4.06 ± 0.34</td>
</tr>
<tr>
<td>HOMA-IR, c.u.</td>
<td>5.90 ± 0.90</td>
<td>3.61 ± 0.62</td>
</tr>
</tbody>
</table>

Data are shown as means ± SEM.

TNF-α, tumor necrosis factor alpha; CRP, C-reactive protein; HOMA-IR, homoeostasis model of assessment-insulin resistance.
IMPACT OF MINERAL BONE PARAMETERS IN COGNITIVE IMPAIRMENT IN DIALYSIS PATIENTS

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University Hospital Center Mother Theresa, Department of Nephrology, Tirana, Albania

Background and Aims: Mineral bone disease and cognitive impairment are related diseases in the CKD population. Vascular calcification, a marker of MBD, may play a role in the early detection of cognitive decline. This study aims to identify a relationship between MBD biomarkers and cognitive function and to identify dialysis patients with a high risk of dementia.

Method: A total of 98 patients participated in this cross-sectional study, with 63 on hemodialysis and 35 on peritoneal dialysis. They underwent the Montreal Cognitive Assessment (MoCA) questionnaire, which categorized mild, moderate, severe, and very severe based on scoring. PTH, P, Ca, ALP, and Mg serum concentrations and vascular calcification were measured as MBD biomarkers. The Adraga score was applied to graphs of the hands and pelvis to evaluate vascular calcification.

Results: The mean MoCA score was 20.28 ± 5.8. Based on the responses, it was concluded that 70% of HD patients had mild cognitive impairment, compared to 63% of PD patients. According to the descriptive data, patients whose underlying CKD was caused by nephroangiosclerosis had the lowest MoCA test results compared to other groups (p < 0.001). The degree of calcification was observed to have an adverse effect on cognitive performance in both groups (p < 0.012); the high Adraga score contributed to the decline in the MoCA test score. In multivariate logistic regression analysis, hypercalcemia and hypomagnesemia were independent variables for cognitive function impairment (p = 0.006 and p = 0.004, respectively). The serum concentration of PTH (p = 0.008) and ALP (p = 0.001) were found to be risk factors for HD patients during the evaluation of the MoCA test in each of the groups.

Conclusion: Vascular calcifications are considered a risk factor for cognitive impairment. In our study, vascular calcification risk is positively impacted by indicators such as hyperparathyroidism, hypercalcemia, high levels of ALP, and hypomagnesemia. Recently research has demonstrated the effectiveness of magnesium as a vascular calcification inhibitor. So, nephrologists should be more careful in monitoring levels of MBD biomarkers.

ASSOCIATION BETWEEN PHYSICAL ACTIVITY LEVEL AND A HISTORY OF FALLS IN PATIENTS ON HEMODIALYSIS

Leda Lucinda1,2, Luciana de Jesus1, Bárbara Alvarenga1, Abner de Castro1, Kéllner Avila1, Rodrigo Garcia1, Cristina Oliveira1, Bruno Pinheiro1 and Maycon Moura Reboredo1
1Federal University of Juiz de Fora, Juiz de Fora, Brazil and 2Barbacena School of Medicine, Barbacena, Brazil

Background and Aims: Patients with end-stage renal disease on hemodialysis have a lower physical activity level in daily life and a higher prevalence of sedentary lifestyle. Moreover, these patients have clinical, musculoskeletal, and physical function complications that contribute to a higher risk of falling. Therefore, the aim of this study was to evaluate the association between physical activity level and history of falls in a retrospective 12-month interval in patients on hemodialysis.

Method: A retrospective study was conducted with patients aged ≥18 years who were undergoing regular hemodialysis treatment for at least three months. Patients were excluded if presented severe and unstable comorbidities, psychiatric or cognitive disorders, uncorrected visual impairments, and hospitalization in the past three months. The retrospective history of falls was assessed for the last 12 months, and a fall was defined as an “unexpected event in which the individual comes to rest on the ground, floor or lower level.” The daily step counts were recorded in the ActiGraph accelerometer (wGT3X-BT) during seven days, and analyzed by excluding the first and last day of recording and calculating the mean among the valid days (≥ 8 hours of wear time). Normativity of data was analyzed by the Shapiro-Wilk test. The Student’s t-test and the Mann-Whitney U test were used for between-group comparisons (patients with and without a history of falls). The univariate and multivariate linear regression models investigated the association between daily step counts and a history of falls. A p value < 0.05 was considered as statistically significant.

Results: This study included 103 patients (59.2 ± 12.6 years, 59.2% male). Of these patients, 49.5% had a history of falls. Patients with a history of falls showed lower prevalence of workers (9.8% vs. 26.9%, p = 0.025) and daily step counts [2989 (2595) vs. 4550 (2966) steps, p = 0.018], and higher educational level [9 (7) vs. 5 (5) years, p = 0.033] compared to patients without a history of falls. The univariate linear regression model showed that daily step counts was significantly associated with a history of falls (p = 0.017). After adjusting for age, gender, educational level, work status, hemoglobin, and diabetes mellitus, this association remained significant in multiple linear regression model with a coefficient of determination of 0.21 and an adjusted coefficient of determination of 0.16 (p = 0.001).

Conclusion: Physical activity level was associated with a history of falls in a retrospective 12-month interval in patients on hemodialysis.

PRESCRIBING PATTERNS IN GREEK HEMODIALYSIS PATIENTS: A MULTICENTER PHARMACOEPIDEMIOLOGY STUDY

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11424 General Military Training Hospital, Department of Internal Medicine, Thessaloniki, Greece, 2Democritus University of Thrace, Department of Nephrology, Alexandroupoli, Greece, 3Aristotle University of Thessaloniki, Department of Nephrology, Thessaloniki, Greece, 4Democritus University of Thrace, Laboratory of Pharmacology, Alexandroupoli, Greece and 5Democritus University of Thrace, Department of Nephrology, Alexandroupoli, Greece

Background and Aims: The aim of the study is to investigate the prescribing patterns and polypharmacy in Greek hemodialysis patients and make comparisons between renal units. Polypharmacy and hyperpolypharmacy emerged as a concerning problem, that affects patient’s adherence, causes drug-drug interactions, adverse drug events, increases morbidity and economically strains the health system. Patients in Europe are prescribed on average 10-12 drugs despite recommendations on polypharmacy.

Method: This is a multicenter retrospective study (2018-2021), in Northern Greece, of 270 patients (male = 168, female = 102) with mean age of 63.8±15 years and median dialysis duration of 45(18-96) months. The medications and laboratory values were documented for a period of 12 months, provided that there were no major changes on their therapy at that time. The 24 public health dialysis units participating in the survey, were classified as secondary (179 patients) and tertiary care (91 patients) depending on the bed capacity (>600) and the availability of health services. Statistical analysis was conducted using SPSS ver 26.

Results: The mean number of prescribed medications was 10.4 (SD 2.9, range 2–20). Of the participants, 97.4% were experiencing polypharmacy (>5 medications per person) and 62.6% hyperpolypharmacy (>10 medications). The average number of prescribed medications in tertiary care was substantially lower comparing with secondary care (mean: 8.7 vs 11.3, p < 0.001). The difference in the mean number, remained significant even when the result was adjusted for age, gender, cardiovascular disease, primary disease and dialysis duration. Notably, despite the fewer medications, there was no statistically significant difference between the two groups, in achieving the most recent Kidney Disease Improving Global Outcomes (KDGIO) guidelines for URR (Urea Ruction Ratio), renal mineral bone disease and renal anemia (chi-square, p>0.05 for all variables). The most frequently prescribed group of medications were EPO analogues (87%), Vitamin D supplements (83%), Proton Pump Inhibitors (68%), β-blockers (56%), Antipatelets (45%) and Loop diuretics (37%). It is important to note the alarming number of patients receiving medication for mental illness (35.2%), mainly benzodiazepines (26%), with women to be more vulnerable (42.2% vs 30.1%, OR 1.63).

Conclusion: This study reports that Greek prescribing practices follow the same worrisome patterns as other European countries. Rural hospitals appear to prescribe more drugs than tertiary facilities.

PREDICTION OF MAJOR GASTROINTESTINAL BLEEDING EVENTS IN HEMODIALYSIS

John Larkin1, Suman Lama1, Sheetal Chaudhuri2, Joanna Willetts3, Anke Winter1, Yue Jiao1, Manuela Stauss-Grabo2, Len Usvayt1, Jeffrey Hymes1, Franklin Maddux3, David C. Wheeler4, Peter Stenvinkel5 and Jürgen Floege6
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Background and Aims: IiNatiVeS on advancing Patients’ outcomes In REnal disease (INSPIRE) is an academia and industry collaboration set forth to identify critical investigations needed to advance the practice of...
The model showed an area under the curve (group mean GIB event) of 0.69, sensitivity = 68.9%, specificity = 68.8% and balanced accuracy = 63.4%. Exposures with largest effect size observed via SHAP values were older age and iron indices, longer dialysis vintage, and proton pump inhibitor use (Fig. 1).

Conclusion: The machine learning model appears suitable for early detection of GIB event risk in HD, yet prospective testing is needed. The association between higher 25OH vitamin D and GIB events was unexpected and warrants investigation. A consistent signal has been observed in warfarin users without kidney disease among which 25OH vitamin D levels of 30–100 ng/mL were shown to associate with the highest GIB risk [3].

REFERENCES


#3706 EFFECT OF CHOLECALCIFEROL INTAKE ON NOVEL INFLAMMATORY INDICATORS IN HEMODIALYSIS PATIENTS

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2Faculty of Medicine - Ain Shams University, Nephrology, Egypt

Background and Aims: Hemodialysis patients (HD) are in a chronic state of systemic inflammation, with vast majority of these patients are vitamin D deficient. Vitamin D appears to be a strong controller of inflammation. It’s well known that C-reactive protein (CRP) is considered the gold of inflammatory markers. Recently, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been shown to be inexpensive, readily available indicators of systemic inflammation. This study is to demonstrate the pleotropic effects, the efficacy and the safety of two dosing regimens of cholecalciferol; (weekly regimen vs monthly regimen) on novel inflammatory indicators in HD population.

Method: A prospective, randomized trial was carried out to evaluate the effect of weekly versus, monthly oral cholecalciferol, on vitamin D (25(OH)D) levels, on inflammatory markers and secondary hyperparathyroidism in HD patients. Fifty eligible HD patients were randomly assigned to either Group A (Once weekly oral 50,000IU Cholecalciferol) or Group B (One monthly, oral 200,000IU Cholecalciferol), for 3 months’ period. Serum levels of high sensitive CRP (hsCRP), NLR, PLR, were all assessed at baseline and at the end of the study.
Results: Cholecalciferol significantly increased serum levels of 25(OH)D in both groups. A significant decrease in serum hsCRP levels ($p < 0.001$) and NLR was noted only in Group A. No significant difference in calcium or phosphorus levels was noticed. No side effects or adverse events were reported.

Conclusion: Weekly (50,000 IU) oral cholecalciferol appears to have a beneficial action on replenishing 25(OH)D levels in HD patients, with an ameliorative action on inflammatory status as well. NLR seems to be an effective, non-expensive inflammatory indicator in HD.

### #3718

**WHAT ARE THE MOST COMMON HEADACHE PROBLEMS IN PATIENTS RECEIVING DIALYSIS?**

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Tashkent Pediatric Medical Institute, Internal Medicine, Nephrology and Hemodialysis, Tashkent, Uzbekistan

**Background and Aims:** Analysis of the clinical features of headache in patients on the program dialysis.

**Method:** The study included 40 males and 40 females with CKD on program dialysis for more than 12 months in 2022, each session lasting 4 hours. The exclusion criteria were patients receiving drugs that can cause headache and with any type of primary headache not associated with the HD procedure, diabetes mellitus, and others. Patients with DH were further compared with patients without DH in terms of BP and blood values such as urea, creatinine, Na+, K+.

**Results:** 45% ($n = 36$) reported DH, which was common in women 60%. Differences between pre- and post-dialysis urea values in patients with DH were statistically significant ($p < 0.05$). Patients with DH showed significantly higher mean SBP and DBP values before dialysis compared with patients without DH (systolic, $P < 0.001$; diastolic, $P < 0.01$). 80% of patients ($n = 64$) reported the quality of their headaches as being throbbing, whereas (20%), 58% and severe in 27% ($n = 22$). The headache duration was reported to last less than 4 hours in 63% ($n = 50$) and 4 to 36 hours in 37% ($n = 30$), Table 2.

**Conclusion:** We determined that DH is a common type of headache among HD patients, female predominance, begins after several hours of therapy, with progressive intensity and throbbing character, which is not associated with a coexisting primary headache, but may be related to differences in urea levels and BP before and after treatment.

### #4287

**GASTROINTESTINAL SYMPTOMS IN PATIENTS RECEIVING HEMODIALYSIS: PREVALENCE, SEVERITY AND ASSOCIATED FACTORS**

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**Background and Aims:** Gastrointestinal (GI) symptoms are common among patients with chronic renal failure, especially in those treated with maintenance hemodialysis (HD), and may adversely affect patients’ quality of life. A variety of GI symptoms has been reported, but previous studies present conflicting results regarding their association with age, sex, comorbidities, concomitant medications and dialysis modality. This study aimed to assess the prevalence and severity of GI symptoms in the maintenance HD population and explore possible associated factors.

**Method:** A total of 188 stable patients (55.3% male, 53.7% ≥65 years of age, age range 24–85, 30.9% with diabetes, 19.9% smokers) from three HD centres were enrolled in this observational cross-sectional study. Gastrointestinal symptoms were assessed by the self-administered Gastrointestinal Symptoms Rating Scale (GSRS). The scale includes 15 items graded by a 7-point Likert scale that can be grouped into five dimensions: abdominal pain syndrome, reflux syndrome, indigestion syndrome, diarrhoea syndrome, and constipation syndrome. A dimension score is calculated as the mean value of the items belonging to the specific syndrome, and the final score is the mean of dimension scores. Standard blood analyses, Kt/V, body mass index (BMI) and malnutrition-inflammation-inflammation score (MIS) were determined in all patients. Other relevant demographic and clinical data were obtained from the patient’s medical records. The results were analyzed with SPSS software, version 22 (IBM Corporation, New York, USA).

**Results:** The average BMI was 25.04 ± 4.29. Half of the patients (50.3%) were overweight, 45.3% had normal weight, and 4.3% were underweight. The average MIS was 5.64 ± 2.87. The average number of symptoms per patient was 4.01 ± 3.20 (range 0 – 15). At least one GI symptom was reported by 84.6% of patients (33.0% reported 1 – 3 symptoms, and 49.5% reported 4 or more symptoms). The mean GSRS scores for eating dysfunctions were 1.59 ± 1.08 for reflux, 1.74 ± 0.98 for abdominal pain, 1.75 ± 1.14 for constipation, 1.94 ± 1.01 for indigestion, and 1.38 ± 0.90 for diarrhoea. Total GSRS was 1.70 ± 0.61. Elderly patients had a significantly lower overall number of GI symptoms (3.49 ± 2.83 vs 4.57 ± 3.31; $p = 0.023$), lower abdominal pain score (1.60 ± 0.96 vs 1.91 ± 1.09; $p = 0.031$), and indigestion score (1.74 ± 0.85 vs 2.18 ± 1.15; $p = 0.005$), but higher constipation (1.94 ± 1.27 vs 1.54 ± 0.96; $p = 0.017$) score than individuals under 65 years of age. Patients smoking cigarettes and those...
longer on HD had a significantly higher overall number of GI symptoms (3.64 ± 0.56 vs 3.10 ± 0.25; p = 0.035 and 3.78 ± 1.29 vs 2.46 ± 2.23; p = 0.016 respectively). Average abdominal pain score was significantly higher in non-diabetic (1.87 ± 1.04 vs 1.44 ± 0.75; p = 0.002) and underweight (2.62 ± 1.51 vs 1.71 ± 0.94 vs 1.65 ± 0.90; p = 0.023) compared to diabetic, normal weight and overweight patients respectively. Patients taking ASA or NSAIDs had significantly higher total GSRs scores (1.84 ± 0.72 to 1.60 ± 0.50; p = 0.016 and 1.80 ± 0.64 vs 1.65 ± 0.59; p = 0.044 respectively). Sex, dialysis adequacy and malnutrition-inflammation status were not significantly related to any of the GSRs dimensions.

Conclusion: The present study demonstrates a high prevalence of GI symptoms in maintenance HD patients and identifies age, cigarette smoking, diabetes, dialysis vintage, and certain medications as important elements to consider when addressing specific groups of GI symptoms in this population.

#5742

MID-ARM CIRCUMFERENCE AS A CORRELATE TO DIFFERENT: ASPECT NEUROCognitive IMPAIRMENT IN HEMODIALYSIS PATIENTS

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Background and Aims: Malnutrition is associated with poor cognitive function (CI) in Hemodialysis (HD) patients. Both have multiple ways of assessment scaled from simple bedside screening tests to more sophisticated time- and cost-consuming measures. This work aims to define the best nutritional assessment measure that correlates to the degree of CI.

Method: A cross-sectional study was carried out on 116 patients in 4 different HD units from Delta Nile, Egypt. The nutritional status was examined after the dialysis session in euvoletic patients using (1) anthropometric measurements, including body mass index (BMI), mid-arm circumference (MAC), skin fold thickness (SFT), and mid-arm muscle circumference (MAMC); (2) bioelectrical impedance analysis for assessment of skeletal muscle mass (SMM), skeletal muscle index (SMI), free fat mass (FFM), body fat mass (BFM), and total body water (TBW); (3) Hand grip strength was used to assess muscle power. The assessment of cognition was made using (1) a mini-mental state examination (MMSE) for orientation, registration, attention, recall, language, and copying; (2) Saint Louis University Mental Status Exam (SLUMS) for early CI and executive functioning; (3) Arabic version of Penn Web-Based Computerized Neurocognitive Battery (WebCNNP) for those who scored no CI in the previous two tests.

Results: The results of MMSE and SLUMS tests showed that 34.5% of our cohort (n = 40) had no CI, 34.5% (n = 40) had mild to moderate degrees of CI, and 31% (n = 36) had a severe form of CI. Comparing the nutritional assessment parameters between the categories of cognitive scores revealed that there were no significant differences except in significantly lower median values of MAC (P 0.01), SMI in bioelectrical impedance analysis (P0.01), and hand grip strength (P 0.002) in severe CI group than the normal to patients without CI. In correlation statistics, MAC and hand grip strength were negatively correlated to the degree of CI (r = -0.3, P 0.006 and r = -0.26, P 0.009, respectively). MAC was the only parameter correlated with attention, emotional recognition, and differentiation functioning in the forty patients with no CI who underwent computerized neurocognitive assessment. The highest reported positive correlations reported were between the MAC and response time of both emotion recognition (r = 0.57, P < 0.001) and different emotion recognition (r = 0.55, P < 0.001).

Conclusion: Of the different parameters of nutritional state assessment, MAC, the simple bedside measurement, was the best correlate with the degree of cognitive impairment in HD patients, even in its mild primitive forms.

#2768

DIFFERENT EFFECTS OF HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITORS ON SERUM LIPOIDS LEVELS IN HEMODIALYSIS PATIENTS

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Background: The activity of hypoxia-inducible factor (HIF), an oxygen-sensing transcription factor involved in erythropoiesis, is regulated by HIF-prolyl hydroxylases. With reduced oxygen tension, the activity of these enzymes is suppressed, resulting in increased erythropoiesis. Chen et al. reported that the decrease in that total cholesterol (TC) was greater with roxadustat than with epoetin alfa, as was the decrease in low density lipoprotein-cholesterol (LDL-C) in patients undergoing dialysis [1]. Cuzy et al. reported roxadustat was superior to erythropoiesis-stimulating agent (ESA) in decreasing LDL-C in accordance to a previous study [2]. Roxadustat is an oral HIF-prolyl hydroxylase inhibitor (HIF-PHI) developed for dialysis-dependent chronic kidney disease (CKD) anemia. While the impact of HIF-PHI on mean hemoglobin (Hb) change in patients on hemodialysis (HD) has been investigated [1], its effects on serum lipid levels have yet to be explored. Clarifying such effects is particularly important because HD patients usually have lower plasma high-density lipoprotein-cholesterol (HDL-C) levels than healthy individuals. Low HDL-C levels are associated with an increased risk of death in HD patients. The effects of HIF-PHIs on dyslipidemia in patients on HD are unclear. This study aimed to investigate the effects of HIF-PHIs on serum lipid levels in HD patients.

Methods: We investigated the effect of HIF-PHIs in three groups by measuring the levels Hb, serum TC, LDL-C, HDL-C, triglycerides (TG), iron, total iron-binding capacity (TIBC), transferrin saturation (TSAT), ferritin. Study 1: We evaluated the efficacy of roxadustat in 13 patients (1 female and 12 males) with HD-dependent CKD anemia and dyslipidemia over 24 weeks. Study 2: We evaluated the efficacy of daprodustat in 9 patients (2 females and 7 males) with HD-dependent CKD anemia and dyslipidemia over 24 weeks. Study 3: We evaluated the efficacy of enarodustat in 15 patients (3 females and 12 males) with HD-dependent CKD anemia and dyslipidemia over 12 weeks.

Results: Study 1: The mean age and mean HD vintage were 77.7 and 6.6 years, respectively. After roxadustat treatment, the mean Hb values (from 10.4 to 10.7 g/dL) did not significantly change. There were no significant changes in mean serum iron, TG, ferritin. However, the following parameters showed a significant decrease: mean TC (from 138.4 to 106.6 mg/dL, p = 0.0002), LDL-C (77.7 to 53.8 mg/dL, p = 0.0002), HDL-C (from 43.3 to 35.9 mg/dL, p = 0.0005), and TSAT (from 32.6 to 31.2%, p = 0.0479). There was a significant increase in the mean TIBC (from 220.5 to 265.1 μg/dL, p = 0.0002). Study 2: The mean age and mean HD vintage were 74.6 and 3.2 years, respectively. After daprodustat treatment, the mean Hb values did not significantly change. There were no significant changes in the mean TC, LDL-C, TG, TSAT, ferritin. However, the following mean HDL-C levels showed a statistically significant decrease (from 50.4 to 45.3 mg/dL, p = 0.0117). Furthermore, there were significant increases in the serum iron level (from 72.5 to 89.1 μg/dL, p = 0.0078) and the mean TIBC level (from 229.7 to 272.8 μg/dL, p = 0.0039). Study 3: The mean age and mean HD vintage were 69.3 and 8.9 years, respectively. After enarodustat treatment, the mean Hb values did not significantly change. There were no significant changes in the mean TC, LDL-C, HDL-C, TG, TSAT, ferritin. There was a significant increase in the mean TIBC (from 230.0 to 259.4 μg/dL, p = 0.0151).

Conclusions: We found that HIF-PHIs had different effects on serum lipids levels in HD patients. Roxadustat treatment improved iron metabolism stabilized Hb levels, and significantly decreased LDL-C levels. Daprodustat and enarodustat treatment improved iron metabolism, maintained stable Hb levels.

REFERENCES

#2875

CONGESTION PHENOTYPES AND DECONGESTION PATTERNS ASSOCIATED BY FOCUS IN HAEMODIALYSIS PATIENTS: A PILOT STUDY

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Background and Aims: Despite the evolution of hemodialysis (HD) in recent years, cardiovascular diseases continue to be the main cause of death in this group of patients. Congestion is one of the factors associated with the highest morbidity and mortality. Unfortunately, there is no gold standard for the proper assessment of dry weight; in fact, physical examination, and even newer techniques such as bioimpedance have poor sensitivity, are difficult to interpret in some cases and fail to discriminate between tissue and vascular congestion. Recently, the use of Point-of-care Ultrasonography (PoCUS) has emerged as the fifth pillar of the conventional physical examination that allows dynamic assessment of congestion and enables congestion to be phenotyped. The aims of the present study were: 1. to phenotype congestion in HD patients and 2. to establish patterns of decongestion according to changes in phenotypes over the course of a HD session.

Method: Descriptive study carried out in HD units of two tertiary hospitals. Patients with more than three months on HD were included. Excluding patients with short life expectancy or who had an acute complication. In addition to the congestive composite score (CCS), a PoCUS evaluation was performed at the beginning and the end of the HD session on long dialysis interval. Tissular congestion was assessed by lung ultrasound and vascular congestion was assessed by evaluation of the inferior vena cava diameter and portal vein pulsation by pulsed Doppler. Four phenotypes of congestion were established: phenotype A: no congestion, phenotype B: predominance of tissue congestion, phenotype C: predominance of vascular congestion and phenotype D: mixed congestion. In addition, 4 patterns of decongestion were established: pattern 1: absence of congestion at the beginning and end of the HD session, pattern 2: change of phenotype from B, C or D to A, pattern 3: change in congestion phenotype and pattern 4: persistence in the same congestion phenotype as at the beginning.

Results: 20 patients were included, mean age: 70.5 ± 11.3 years, 14 (70%) were male, CCS: 3 (1.5 – 7.5), interdialysis weight gain: 2.93 ± 0.95 kg and mean UF: 2,570 ± 868 mL. 75% of patients reached the prescribed dry weight. At the beginning of the session the distribution of phenotypes was: phenotype A: 35%, phenotype B: 25%, phenotype C: 25% and phenotype D: 15%. At the end of the HD session: phenotype A: 55%, phenotype B: 30%, phenotype C: 10% and phenotype D: 5%. At the end of the HD session 45% of the patients persisted with some phenotype of congestion at the end of the session. An inverse correlation was found between age and phenotype at baseline (Rho: -0.506; p = 0.023). No correlation was found between dry weight and UF with decongestion patterns.

Conclusion: These results show the persistence of echographic congestion at the end of the HD session in a significant number of patients, suggesting that subclinical congestion is more frequent than clinically observed. Further studies are warranted to confirm these results.

#3712
INTRAVASCULAR VOLUMES AND THE INFLUENCE ON ANAEMIA IN PATIENTS UNDERGOING MAINTENANCE HAEMODIALYSIS
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Background and Aims: Fluid overload is a major challenge in haemodialysis (HD) patients and might cause hypervolaemia. We speculated that HD patients reaching dry weight could have undetected hypervolaemia and low haemoglobin concentration (Hb) due to haemodilution.

Method: The study included HD patients (n = 22) and matched healthy controls (n = 22). Blood volume, plasma volume, red blood cell volume, and total haemoglobin mass (Hb mass) were determined using a carbon monoxide (CO)-rebreathing method in HD patients reaching dry weight and controls. Blood volume measurements were also obtained by a dual-isotope labelling technique in a subgroup for validation purposes.

Results: Blood volume was higher in 16 out of the 22 HD patients compared to controls. In the HD group, the median blood volume was 89.3 mL/kg (interquartile range (IQR) 76.7–95.4 mL/kg) and was higher than in the control group (79.9 mL/kg (IQR 70.4–88.0 mL/kg); P = 0.037) (Table 1). The median plasma volume was 54.7 mL/kg (IQR 47.1–61.0 mL/kg) and 44.0 mL/kg (IQR 38.7–49.5 mL/kg) in the HD and control groups, respectively (P < 0.001). Hb was lower in HD patients (P < 0.001), whereas no difference in total Hb mass was observed between groups (P = 0.11). Changes in Hb levels during and after dialysis were observed in the HD group and is shown in Fig. 1. A correlation was found between blood volume measured by the CO-rebreathing test and the dual-isotope labelling technique in the control group (r = 0.83, P = 0.015), but not the HD group (r = 0.25, P = 0.60).

Conclusion: The HD group had increased blood volume at dry weight due to high plasma volume, indicating a hypervolaemic state. The total Hb mass was similar between HD patients and controls, unlike Hb, which emphasizes that Hb is an inaccurate marker of anaemia among HD patients.
Table 1: Haemoglobin concentration and measures of CO-rebreathing test.

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Haemodialysis Group</th>
<th>Control Group</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline haemoglobin (g/dL)</td>
<td>11.4 (10.8-12.6)</td>
<td>14.5 (13.7-15.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CO-rebreathing test

<table>
<thead>
<tr>
<th>Measure</th>
<th>HD Group</th>
<th>Control Group</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>BV (mL/kg body weight)</td>
<td>89.3 (76.7-95.4)</td>
<td>79.9 (70.4-88.0)</td>
<td>0.037</td>
</tr>
<tr>
<td>PV (mL/kg body weight)</td>
<td>54.7 (47.1-61.0)</td>
<td>44.0 (38.7-49.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total haemoglobin mass (g)</td>
<td>902.5 (783.0-982.0)</td>
<td>964.0 (830.5-1088.0)</td>
<td>0.40</td>
</tr>
<tr>
<td>Total haemoglobin mass (g/kg)</td>
<td>10.6 (9.5-12.6)</td>
<td>11.7 (10.8-13.1)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

All values are given as the median and interquartile range. Mann-Whitney test was used to compare measured volumes in HD group and control group. BV = blood volume; PV = plasma volume; RBCV = red blood cell volume; HbCO = carboxyhaemoglobin.

Figure 1: Changes in haemoglobin concentration (g/dL) during dialysis in the HD group. Pre-dialysis Hb was obtained immediately before the HD session and post-dialysis Hb immediately after.

#2918

SERUM 25(OH)-VITAMIN D AND 1,25(OH)2 VITAMIN D IN HEMODIALYSIS PATIENTS: FACTORS AFFECTING THEIR CONCENTRATIONS AND THEIR EFFECT ON SURVIVAL

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Background and Aims: In haemodialysis patients, serum levels of vitamin D metabolites, 25-hydroxy-vitamin D (25D), a nutritional status of vitamin D, and 1,25-dihydroxy-vitamin D (1,25D), an active form of vitamin D, are previously reported to be low. In recent years of new CKD-MBD guidelines utilizing calcimimetics, vitamin D receptor agonists (VDRA) and new phosphate binders, relationship between serum 25D, 1,25D concentrations and clinical parameters in haemodialysis patients are not well known. We measured both serum 25D and 1,25D concentrations in chronic haemodialysis patients, and examined their association with several clinical factors and also with survival, in both cross-sectional and longitudinal analyses.

Method: A total of 108 stable haemodialysis patients (72 ± 10 year-old, 64 males, haemodialysis duration 6.9 ± 7.5 years, 45 with type 2 diabetes) were examined. Serum 25D was measured by a ECRIA method, and 1,25D by a RIA2 antibody method, and serum PTH by a IRMA assay. In a cross-sectional analysis, association of these vitamin D metabolites with clinical parameters was examined. In a longitudinal study, patients were followed for 3 years and survival of the patients was examined in relation with these vitamin D metabolites.

Results: Serum 25D concentrations were 12.0 ± 4.0 ng/ml, being hypovitaminosis D (<30 ng/ml) in all patients. Serum 1,25D concentrations were 14.7 ± 8.7 pg/ml, being lower than normal ranges (60-120 pg/ml) in 93% of the patients. There was no significant differences in 25D or 1,25D between those with diabetes and without. Although there was no significant correlation between 25D and haemodialysis duration, there was a significant negative correlation between 1,25D and haemodialysis duration (r = -0.187, p = 0.042). Neither of 1,25D or 25D was significantly correlated with serum calcium or phosphate concentrations. There was a significant, positive correlation between 25D and serum albumin (r = 0.172, p = 0.0454), although there was no significant correlation between 25D and serum PTH, there was a significant, negative correlation between 1,25D and serum PTH (r = -0.310, p = 0.003). Similarly, although there was no significant correlation between 25D and serum intact PTH, there was a significant, negative correlation between 1,25D and serum alkaline phosphatase (r = -0.309, p = 0.001). There were no significant differences in serum two vitamin D metabolites between patients with (n = 65) and without VDRA treatment, nor between those with (n = 12) and without calcimimetics. In a multiple regression analysis after adjustment of age, gender, haemodialysis duration, and VDRA treatment, serum 25D concentrations were significantly, independently associated with serum albumin (β = -0.244, p = 0.0149) (R² = 0.123, p = 0.007). In a multiple regression analysis after the same adjustment, serum 1,25D concentrations were significantly, independently associated with serum intact PTH (β = -0.310, p = 0.003) (R² = 0.200, p = 0.002). In the follow-up of three year, 16
patients died. Kaplan Meier analysis revealed that there tended to be better survival in patients with higher 25D concentration (n = 52) than those with lower concentration (p = 0.1936), although no significant association was seen between 1,25D and survival.

Conclusion: These results indicate that hypovitaminosis D (low 25D<30 ng/ml) is seen in all haemodialysis patients, and in most of these patients, serum 1,25D concentrations are low. Lower serum 25D concentrations are significantly associated with lower serum albumin, i.e., poorer nutritional status. Higher serum 1,25D, even in low ranges, is significantly associated with lower intact PTH and alkaline phosphatase, i.e., lower bone metabolism status. The results suggest that, in the era of new CKD-MBD treatments with calcimimetics and new VDRA, serum 25D may represent a nutritional status, and that serum 1,25D concentrations with regard to bone metabolism may be re-considered for the assessment of CKD-MBD, particularly in regards to prevention of secondary hyperparathyroidism.

#5745
CORRELATION BETWEEN MATRIX GLA PROTEIN LEVEL AND EFFECT OF VITAMIN K2 THERAPY ON VASCULAR CALCIFICATION IN HEMODIALYSIS PATIENTS
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Background and Aims: In hemodialysis patients, vascular calcifications are precocious, frequent, and excessive. The association between the level of vascular calcifications and mortality has been described in dialysis patients. The dephosphorylated and uncarboxylated matrix GlA protein (dp-ucMGP) is an indicator of vitamin K2 status and correlates with markers of vascular calcification. It is activated by γ-glutamyl carboxylase that converts inactive matrix GlA protein into an active form, and vitamin K2 is a cofactor of this reaction. The active form of matrix GlA protein is a known inhibitor of arterial wall calcification and plays an essential role in bone turnover. The biological activity of the calcification-inhibitory matrix GlA protein can be achieved by simple administration of oral vitamin K2.

Aim: To assess the effect of vitamin K2 supplementation on vascular calcification and matrix GlA protein in hemodialysis patients. In addition, we wanted to clarify the role of vitamin K2 as prophylaxis against vascular calcification in hemodialysis patients not suffering from vascular calcifications.

Methods: The study included 112 hemodialysis adult patients not receiving vitamin K antagonists. The study was conducted at the Urology and Nephrology Center, Mansoura University. Patients who suffered from vascular calcification (68 patients) received oral 180 μg of vitamin K2 every day for one year. Uncarboxylated matrix GlA protein concentrations were quantified using ELISA before administering vitamin K2 and after 12 months of treatment.

In addition, we used an abdominal CT scan to assess aortic calcification with Agatston score. The scan was performed at the beginning of the study and after 12 months of follow-up. Patients who did not suffer from vascular calcification (44 patients) were randomly assigned to either receive oral vitamin K2 or no treatment. Uncarboxylated matrix GlA protein concentrations were quantified using ELISA at randomization and 12 months after treatment.

Aortic calcification was evaluated using Agatston score after an abdominal CT scan that was performed at the beginning and at 12 months of follow-up.

Results: There was a positive and statistically significant correlation between un-carboxylated matrix GlA protein level and vascular calcification (r = 0.64, P-value < 0.001). Among patients with vascular calcification, the baseline plasma (dp-ucMGP) significantly decreased by 21.3% after treatment of vitamin K2 for one year. Besides, the median baseline calcium score significantly decreased by 15.1% after 1 year of vitamin K2 treatment. On the other hand, patients without vascular calcification had their 1-year matrix GlA protein comparable between the two groups. Despite the reduction of matrix GlA protein in the vitamin K2 naïve group, there was no statistically significant difference. In addition, the calcium score after one year was comparable between both groups.

Conclusion: Hemodialysis patients are at risk of vascular calcification. There is a positive correlation between (dp-ucMGP) protein and vascular calcification. Supplementation of vitamin K2 is safe and improves the serum markers of its deficiency. Also, vitamin K2 supplementation slow the progression of calcification. On the other hand, there is a lack of strong evidence that vitamin K2 supplementation slows down the calcification progression in dialysis patients. Therefore, we recommend further studies to delineate the efficacy and cost-effectiveness of the drug.

#3720
ON THE DEVELOPMENT OF SOME PAIN SYNDROMES IN PATIENTS ON DIALYSIS
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Background and Aims: To study the incidence and intensity of cramps in patients with end-stage CKD during dialysis.

Method: In a cross-sectional study in 2021, 160 male and female patients on program dialysis (PD), aged 22 to 77 (53.±7.11) receiving for 7.7 ± 1.83 (1 to 25) lasting 12 ± 0.24 hours per week (average KT / V 1.4 ± 0.03) on Fresenius and B. Braun devices. The incidence of cramps was assessed according to a numeric rating scale (NRS) from 0 to 10, as well as its impact on quality of life. To identify patients with intradialytic hypotension (IDH), we used the KDOQI guidelines, which define IDH as a 20 mm Hg decrease in systolic blood pressure (BP) from the origin, assessed over 3 consecutive sessions. All patients’ blood serum was checked for phosphorus (P), calcium (Ca), parathyroid hormone (PTH).

Results: Patients were divided into 2 groups, presence 81 (51.0%) or absence 79 (49.0%) of cramps (Table 1). Among patients with diabetes, the frequency of absence of cramps is 2 times higher than among patients with diabetes (6% vs. 94%, respectively) (Table 2). Among patients with hypotension, only in 15% there were no cramps, while without hypotension 85% (Table 3). No statistically significant difference was found between the groups for any of the 3 parameters (PTH, P, Ca).

Conclusion: Painful muscle spasms have been insufficiently studied, although their impact on the quality life of dialysis patients is clinically significant.
Background and Aims: In a normal physiological state, there are many Tashkent Pediatric Medical Institute, Internal Disease, Nephrology and Barno Mirzaeva and Botir Daminov HEMODIALYSIS CHRONIC KIDNEY DISEASE RECEIVING PROGRAMMED THE COURSE OF OSTEODYSTROPHY IN PATIENTS WITH STAGE 5 #2886

THE COURSE OF OSTEODYSTROPHY IN PATIENTS WITH STAGE 5 CHRONIC KIDNEY DISEASE RECEIVING PROGRAMMED HEMODIALYSIS

Barno Mirzaeva and Botir Daminov

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Background and Aims: In a normal physiological state, there are many regulatory molecules that act as inhibitors of mineral formation to prevent the spread of tissue hardening. In patients with CKD, the levels or functions of these inhibitors may be abnormal, which in turn may predispose to or enhance ectopic calcification. To increase the effectiveness of early diagnosis of demineralization of the bone skeleton in patients with stage V chronic kidney disease receiving hemodialysis.

Method: The study included 94 CKD patients receiving hemodialysis for 15 months. The average age of the patients was 42.13 ± 12.16 years. Etiologically, the etiology of patients included in the study was diverse, with a significant predominance of chronic glomerulonephritis as the cause of CKD in 72 patients, chronic pyelonephritis in 22 patients occupied the second place among the causes of CKD, the remaining causes occurred with a single frequency. Anemia was diagnosed in 71 patients. The observation lasted 12 months. Pathological changes in phosphorus-calcium metabolism and secondary hyperparathyroidism in patients were associated with a significant decrease in bone mineral density; it was shown both for the bodies of the lumbar vertebrae and for the femoral neck, the significance of the difference from the control group for absolute values of mineral density and relative deviation.

Results: In dynamics for 6 months in the general cohort of patients, there was a significant increase in the absolute mineral density of the femoral neck by 11.38%, p < 0.01 the reliability of the difference with the baseline data, and a decrease in the degree of deviation of the mineral density index from the age norm -3.13%, p < 0.05 for the bodies of the lumbar vertebrae and -4.01%, p < 0.01 for the femoral neck, which confirms the effectiveness of osteoporosis therapy. In the present study, in 45 patients 37.5% at the time of inclusion in the study in the bodies of the lumbar vertebrae, the T-index was higher than -2.5 SD; in respect of the femoral neck – in all patients, the T was lower than 2.5 ST. The study of bone mineral density in patients with HCBP, the decrease of which reflects the syndrome of renal osteodystrophy, developing in response to secondary hyperparathyroidism, against the background of osteoporosis therapy.

Conclusion: In patients with CKD, against the background of programmed hemodialysis, there is a decrease in bone mineral density (1.93 times the bodies of the lumbar vertebrae and 2.83 times the femoral neck). The use of calcium carbonate, biphosphonate and vitamin D3 contributes to an increase in the mineral density of the femoral neck by 8.64% (p < 0.05). The introduction of sevelamer hydrochloride into the therapy regimen increases the effectiveness of therapy and increases the mineral density of the bodies of the lumbar vertebrae by 5.96% (p < 0.05) and the femoral neck by 14.04% (p < 0.05).

#3520

THE RELATIONSHIPS OF BONE TURNOVER MARKERS AND CEREBRAL WHITE MATTER ALTERATIONS IN PATIENTS UNDERGOING HEMODIALYSIS

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Background and Aims: Patients with end-stage kidney disease (ESKD) have a higher prevalence rate of cognitive impairment than the general population. ESKD patients also present a worsening brain white matter damage than healthy subjects. Some studies showed a lower bone marrow density was associated with cognitive impairment, but limited studies investigated the relationship between bone turnover biomarkers and brain white matter damage in ESKD patients.

Method: Hemodialysis participants were enrolled in two hemodialysis units from August 2016 to January 2017. Participants’ baseline characteristics, bone-turnover proteins, and Fazekas scale of brain magnetic resonance imaging (MRI) white matter lesions were recorded. Fazekas scale of periventricular lesions was defined as cerebral white matter hyperintensities in MRI from grade 0 to grade 3. Multivariable ordinal regression and logistic regression models were analyzed to identify the independent association between bone turnover proteins and the Fazekas scale of periventricular lesions.

Results: In 59 hemodialysis patients, a higher Fazekas scale of periventricular lesions was found in elderly patients and correlated to a lower Mini-Mental State Examination (MMSE). Among 8 bone turnover proteins, the serum level of sclerostin (SOST) showed a dose-response effect (P value for trend = 0.004), corresponding to a higher level of SOST correlated with a lower grade on the Fazekas scale. After full adjustment with potential confounders, a negative association between SOST and Fazekas scale of periventricular lesions remained in the ordinal regression model (Odds ratio [OR] 0.886; 95% confidence interval [CI] 0.828-0.947, P value <0.001) and in the logistic regression model (OR 0.828; 95% 0.712-0.963, P value = 0.014).

Conclusion: The circulating SOST level was negatively associated with brain white matter damage. Our study result provided a potential link between bone turnover markers and brain damage.
RELATIONSHIP BETWEEN EXTRACELLULAR WATER PERCENTAGE AND MORTALITY IN PATIENTS UNDERGOING CHRONIC HEMODIALYSIS

Silverio Rotondi, Lida Tartaglione, Adolfo Perrotta, Miriana Moscatelli, Emanuela Paoloni, Marzia Pasquali, Silvia Lai and Sandro Mazzaferrro

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Background and Aims: Chronic hemodialysis (HD) patients have a high cardiovascular and mortality risk. This is secondary to numerous risk factors specific to the HD population. Relevant on cardiovascular disease and mortality in HD, is the sodium intake and the extent of the sodium pool of patients. An increase in the total sodium pool may have a negative action on cardio vascular system directly and mediated by the increase in total body water associated with an increase in the sodium pool. However, the assessment of the sodium pool in patients is clinically complex. Some evidence has suggested that the assessment of the extracellular water percentage (ECW%) in the HD patient may be a marker of the sodium pool. In fact, the increase in extracellular sodium is followed by a shift of water from the intracellular compartment to the extracellular compartment. The assessment of ECW% could therefore identify patients with greater ECW increase secondary to the greater sodium pool and therefore with high clinical risk. Primary aim: to evaluate the relationship between extracellular water percentage and mortality in patients on chronic hemodialysis.

Method: This is an observational prospective cohort study. The inclusion criteria were chronic HD for at least three months, minimum follow-up of six months, age greater than 18 years. In all of the included patients we performed the bioimpedance examination with a dedicated instrument after hemodialysis session, after the long interdialytic interval, for the evaluation of ECW (L), ECW (%), TBW (L/m), ICW (L). The protocol involved dividing the population into two groups based on normal or pathological ECW%, according to values calculated by gender and age and then evaluating the incidence of death in a 36-month follow-up.

Results: We enrolled 101 patients with an average age of 71 ± 14 years in HD for 51 ± 15 months. During the average follow-up of 19 months we observed 31 deaths (30% of the population) with an annual mortality of 15%. ECW % correlated positively with age (R: 0.498 P<0.01) and differential post-dialysis pressure (R: 0.260; P<0.01). 41 patients (aged 64 ± 13 years) had a normal ECW% (ECW-N) and 60 patients (75±13 years) had pathological ECW% (ECW-P). ECW-P patients had an increased mortality respect to ECW-N patients (60% vs 20%; P<0.01). The survival curve confirmed higher mortality in the ECW-P group (log-rank test P=0.02). These results were confirmed in a sub-analysis of two age-matched ECW-N (n. 20 age 64±10 years) vs ECW-P (n. 20 age 65±12 years) subgroups (log-rank test P<0.05).

Conclusion: Our data showed that ECW% identifies HD patients at increased mortality risk in 36-month follow-up. These data are also confirmed in age-related subgroups, suggesting the ECW% assessment can be a simple and useful parameter to evaluate for targeted treatment choices in patients with chronic HD.

AMBULATORY BLOOD PRESSURE LEVELS AFFECT THE ASSOCIATION OF INTRADIALYTIC HYPERTENSION WITH ADVERSE CARDIOVASCULAR EVENTS IN HEMODIALYSIS PATIENTS

Foteini Iatridi1, Marieta Theodorakopoulou1, Areti Georgiou1, Antonios Karpetas2, Eva Pella3, Ioannis Tsouchnikas4, Panagiotis Giamalis1, Alkaterini Papagiani2 and Pantelis Sarafidis1

1Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Thessaloniki, Greece and 2Therapeutiki Hemodialysis Unit, Thessaloniki, Greece

Background and Aims: Patients with intradialytic hypertension (IDH) display also higher ambulatory blood pressure (BP) levels during the whole 44-h interdialytic interval compared to patients without the phenomenon. Sustained high 44-h ambulatory BP levels is a potential risk factor for cardiovascular events and mortality in these individuals. The aim of this study is to evaluate the influence of elevated 44-h BP levels on the high cardiovascular risk of individuals with IDH.

Method: A total of 242 hemodialysis patients with valid 48-h ABPM with Mobil-O-Graph-NG had an extended follow-up for a median of 57.8 months. HD was defined as: rise in SBP greater or equal to 10 mmHg from pre-to-post dialysis and post-dialysis SBP greater or equal to 150 mmHg. The primary end-point was a composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, resuscitation after cardiac arrest, hospitalization for heart failure, coronary or peripheral revascularization procedure. The secondary endpoint was cardiovascular mortality.

Results: 5 patients with and 197 without were included in this prospective analysis. Cumulative freedom from the primary and secondary endpoint was significantly lower for patients with IDH (log-rank p = 0.019), while freedom from the secondary endpoint did not differ significantly between the two groups (log-rank p = 0.321). Patients with IDH presented a significantly higher risk for the composite endpoint (HR = 1.651, 95%CI[1.083, 2.516]), while, however, showing a significant difference in the risk for cardiovascular mortality (HR = 1.320, 95%CI[0.762, 2.288]). After adjustment for 44-h SBP, the association of IDH with the primary endpoint slightly attenuated, while the association with the secondary outcome had no significant changes (HR = 1.421, 95%CI[0.906, 2.228] and HR = 1.270, 95%CI[0.708, 2.276], for primary and secondary outcome respectively).

Conclusion: IDH is associated with higher risk for adverse cardiovascular outcomes. High ambulatory BP during the interdialytic interval contributes to the excess cardiovascular risk observed in this population.

EFFECT OF IMMUNO-NUTRITION ON SYSTEMIC INFLAMMATION AND MUSCLE MASS IN A HAEMODIALYSIS POPULATION: A FEASIBILITY STUDY

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1Centre for Kidney Research and Innovation, Academic Unit for Translational Medical Sciences, School of Medicine, University of Nottingham, Derby, United Kingdom, 2Academic Unit of Injury, Recovery and Inflammation Sciences, School of Medicine, University of Nottingham, Derby, United Kingdom and 3Department of Renal Medicine, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, United Kingdom

Background and Aims: Decreased skeletal muscle mass (SMM) and systemic inflammation are frequent complications associated with poor outcomes in people receiving haemodialysis. Although these problems are widely acknowledged, it has become clear that simply providing conventional oral nutritional supplements (ONS) is often not effective in increasing SMM. This is partly because systemic inflammation causes "anabolic resistance", a condition that inhibits optimal rates of muscle protein synthesis being achieved despite adequate protein intake/availability. Immuno-nutrition supplements are high in energy and protein (similar to conventional ONS), but also contain a unique combination of nutrients that have shown to reduce inflammation in people with cancer. Therefore, the purpose of this feasibility study is to explore the potential effect of immuno-nutrition on systemic inflammation and SMM in a haemodialysis population.

Method: This was a single-centre, non-randomised, interventional feasibility study where 14 haemodialysis patients received 1 sachet per day (74 g dissolved in 125 ml of water) of a commercially available immuno-nutrition supplement (Oral Impact®, Nestlé) for 6 weeks. C reactive protein (CRP), skin autofluorescence (SAF, a marker of systemic inflammation), body composition assessment using bioelectrical impedance analysis (InBody 770), weight, body mass index (BMI), handgrip strength (HGS), routine biochemical variables (pre-dialysis), and energy, protein and fat intake were measured at baseline and after the 6-week intervention.

Results: Mean participant age was 69 ± 13 years and median dialysis vintage was 26 (interquartile range 9 to 94) months. Twelve participants (86%) were male and of white ethnicity. Diabetes and heart disease were present in 9 (64%) and 7 (50%) participants, respectively. Adherence to the intervention was high (98%). Participants reported that the taste of the supplement was nice and acceptable. No safety issues were observed in terms of development of hyperkalaemia or fluid overload. We observed a significant increase in HGS and urea. Fat-free body mass and SMM remained stable, while body weight, BMI and body fat mass tended to increase, though changes did not reach statistical significance. Markers of systemic inflammation and dietary intake did not show any significant change (Table 1).

Conclusion: In this interventional feasibility study, we observed that provision of an immuno-nutrition supplement was associated with an improvement in muscle strength, as well as maintenance of SMM. This suggests that immuno-nutrition may be effective in preventing SMM loss over time in people on haemodialysis. The findings of this feasibility study will help design a randomised controlled clinical trial investigating whether immuno-nutrition supplementation can improve SMM and other nutritional markers, and to evaluate the impact on long-term outcomes, including quality of life.
Table 1: Changes in markers of systemic inflammation and nutritional status from baseline to 6 weeks of treatment with an immuno-nutrition supplement.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>6 weeks</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C reactive protein (mg/L)</td>
<td>7.6 (4.8 to 32.3)</td>
<td>7.3 (2.9 to 22.0)</td>
<td>0.8</td>
</tr>
<tr>
<td>Skin autofluorescence (AU)</td>
<td>4.0 (3.2 to 4.6)</td>
<td>3.5 (3.1 to 4.0)</td>
<td>0.2</td>
</tr>
<tr>
<td>Handgrip strength (kg)</td>
<td>23.8 (17.1 to 27.9)</td>
<td>24.4 (18.9 to 30.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Post-dialysis weight (kg)</td>
<td>68.1 (60.8 to 81.7)</td>
<td>70.2 (61.0 to 84.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.7 (21.8 to 27.0)</td>
<td>24.2 (21.8 to 27.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>Fat-free body mass (kg)</td>
<td>49.2 (46.2 to 61.3)</td>
<td>50.2 (44.5 to 59.9)</td>
<td>0.7</td>
</tr>
<tr>
<td>Skeletal muscle mass (kg)</td>
<td>26.7 (25.3 to 33.6)</td>
<td>26.7 (23.9 to 32.3)</td>
<td>0.7</td>
</tr>
<tr>
<td>Body fat mass (kg)</td>
<td>17.9 (13.2 to 23.6)</td>
<td>21.1 (13.0 to 24.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>13.1 (10.7 to 15.0)</td>
<td>18.7 (14.9 to 23.0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Serum creatinine (μmol/L)</td>
<td>563 (425 to 666)</td>
<td>611 (498 to 706)</td>
<td>0.3</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>30.0 (29.0 to 35.0)</td>
<td>32.0 (29.5 to 33.3)</td>
<td>0.9</td>
</tr>
<tr>
<td>Energy intake (kcal/kg/d)</td>
<td>26.6 (22.5 to 33.8)</td>
<td>27.2 (22.3 to 31.6)</td>
<td>0.9</td>
</tr>
<tr>
<td>Protein intake (g/kg/d)</td>
<td>1.0 (0.9 to 1.3)</td>
<td>1.1 (1.0 to 1.4)</td>
<td>0.1</td>
</tr>
<tr>
<td>Fat intake (g/day)</td>
<td>86.0 (57.4 to 101.7)</td>
<td>72.2 (57.6 to 85.7)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Data expressed as median (interquartile range).
Abbreviations: AU, arbitrary units.

#4306
DIALYSIS ADEQUACY AND INCIDENT ATRIAL FIBRILLATION IN HEMODIALYSIS PATIENTS
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1 Yonsei University College of Medicine, Department of Internal Medicine, Rep. of South Korea, 2 Health Insurance Review and Assessment Service, Healthcare Review and Assessment Committee, Rep. of South Korea and 3 Health Insurance Review and Assessment Service, Quality Assessment Department, Rep. of South Korea

Background and Aims: Atrial fibrillation (AF) can lead to stroke, heart failure, and mortality, and has a greater prevalence in dialysis patients than in the general population. Several studies have proposed that uremic toxins might promote AF development. However, the association between dialysis adequacy and incident AF has not been well established.

Method: In this retrospective study, we analyzed 27,475 patients receiving maintenance hemodialysis, included in the Periodic Hemodialysis Quality Assessment by Health Insurance Review & Assessment Service (HIRA). The main exposure was single pooled Kt/V and the primary outcome was the development of AF.

Results: During a median follow-up of 4.8 years, incident AF occurred in a total of 4,229 (15.4%) patients. Participants with higher single pooled Kt/V tended to have lower AF incidence. In survival analysis, there was a graded association between the risk of incident AF and single-pool Kt/V quartiles: subdistribution hazard ratios and 95% confidence intervals (CI) for the second, third, and the highest quartile compared with the lowest quartile were 0.90 (95% CI, 0.83-0.98), 0.85 (95% CI, 0.78-0.93), and 0.80 (95% CI, 0.73-0.89), respectively. When treating single-pool Kt/V as a continuous variable, a similar association was found. In addition, the risk of incident AF in the highest quartile of urea reduction ratio was 0.83-fold (95% CI, 0.76-0.91) lower than in the lowest quartile. Sensitivity analyses showed consistent results. This association was more pronounced in men.

Conclusion: As the part of the Joint Project on Quality Assessment Research by HIRA, this nationwide cohort study showed that lowering uremic toxin burden through increased dialysis clearance could be associated with a lower AF development risk in patients receiving maintenance hemodialysis.

Table 1: Incidence rates of atrial fibrillation according to quartile of spKt/V.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Total</th>
<th>Q1 (&lt;1.33)</th>
<th>Q2 (1.33 to 1.49)</th>
<th>Q3 (1.50 to 1.70)</th>
<th>Q4 (≥1.70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of participants, n (%)</td>
<td>27475</td>
<td>6869</td>
<td>6869</td>
<td>6869</td>
<td>6869</td>
</tr>
<tr>
<td>Person-year</td>
<td>131808</td>
<td>32782</td>
<td>32516</td>
<td>33179</td>
<td>33331</td>
</tr>
<tr>
<td>Incident Atrial fibrillation</td>
<td>4229 (15.4)</td>
<td>1122 (16.3)</td>
<td>1064 (15.5)</td>
<td>1050 (15.3)</td>
<td>993 (14.5)</td>
</tr>
<tr>
<td>Incidence rate per</td>
<td>32.1</td>
<td>34.2</td>
<td>32.7</td>
<td>31.7</td>
<td>29.8</td>
</tr>
<tr>
<td>1000 person-years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>9286 (33.8)</td>
<td>2328 (33.9)</td>
<td>2404 (35.0)</td>
<td>2312 (33.7)</td>
<td>2242 (32.6)</td>
</tr>
<tr>
<td>Incidence rate per 1000 person-years</td>
<td>70.5</td>
<td>71.0</td>
<td>73.9</td>
<td>69.7</td>
<td>67.3</td>
</tr>
</tbody>
</table>

Abbreviations: spKt/V, single-pool Kt/V.
Table 2: Associations of dialysis adequacy with incident atrial fibrillation.

<table>
<thead>
<tr>
<th>Dialysis adequacy</th>
<th>Model 1</th>
<th></th>
<th>Model 2</th>
<th></th>
<th>Model 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sHR (95% CI)</td>
<td>P value</td>
<td>sHR (95% CI)</td>
<td>P value</td>
<td>sHR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>spKt/V</td>
<td></td>
<td></td>
<td>spKt/V</td>
<td></td>
<td></td>
<td>spKt/V</td>
</tr>
<tr>
<td>Quartile</td>
<td></td>
<td></td>
<td>Quartile</td>
<td></td>
<td></td>
<td>Quartile</td>
</tr>
<tr>
<td>Q1 (&lt;1.33)</td>
<td>1.00 (Reference)</td>
<td>-</td>
<td>1.00 (Reference)</td>
<td>-</td>
<td>1.00 (Reference)</td>
<td>-</td>
</tr>
<tr>
<td>Q2 (1.33 to 1.49)</td>
<td>0.92 (0.84-0.99)</td>
<td>0.039</td>
<td>0.90 (0.82-0.98)</td>
<td>0.013</td>
<td>0.90 (0.83-0.98)</td>
<td>0.015</td>
</tr>
<tr>
<td>Q3 (1.50 to 1.69)</td>
<td>0.89 (0.81-0.97)</td>
<td>0.007</td>
<td>0.85 (0.78-0.93)</td>
<td>&lt;0.001</td>
<td>0.85 (0.78-0.93)</td>
<td>0.001</td>
</tr>
<tr>
<td>Q4 (≥1.70)</td>
<td>0.83 (0.76-0.92)</td>
<td>&lt;0.001</td>
<td>0.80 (0.73-0.89)</td>
<td>&lt;0.001</td>
<td>0.80 (0.73-0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Continuous</td>
<td>per 0.1 increase</td>
<td></td>
<td>0.98 (0.97-0.99)</td>
<td>&lt;0.001</td>
<td>0.98 (0.96-0.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>URR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile</td>
<td></td>
<td></td>
<td>Quartile</td>
<td></td>
<td></td>
<td>Quartile</td>
</tr>
<tr>
<td>Q1 (&lt;67.3)</td>
<td>1.00 (Reference)</td>
<td>-</td>
<td>1.00 (Reference)</td>
<td>-</td>
<td>1.00 (Reference)</td>
<td>-</td>
</tr>
<tr>
<td>Q2 (67.3 to 71.5)</td>
<td>0.93 (0.86-1.00)</td>
<td>0.058</td>
<td>0.93 (0.86-1.01)</td>
<td>0.065</td>
<td>0.93 (0.86-1.01)</td>
<td>0.076</td>
</tr>
<tr>
<td>Q3 (71.6 to 75.8)</td>
<td>0.88 (0.81-0.96)</td>
<td>0.002</td>
<td>0.88 (0.81-0.95)</td>
<td>0.002</td>
<td>0.88 (0.81-0.96)</td>
<td>0.003</td>
</tr>
<tr>
<td>Q4 (≥75.9)</td>
<td>0.83 (0.75-0.90)</td>
<td>&lt;0.001</td>
<td>0.83 (0.76-0.91)</td>
<td>&lt;0.001</td>
<td>0.83 (0.76-0.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Continuous</td>
<td>per 10 increases</td>
<td></td>
<td>0.87 (0.83-0.92)</td>
<td>&lt;0.001</td>
<td>0.87 (0.83-0.92)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: Model 1: minimally adjusted for age and sex. Model 2: Model 1 + medical aid, dialysis vintage, body mass index, predialysis systolic blood pressure, ultrafiltration, and a history of diabetes mellitus, congestive heart failure, myocardial infarction, cerebrovascular disease, and chronic obstructive pulmonary disease. Model 3: Model 2 + the use of medications (antihypertensive drugs and statins), and laboratory measurements (hemoglobin, serum albumin, and serum calcium).

Abbreviations: sHR, subdistribution hazard ratio; CI, confidence interval; spKt/V, single pooled Kt/V; URR, urea reduction ratio.
duration of the dialysis session emerged as risk factors for IDH. Indeed, when the number of antihypertensives increased by 1 unit, the IDH score was multiplied on average by 2.74 ($p < 0.001$), and when the session duration (h) increased by 0.1 units, the IDH score was multiplied by an average of 1.39 ($p = 0.019$). Residual natriuresis appeared as a protective factor against interdialytic weight gain, because when urinary sodium (mEq/l) increased by 10 units, mean interdialytic weight gain (kg) decreased by an average of -0.116 ($p = 0.043$).

**Conclusion:** Intradialytic hypertension is common and multifactorial. Antihypertensive combination therapy, usually reflecting resistant high blood pressure, is a major risk factor. The present study, at the expense of the definition criteria used, did not find significant associations with peridialytic natremia and residual natriuresis. However, the latter remains protective against interdialytic hypervolemia. Hence, the need for its preservation.

#4472

**POLYMORPHISMS OF THE GENE FOR GALECTIN-3 IN PATIENTS IN THE TERMINAL PHASE OF RENAL INSUFFICIENCY**

Zoran Kovacevic1, Tatjana Lazarevic2, Biljana Ljubic3, Petar Canovic4, Marina Miletic Kovacevic3, Nela Maksimovic3, Marina Gazdic Jankovic5, Svetlana Djukic5 and Milos Glisic6

1 University Clinical Center, Department of Nephrology, Kragujevac, Serbia, 2 Faculty of Medical Sciences, University of Kragujevac, Department of Internal Medicine, Kragujevac, Serbia, 3 Faculty of Medical Sciences, University of Kragujevac, Department of Genetics, Kragujevac, Serbia, 4 Faculty of Medical Sciences, University of Kragujevac, Department of Biochemistry, Kragujevac, Serbia, 5 Faculty of Medical Sciences, University of Kragujevac, Department of Hystology and Embryology, Kragujevac, Serbia, 6 Faculty of Medicine, University of Belgrade, Department of Human Genetics, Belgrade, Serbia, 7 Faculty of Medical Sciences, University of Kragujevac, Department of Genetics, Kragujevac, Serbia, 8 Faculty of Medical Sciences, University of Kragujevac, Department of Internal Medicine, Kragujevac, Serbia and 9 Faculty of Medical Sciences, University of Kragujevac, Department of Physiology, Kragujevac, Serbia

**Background and Aims:** Chronic kidney disease (CKD) is a major health problem worldwide. The last stage of CKD is end-stage renal disease (ESRD), which is characterized by a progressive decrease in glomerular filtration rate (GFR). End-stage renal failure is often complicated by anemia, uremic cardiomyopathy, and renal osteodystrophy, which can be fatal. Therefore, it is necessary to identify the risk factors that can lead to ESRD or death. In addition to well-defined early markers such as diabetes, hypertension, and obesity, it is necessary to identify other markers that would help in the prediction of the disease. It has been shown that genetic factors also have an influence on renal function, pathogenesis, and disease progression, which is confirmed by the results of genome-wide association studies (GWASs). The results of GWASs show that glomerular filtration rate and renal function are affected by several gene loci. Galectin 3 (Gal-3) is the only representative chimera type of the galectin family, which forms a pentameric structure on
the cell surface after binding to glycoproteins or glycolipids. The results of numerous studies have shown that Gal-3 plays a significant role in fibrosis, inflammation, and proliferation. Increased circulating levels of Gal-3 have been associated with various diseases, including cancer, immunological disorders, and cardiovascular disease.

Method: A total of 108 ESRD patients and 38 healthy controls were enrolled in the study. Genotyping of LGALS3 geners 4644, rs4652, and rs11125 polymorphisms was performed by polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP).

Results: By multivariate logistic regression analysis, we found that LGALS3 rs4644 CC and rs4652 AA genotypes were significantly associated with a higher risk for lower hemoglobin, higher level of parathyroid hormone, and also occurrence of diabetes mellitus and arterial hypertension. The CAA haplotype was significantly more common in patients with diabetes, low hemoglobin level, and normal PTH level. It has been observed as well that the ACT haplotype was more common in patients with low glomerular filtration, lowPTH, and normal hemoglobin level.

Conclusion: We found that the LGALS3 rs4644 and rs4652 gene polymorphism may be involved in the pathogenesis and appearance of complications in ESRD patients and thus could be considered a new genetic risk factor in this population.

THE USE OF REGDANVIMAB FOR THE PREVENTION OF SEVERE COVID-19 IN PATIENTS ON HEMODIALYSIS

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1City Clinical Hospital named after S.P.Botkin, Moscow, Russia and 2Federal State Budgetary Educational Institution of Further Professional Education

"Russian Medical Academy of Continuous Professional Education" of the Ministry of Healthcare of the Russian Federation., Moscow, Russia

Background and Aims: A new coronavirus infection has become a serious threat leading to increased mortality worldwide. COVID-19 is an acute airborne disease caused by severe acute respiratory syndrome virus (SARS-CoV-2). Evolution of the virus, emergence of new mutant strains, changes in virulence dictate the need to search for new tools both in treatment and prevention of severe disease. The aim of our study was evaluation of the efficacy of Regdanvimab (Regkirona, Samsung BioLogics) to prevent severe COVID-19 in patients receiving ambulatory hemodialysis in the period of increasing morbidity.

Method: The study included 20 patients on program hemodialysis, mean age 54.9±17.6 years, vaccinated or who underwent COVID-19 more than six months ago. All subjects of the study received Regkirona at a standard dose of 40 mg/kg of body weight intravenously once at the end of the hemodialysis procedure after the physician assessed the feasibility of prophylaxis. All subjects were assessed for humoral immunity before Regkirona administration and after Regkirona administration according to the level of total SARS-CoV-2 IgG and IgG antibodies to the subunit of the S1 receptor-binding domain of the SARS-CoV-2 protein.

Results: Total SARS-CoV-2 IgG level and IgG level of antibodies to SARS-CoV-2 receptor-binding subunit S1 was 83.9±69.5 U/ml and 260.7±199.5 BAU/ml respectively before drug administration. During the 6-month follow-up period from July to November 2022, which paralleled the next round of increased morbidity, four patients with SARS-CoV-2 PCR test positive reported mild to moderate symptoms of SARS (marked weakness, fever, loss of smell, catarrhal symptoms, cough, shortness of breath, and chest pain unassociated with other causes). None of the subjects required hospitalization. We evaluated IgG antibody titers to the receptor-binding domain of the SARS-CoV-2 protein subunit S1 after 1, 3 and 6 months and demonstrated a nonlinear decline titers from 5104±2257.1 BAU/ml, 1988.7±1440.4 BAU/ml
to 407.8±350.2 BAU/ml respectively, which may indirectly reflect short half-life of Regdanvimab.

Conclusion: The results of our study showed the efficacy of Regdanvimab to prevent the severe disease of COVID-19 in high-risk patients during the period of rising morbidity.

#4880
SUCCESSFUL LIMB SALVAGE IN A CHALLENGING PATIENT ON DIALYSIS BY IMPLANTATION OF AUTOLOGOUS PERIPHERAL BLOOD MONONUCLEAR CELLS: A CASE REPORT
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SS Annunziata Hospital, Nephrology Division, Chieti, Italy

Background and Aims: Peripheral arterial disease (PAD) is an extremely common condition in patients with End-Stage Renal Disease (ESRD) on dialysis. Concomitant comorbidity such as diabetes may be associated with complex vascular dysfunction, and ESRD itself is a recognized risk factor for PAD leading to non healing ulcers and lower limb amputation, which occurs in a high rate of patients [1]. Despite improvement in endovascular techniques for lower extremity revascularization, the incidence of limb salvage among dialysis patients remains poor. Furthermore, lower extremity amputation in these patients is associated with higher mortality rates [2], in addition to important social and economic implications. In this Case Report, an emergent therapy approach was applied aiming to limb salvage in a 74 years old female patient on hemodialysis suffering from lower extremity critical ischemia in diabetic foot infection, otherwise candidate for major amputation, after ineffective angioplasty and Negative Pressure Wound Therapy (NPWT).

Method: After surgical debridement of the ischemic lesion, an innovative therapeutic approach [3] was performed. It consisted in implantation, in the perifemoral area of the affected lower limb, of a concentrate of autologous peripheral blood mononuclear cells (PBMCN) taken from 120 ml of peripheral blood of the patient, by using a selective filtration separation system. This procedure was managed in the operating room and was repeated three times at intervals of 15 days from each other. Since concomitant osteomyelitis occurs in the ischemic diabetic foot under treatment, it was managed with a 2-dose regimen of weekly Dalbavancin, reaching infection control. The patient was followed twice a week for 7 months for regular medications.

Results: After the treatment approach, the granulation tissue improved gradually, obtaining complete surgical wound healing. Since toess gangrene occurs, amputation of the toes was necessary, but limb rescue was successfully reached.

Conclusion: The autologous implantation of PBMCN resulted in limb salvage in this patient on dialysis affected by critical peripheral arterial disease in diabetic foot. This approach has not been described in literature among patients on dialysis, despite the higher mortality rate associated with lower limb amputation in these patients. It seems to be a very promising therapy, with the potential to modify the natural history of no-options critical limb with diabetes complications, in terms of major amputation and overall survival rates. After thorough validation, the reported management could be considered for similar cases.

REFERENCES

#5584
FIRST EXPERIENCES IN REAL LIFE WITH DIFELIKEFALIN IN GABAPENTIN RESISTANT UREMIC PRURITUS (CKD-aP)
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Background and Aims: Chronic kidney disease associated pruritus (CKD-aP) has been recognized for over a century. The actual proposed off-label therapeutic option is gabapentin, that showed relevant efficacy in some small trial. Recently difelikefalin (DFK), a k-opioid receptor agonist, has been the first FDA and EMA approved drug for CKD-aP treatment. We report the first three treated patients suffering gabapentin-resistant CKD-aP in our dialysis center.

Method: Since March 2022, 2 patients have been treated with DFK. Before starting the treatment and every week thereafter until now, the patients completed the following scales: Worst-Itch Numerical rating scale (WI-NRS, 0 = no Itch, 10 = worst itch), and the sleep quality scale (SQS) (from 0 = worse to 10 = best quality).

Results: Case 1 (Male, 58-years old). The patient started hemodialysis (HD) 5 years ago. He was suffering gabapentin resistant CKD-aP (WI-NRS 10, SADS = C, SQS = 3). As soon as DFK was available the patient started DFK 0.5 mcg/kg/Every HD Session. There was immediate and persistent treatment efficacy. After 1 month gabapentin was stopped and after 4 months of DFK therapy, WI-NRS = 0 and SQS = 10, in the absence of side effects. After 6 months DFK was stopped but 4 weeks later CKD-aP returned (WI-NRS 7, SQS = 7). DFK was administered again with immediate response (Fig.1a). Case 2 (Female, 81-years-old). The patient started HD 5 years ago. Two years after she started suffering moderate to severe gabapentin-resistant CKD-aP. Before starting DFK 0.5 mcg/kg/Every HD WI-NRS = 6 and SQS = 3. In the next weeks we obtained a progressive reduction of CKD-aP. After 3 months WI-NRS = 3, SQS = 6. At 6 month follow up CKD-aP ameliorated significantly (WI-NRS 0 and SQS = 9) (Fig. 1b). Case 3. (Male, 75-years-old). The patient suffers initial dementia. He started hemodialysis 1 year ago. He presented with scratching lesions on his arms and legs and complained of itching. After an initial period treated with Gabapentin without success Difelikefalin was tried. At the first assessment WI-NRS 7 and SQS 5; after an initial apparent benefit the rating scales were particularly fluctuating. There was also a dissociation between the improvement of the scratching lesions and the persistence of high values on the WI-NRS (after 3 months WI-NRS = 8). At 6 months’ follow-up the patient presented WI-NRS 9 and SQS 6 (Fig. 1c). The scratching lesions had almost disappeared.

Conclusion: Our initial experience with DFK in the treatment of CKD-aP in 3 gabapentin-resistant patients seems to recognize a remarkable efficacy of the drug. In particular, Case 1 showed a complete, immediate and lasting response, whereas no other drug had been able to improve very severe CKD-aP. Case 2 showed a slowly reduction but achieved complete response at 6 months. In Case 3 the improvement of the scratching lesions suggests a partial benefit of DFK, but to date no relevant results with the adopted scales has been achieved. In conclusion DFK seems to show promising efficacy particularly in CKD-aP resistant to gabapentin. In older patients with cognitive problems the actual tools identified to measure CKD-aP seems inadequate.
Exercise Physiology & Biochemistry Laboratory, Department of Sport Sciences at Thessaloniki, Greece and "Papageorgiou General Hospital, Department of Nephrology, Greece".

Background and Aims: Cardiac arrhythmias and sudden death are the leading causes of cardiovascular mortality in end-stage-kidney-disease (ESKD). Autonomic dysfunction contributes to the arrhythmogenic background of ESKD patients. This is the first study to compare linear and non-linear heart-rate-variability (HRV) indices between hemodialysis (HD) and peritoneal (PD) patients, both at rest and in response to mental- and physical-stimulation maneuvers.

Method: Thirty-four HD and 34 PD patients matched for age, sex, and dialysis-vintage, as well as 17 age- and sex-matched controls were studied. Autonomic function was examined by linear and non-linear-HRV indices. Heart-rate was recorded continuously with Finometer-PRO at rest and during orthostatic, mental-arithmetic, sit-to-stand, and handgrip-exercise tests.

Results: No significant between-group differences were observed in resting HRV indices (RMSSD: HD:57.1±81.1 vs PD:69.6±113.4ms; p = 0.792) except for DFA-a1 index (HD:0.87±0.40 vs PD:0.70±0.20, p = 0.047). All HRV indices during the mental arithmetic test (RMSSD HD:128.2±346.0 vs PD:87.5±150.0ms; p = 0.893) and the physical stress tests were similar between HD and PD patients. Both dialysis groups presented similar patterns of HRV responses to orthostatic and handgrip exercise tests; however, after the sit-to-stand test RMSSD, SD1,SD2 and DFA-a2 indices were higher compared to rest only in HD patients (RMSSD: HD:57.1±81.1 vs PD:126.7±185.7ms, p = 0.028), suggesting a greater difficulty of HD patients in recovering normal ANS function following a physical stress-test.

Conclusion: HRV indices at rest and after mental and physical stimulation did not differ between HD and PD patients, however the ANS response following the sit-to-stand test was more impaired in HD. These findings suggest that ANS dysfunction is not largely affected by dialysis modality but small differences in normal ANS recovery may exist.

Heart rate variability at rest and in response to physical and mental stress: a comparative study between hemodialysis and peritoneal dialysis patients

#6068

ERYTHROPOIETIN RESISTANCE IN HAEMODIALYSIS PATIENTS POST SARS-COV-2 INFECTION

Guido Gembilo, Vincenzo Labbrozetta, Luigi Peritore, Alfonso Edoardo Giuffrida, Adolfo Romeo, Antonella Lipari, Claudia Spinella, Alessia Tigan, Eugenia Spallino, Vincenzo Calabrese and Domenico San FOLLOW

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Background and Aims: During the SARS-CoV-2 pandemic, patients undergoing chronic haemodialysis treatment were at particularly high risk of infection. This was due to their vulnerability given their state of immunosuppression and multiple comorbidities, on the one hand, and the circumstances that limited physical distancing during treatment, on the other. Even after negativation, patients with a previous infection experience symptoms such as persistent asthenia, muscle weakness, widespread pain and deterioration in perceived health status. In our study, we aimed to investigate the parameters of anaemia and the change in the erythropoietin resistance index (ERI) in haemodialysis patients with previous infection.

Method: We included 25 patients with a dialysis age >6 months, giving a total of 72 measurements. The distribution was assessed with the Kolmogorov-Smirnov test and with a graphical evaluation of the same. We calculated the ERI 3 months before the date of infection and in the 3 and 6 months after. These data were also compared with a control group. Patients were divided into 2 groups: Group A (patients with previous infection) and Group B (control group). Linear mixed models were performed to calculate the slope between the group and the ERI index.

Results: No statistically significant differences were found. The LMMs showed a significant interaction between the scores obtained at the visits performed and the study group, with a decrease in ERI over time of 0.21 at each visit.

Conclusion: Our results show that patients with previous Covid 19 infection have higher resistance to erythropoietin and require higher doses even months after infection. The response to erythropoietin in this population should be investigated in studies with larger cohorts, as anaemia is an important factor affecting the quality of life of our patients.

Erythropoietin resistance in haemodialysis patients post SARS-COV-2 infection

#6829

DIFFERENTIAL LIPIDIC PROFILE WITH THE USE OF CITRATE OR ACETATE DIALYSATES

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Background and Aims: Unlike other high-cardiovascular-risk populations, the efficacy obtained from lipid-lowering therapy remains uncertain in dialysis-dependent chronic kidney disease (DD-CKD) patients. This is probably due to the exclusion in clinical trials of patients with very high LDL levels, their population heterogeneity, accompanying cardiovascular morbidities, and the higher mortality risk explained partly by chronic inflammation. The latter has been associated with the accumulation of uremic toxins, membrane biocompatibility, and acetate-based dialysates, which promote inflammation. Different dialysate weak acidifying agents such as lactic, pyruvic, hydrochloric, or citric acids have surged as less-inflammatory alternatives to acetate. This study aims to evaluate the effects of the metabolism of acetate and citrate in the lipidic profile of DD-CKD patients.

Method: In a unicentric, cross-over prospective study, we compared the lipidic profile by assessing the plasma levels of total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG), high-density (HDL) and very low-density (VLDL) lipoprotein cholesterol, and lipoprotein (a) (Lp[a]) comparing the use of citrate (CD) vs. acetate (AD) as dialysate buffers, after twelve sessions with each one. Prealbumin was also measured to rule out malnutrition as a potential confounding factor. Prevalent (i.e., dialysis vintage >3 months) adult patients on maintenance haemodialysis were included. The dialysis prescription parameters and additional medical treatments remained unchanged during their sessions with both dialysates. Quantitative values are reported with mean and standard deviation. Normal distribution was assessed with the Shapiro-Wilk test, and the comparisons were made with the Student's paired T-test or Wilcoxon's signed-rank test, accordingly. A two-sided p-value ≤0.05 was considered statistically significant.

Results: After twelve dialysis sessions with CD, compared to AD, there was a statistically significant decline in TG and HDL and an increase in LDL. There was also a notable but non-significant reduction in VLDL (Table 1).

Conclusion: There were noteworthy differences in the lipid profile that can only be attributed to the change of dialysis fluid, as we avoided inter-individual (with a cross-over design) and intra-individual (different inflammatory or nutritional profiles would not be expected with this short-term setting)
Table 1: Measured lipidic plasma levels after twelve dialysis sessions with each dialysate.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acetate</th>
<th>Citrate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>140.33 ± 30.56</td>
<td>142.33 ± 33.4</td>
<td>0.624</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>67.05 ± 30.53</td>
<td>75.71 ± 31.01</td>
<td>0.042</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>110.38 ± 35.79</td>
<td>97.86 ± 29.69</td>
<td>0.046</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>51.19 ± 11.25</td>
<td>47.14 ± 11.99</td>
<td>0.013</td>
</tr>
<tr>
<td>VLDL cholesterol (mg/dL)</td>
<td>22.14 ± 7.36</td>
<td>19.67 ± 5.97</td>
<td>0.057</td>
</tr>
<tr>
<td>Lp(a) (mg/dL)</td>
<td>26.21 ± 30.45</td>
<td>27.04 ± 34.21</td>
<td>0.617</td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>26.21 ± 7.57</td>
<td>24.89 ± 8.09</td>
<td>0.096</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein a; TG, triglycerides; VLDL, very-low-density lipoprotein.

variabilities. Further studies must elucidate if the short-term changes induced in the lipidic profile of DD-CKD patients by the dialysate’s weak acid translate into clinical implications.

#6884

THE BARRIERS TO TRANSPLANTATION IN OUR DIABETIC HAEMODIALYSIS POPULATION AT THE LEEDS TEACHING HOSPITALS NHS TRUST

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Background and Aims: According to the 24th Annual Renal Registry Report, diabetes is the most common identified primary renal disease in patients starting renal replacement therapy (RRT). The prevalence of this underlying disease amounted to 30.5% by the end of 2020, a statistic which increased from 27% in 2015. This highlights the challenges faced by healthcare services in meeting the accrescent demands of this cohort of patients. The Renal Association and British Transplantation Society suggest that patients with a BMI >30 kg/m² are at a heightened risk of complications and is therefore discouraged. Our local transplant centre at St James’s University Hospital accepts recipients with a BMI of up to 35 kg/m² for kidney alone transplantation should no other medical/surgical contraindications to transplantation prevail. Despite this threshold, there remains a significant proportion of patients suspended from the deceased donor transplant waiting list due to an unacceptably raised BMI.

Method: Data was collected through the use of clinic letters or GP records uploaded to Patient Pathway Manager and BHLY (Bradford, Hull, Leeds and York) Renal Patient System. Our patient population consisted of those diabetic patients on home and in-centre haemodialysis (Leeds St James’s University Hospital, Pontefract, Seacroft, Beeston, Dewsbury, Calderdale and Huddersfield). The aims of our study are to assess the demographics of the diabetic haemodialysis (HD) population at the Leeds Teaching Hospitals NHS Trust, to determine the reasons for suspension from the renal transplant waiting list, with a particular interest in obesity. We also assessed the commonest treatment modality (insulin vs other) and the use of continuous glucose monitoring.

Results: The Leeds renal services provide haemodialysis for 631 patients, 248 of these being diabetic patients - 66% of whom are male, with a mean age of 60. Just over 50% of this cohort of patients are Caucasian in ethnicity, while 30% are South Asian. By the end of December 2022, just below 20% (n = 119) of all haemodialysis patients were active on the national deceased transplant waiting list. On the other hand, only 14% (n = 35) of the diabetic haemodialysis subpopulation were active by the end of 2022, while 13% (n = 31) were under assessment, 14% (n = 35) declined and/or disengaged from assessment for transplantation, while the rest were either temporarly or permanently suspended. Almost 10% (n = 24) of all diabetic haemodialysis patients are suspended due to a BMI >35 kg/m².

Conclusion: Our audit reveals that only 14% of the haemodialysis diabetic population is presently active on the deceased transplant waiting list. This remains suboptimal, as renal or simultaneous pancreas kidney transplantation is the gold standard for diabetes-induced ESKD. Obesity (BMI >35) was a reason for temporary suspension in 10% of our haemodialysis diabetic population. Therefore we need to target this comorbidity in a timely manner in order to optimise patients for transplantation. NICE recommend pharmacological weight-lowering therapy for people who have failed to achieve a healthy BMI following conservative methods. Such medical therapy (eg. liraglutide) is still yet to be evaluated in depth in the ESKD-haemodialysis obese population. Only one patient in our cohort was being treated with liraglutide, while the rest was either on insulin, linagliptin, glitazide or non-pharmacological dietary modification. The authors of this study encourage the inclusion of CKD5 patients on liraglutide, before they are started on haemodialysis, in order to pave their way to transplantation before it is too late.

#2779

THROMBOMODULIN IS A SPECIFIC MARKER OF ENDOTHELIAL DISFUNCTION IN HEMODIALYSIS PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is associated with endothelial dysfunction which is a common problem in hemodialysis patients and a risk for high cardiovascular mortality in hemodialysis. Thrombomodulin is a promising marker of endothelial cell injury in different pathological conditions. This study evaluates the additive

Table 1: Risk estimation of endothelial dysfunction using Thrombomodulin in patients with NAFLD.

<table>
<thead>
<tr>
<th>NAFLD &amp; Non- NAFLD</th>
<th>Odd ratio</th>
<th>95.0% C.I. for odd ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombomodulin</td>
<td>2.566</td>
<td>1.304-5.052</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

*: significant p value <0.05.
effect of non-alcoholic fatty liver disease (NAFLD) in prevalent HD patients on endothelial dysfunction.  

**Methods:** A case-control study was conducted on 60 end-stage renal disease (ESRD) patients on conventional hemodialysis: group A: 30 patients with NAFLD, group B: 30 patients without NAFLD, and control group of 30 apparently healthy subjects. Excluding elderly, diabetic patients, chronic liver disease, advanced heart Failure, active infection, COVID-19 infection, autoimmune diseases and patients with hemodialysis catheters. Thrombomodulin was measured for all participants by ELISA technique.

**Results:** Thrombomodulin could detect endothelial dysfunction in patients with NAFLD at Cut off value <0.8 ng/ml with sensitivity 53.33%, specificity 80%, PPV 72.72%, and NPV 63.2%. On comparing Thrombomodulin in patients with NAFLD (4.378±3.762 ng/ml), Non-NAFLD (1.126±0.591 ng/ml), and control (0.755±0.314 ng/ml) there was a significant difference (P-value<0.001). Post hoc analysis showed significantly high Thrombomodulin levels in patients with [NAFLD versus Non-NAFLD] and [NAFLD versus control] with p-value<0.001, 0.001 respectively while there was no significant difference between patients with Non-NAFLD and control p-value 0.792. NAFLD patients with positive thrombomodulin have a risk of 2.5 times having endothelial dysfunction. There was no significant correlation between Thrombomodulin and all variables in the study.

Conclusions: Thrombomodulin can be used as specific marker for endothelial dysfunction in hemodialysis patients with Non Alcoholic fatty liver disease.

### Table 1:

<table>
<thead>
<tr>
<th>Parameters of BIVA</th>
<th>Euhydration</th>
<th>Overhydration</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HD (63)</td>
<td>HDFOL (63)</td>
<td>HD (235)</td>
</tr>
<tr>
<td>TBW (6)</td>
<td>37.77 ± 6.35</td>
<td>39.30 ± 6.99</td>
<td>40.31 ± 8.59</td>
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<td></td>
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<tr>
<td>ECW (7)</td>
<td>18.95 ± 2.84</td>
<td>19.22 ± 3.00</td>
<td>24.34 ± 4.92</td>
</tr>
<tr>
<td></td>
<td>172</td>
<td>172</td>
<td>172</td>
</tr>
<tr>
<td>ICW (8)</td>
<td>18.29 ± 4.29</td>
<td>20.08 ± 4.75</td>
<td>15.97 ± 5.28</td>
</tr>
<tr>
<td></td>
<td>172</td>
<td>172</td>
<td>172</td>
</tr>
<tr>
<td>ECW / ICW (9)</td>
<td>1.04 ± 0.21</td>
<td>0.99 ± 0.18</td>
<td>1.67 ± 0.65</td>
</tr>
<tr>
<td></td>
<td>172</td>
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<tr>
<td>PA (12)</td>
<td>5.13 ± 0.87</td>
<td>5.36 ± 0.91</td>
<td>3.60 ± 0.80</td>
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<tr>
<td>NAK (13)</td>
<td>1.11 ± 0.18</td>
<td>1.08 ± 0.18</td>
<td>1.74 ± 0.52</td>
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<tr>
<td>Cap (27)</td>
<td>533.92±149.76</td>
<td>576.62±177.18</td>
<td>433.96±159.62</td>
</tr>
<tr>
<td>CHI (29)</td>
<td>7.27 ± 2.04</td>
<td>7.85 ± 2.41</td>
<td>5.35 ± 2.01</td>
</tr>
<tr>
<td></td>
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<td>172</td>
<td>172</td>
</tr>
</tbody>
</table>

TBW: Total Body Water; ECW: Extracellular Water; ICW: Intracellular Water; PA: Phase Angle; NaK: quotient Na K; Cap: Capacitance; CHI: Capacitance hydration Index

Euhydration: 6a vs 6b, p = 0.035; 8a vs 8b, p = 0.011; 9a vs 9b, p = 0.013; 12 a vs 12 b, p = 0.019; 13 a vs 13 b, p = 0.013; 27a vs 27 b, p = 0.016; 29a vs 29 b, p = 0.016

Overhydrated: 8c vs 8d, p = 0.019; 9c vs 9d, p = 0.025; 12 c vs 12 d, p = 0.012; 13 c vs 13 d, p = 0.009; 27 c vs 27 d, p=0 0.025; 29 c vs 29d, p = 0.027

HD Euhydration vs Overhydration: 6a vs 6c, p = 0.015; 7a vs 7c, p = 0.000; 8a vs 8c, p = 0.000; 9a vs 9c, p = 0.000; 12a vs 12c, p = 0.000; 13a vs 13c, p = 0.000; 27a vs 27b, p = 0.000; 29a vs 29 b, p = 0.000

HDFOL Euhydration vs Overhydration: 6b vs 6d, p = 0.002; 7b vs 7d, p = 0.000; 8d vs 8d, p = 0.029; 9b vs 9d, p = 0.000; 12b vs 12 d, p = 0.039; 13b vs 13d, p = 0.000; 27b vs 27d, p = 0.004; 29 b vs 29 d, p = 0.000

All patients HD vs HDFOL: 6e vs 6f, p = 0.009; 8e vs 8f, p = 0.001; 9e vs 9f, p = 0.009; 13e vs 13 f, p = 0.009; 27e vs 27 f, p = 0.002; 28e vs 28f, p = 0.002; 29 e vs 29 f, p = 0.002

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Figure 1: ROC of Thrombomodulin in prediction of NAFLD.
D5 - PERITONEAL DIALYSIS & HOME THERAPIES

#3270
TRANSPORT AND HYDROLYSIS OF ICODEXTRIN DURING PERITONEAL DIALYSIS
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Background and Aims: α-amylase, an enzyme present in plasma and peritoneal tissue, takes part in the process of starch digestion. During peritoneal exchange with icodextrin-based solution, polysaccharide chains are hydrolysed to shorter oligosaccharide chains, influencing osmotic properties of peritoneal dialysate. We estimated peritoneal transport parameters and

Figure 1:

Figure 2:
compared them with hydrolytic clearances using a new model that takes into consideration absorption of icodextrin from the peritoneal cavity and its degradation by α-amylase.

**Method:** Frequent dialysate and blood samples were taken in 11 patients (8 icodextrin-naïve, 3 icodextrin-exposed) undergoing 16-hour dwell studies with icodextrin-based dialysis solution and labeled serum albumin (RISA) added as a volume marker. Using data on the intraperitoneal volume and dialysate and blood concentrations of glucose, urea, creatinine, and 7 icodextrin molecular weight (MW) fractions (glucose polymer size classes) and dialysate concentrations of α-amylase the extended three-pore model was applied to estimate individual parameters related to the peritoneal transport induced by dialysis and to hydrolysis of icodextrin by α-amylase. The following MW cut-off values were assumed for icodextrin fractions: up to 1.08, 4.44, 9.89, 21.4, 43.5, 66.7 and over 66.7 kDa, called Fractions 1–7, respectively. The hydrolytic clearances were defined as rate at which dialysate volume is cleared of the fraction by hydrolysis. The time-dependent hydrolytic clearances of icodextrin fractions were calculated and compared with diffusive ones. For the first time the extended three-pore model was validated not only with respect to the peritoneal transport of water and small solutes but also regarding concentration of icodextrin fractions.

**Results:** Mean measured and simulated dialysate to plasma concentration ratios for glucose, urea and creatinine are presented in Figure 1, left panel. The peritoneal kinetic of icodextrin (dialysate concentrations of each fraction over its initial concentration) is presented for mean measured data and numerical simulation results in Figure 1, right panel. The results showed that the model provides a good estimate of the initial domination of PS slowly decreased during the dwell time, being dominated by hydrolysis processes at the end of the exchange, at least partly due to the changes of intraperitoneal volume and α-amylase concentration. In case of polysaccharides from Fractions 6 and 7, their hydrolytic clearances remained higher than the diffusive ones during whole dwell time. Interestingly, the obtained values of H in icodextrin-exposed patients typically remained below 1.2 mL/min except for Fraction 6, for which H increased from initial value of 0.83 ± 0.30 to 1.43 ± 0.64 mL/min at the end of the peritoneal dwell. On the other hand, the estimated final values of H in icodextrin-naïve patients were on average higher than 1.2 mL/min in all fractions except Fractions 4 and 5.

**Conclusion:** The model provided accurate description of peritoneal transport and icodextrin hydrolysis during long icodextrin dwells. The model showed that hydrolytic processes dominate over diffusive ones during whole dwell time in case of Fractions 6 and 7, whereas diffusive processes dominate for Fractions 1–3.

**Figure 1:** Mean measured (symbols) and simulated (lines) **Left panel:** dialysate to plasma concentration ratio, D/P, for glucose (circles), urea (squares), and creatinine (diamonds) and **Right panel:** normalized (by initial value) dialysate concentration, D/D<sub>0</sub>, for icodextrin Fractions: 1 – circles, 2 – plus marker, 3 – filled circles, 4 – crosses, 5 – squares, 6 – diamonds, 7 – triangles, during 16-hour dwell.

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**Background and Aims:** Despite being energy and resource-intensive, hemodialysis (HD) is the most common therapy for end stage kidney disease. Considering the extensive amount of energy, water, and consumables involved, this modality is expected to have a significant environmental impact. Through a comparative lifecycle assessment (LCA), this study aims to analyze the environmental impacts of hemodialysis in British Columbia, Canada.

**Method:** A process-based life cycle assessment was performed for three hemodialysis modalities: i) in-centre HD (ICHD), ii) home HD with NxStage machine (HHD-Nx), and iii) home HD with Baxter AK-98 machine (HHD-B). The scope of study included patient and staff commute, supply transportation, dialysis services, patient training for home hemodialysis, and waste management. The functional unit considered is HD energy and material consumption for one patient per year. Based on the patient's record, two prescriptions including standard (three dialysis sessions per week for 4 hours daily) and extended (six HD sessions per week for 8 hours daily) were considered. LCAs were performed using ISO 14040, 14041 standards in which ReCiPe (world) midpoint method and a cut-off criterion of 0.5% was used to assess the environmental impacts of selected impact categories.

**Results:** For both prescriptions, ICHD had highest impact on all environmental impact categories (climate change, human toxicity, freshwater eutrophication, particulate matter formation, marine ecotoxicity and water depletion), except ozone depletion in which HHD-B had highest impact. The fewest impacts were associated with HHD-Nx. CO<sub>2</sub> emissions observed for a standard HD prescription are 3590 kg carbon dioxide equivalents (CO<sub>2</sub>eq) per patient/year by ICHD, 1350 kg CO<sub>2</sub>eq/patient/year by HHD-Nx and 733 kg CO<sub>2</sub>eq/patient/year by HHD-Nx. For extended prescriptions, the highest impact observed is from HHD-B (2210 kg CO<sub>2</sub>eq/patient/year) followed by HHD-Nx (1110 kg CO<sub>2</sub>eq/patient/year). With respect to ICHD, HHD-Nx only accounts for 13% (standard) and 18% (extended) of total environmental impact. Patient and staff commute in ICHD (40% of total impact) and dialysis services in HHD (75% in HHD-B and 63% in HHD-Nx) are the highest contributors to the majority of environmental impacts.

**Conclusion:** Our study demonstrates the environmental impacts of various modes of HHD through LCA. HD modalities have substantial differences in their environmental impacts as compared to ICHD, both HHD systems have lower impact, with NxStage having less impact than Baxter. Our results also demonstrate that a shift from standard to extended prescriptions increases overall environmental impact by 5%. Combined with existing clinical and economic data, these results could assist policy and decision-makers to optimize the provision of kidney replacement therapies. Lower environmental impact of HHD may add to the patient and provider appeal of these therapies, and when clinical equipoise exists, NxStage may be preferred over Baxter in eligible patients.
LIQUID BIOPSY IN PATIENTS TREATED WITH BIOCOMPATIBLE PERITONEAL DIALYSIS FLUIDS – ITS RELATIONSHIP WITH CYTOLOGICAL AND HISTOLOGICAL FINDINGS

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Background and Aims: Peritoneal fibrosis can limit long term peritoneal membrane function in peritoneal dialysis (PD) patients. It has been related to bioincompatible PD fluids and peritoneal infections. There are no prospective studies regarding correlation between effluent biomarkers and peritoneal biopsy findings. Our aim was to study the possible relation of peritoneal effluent biomarkers and peritoneal morphology alterations.

Method: Multicenter prospective study in a cohort of stable PD patients treated with biocompatible PD fluids who received a kidney transplant. We collected in each patient peritoneal biopsy samples and peritoneal effluent fluid. We analyzed the relation between effluent biomarkers, phenotype of mesothelial cells (MC) cultured ex vivo, and peritoneal biopsy parameters (mesothelial integrity, fibrosis and hyalinizing vasculopathy). We compared them with patient characteristics, including peritoneal transport parameters. The biomarkers tested were Collagen-1 (COL-1), Fibronectin (FN), Collagen-13 (COL-13), Interleukin-6 (IL-6), Trombospondin-1, Cadherin 13 (CDH-13), CA-125, Gremlin-1 (GREM-1), Matrix metalloproteinase 2 (MMP-2), CC chemokine ligand 18 (CCL18), Plasminogen activator inhibitor 1 (PAI-1) and Vascular endothelial growth factor A (VEGF-A).

Results: Forty patients were included (mean age 54.5±15 years, 64% male, 24.1% diabetics). Mean time on PD was 25.5±27 months, 62.1% were on automated PD (APD) and 17.2% had prior peritonitis episodes. A normal MC culture phenotype was observed in 78% of patients. In peritoneal biopsies samples we found partial or total mesothelium preservation in 39%, submesothelial thickness in 42% and vasculopathy in 14% of cases. Effluent PAI-1 levels were significantly lower in patients with mesothelial cell loss than in those with mesothelial preservation (21.62 vs. 38.59 pg/ml respectively; p = 0.031). Patients with peritoneal fibrosis showed significantly higher ef fluent CDH-13 levels (3.51 vs. 2.32 pg/ml; p = 0.048) and supernatant PAI-1 levels (1183 vs. 72.73; p = 0.000) than those without fibrosis. No other statistical differences were found in other biomarkers analysed.

Conclusion: Most patients treated with biocompatible peritoneal dialysis fluids showed normal mesothelial cell phenotype in peritoneal ef fluent culture. Lower PAI-1 ef fluent levels were associated with mesothelial cell loss and higher effluent CDH-13 levels were related to peritoneal fibrosis.

CHARACTERIZING THE RESIDUAL VOLUME IN PERITONEAL DIALYSIS PATIENTS

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Background and Aims: Peritoneal dialysis (PD) is the most common home dialysis treatment, and is associated with lower societal costs and increased patient autonomy. During routine PD, the exact amount of fluid inside the peritoneal cavity is in general unknown, and the peritoneal catheter may also change position, which may lead to a large residual volume, inefficient dialysis, and potentially harmful overfill. A practical, clinical method to estimate the residual volume is from the dilution of a marker molecule before and after fill of a known volume of fresh dialysis fluid. However, ultrafiltration and transport of the marker molecule during the fill phase may introduce large errors, especially when low molecular weight marker molecules are utilized.

Method: Here we performed a retrospective analysis of clinical data consisting of 56 residual volume estimations utilizing either 1.5% glucose (n = 28) or 4.25% glucose fluid (n = 28). Residual volumes were estimated using creatinine, urea and albumin. The contribution of ultrafiltration and mass transport of the marker molecules were quantified using the Three-pore model.

Results: During the fill phase, the median ultrafiltration volume was 16 mL (IQR 3 to 31) in 1.5% glucose dwells, compared to 52 mL (IQR 38 to 66) during 4.25% glucose dwells (Fig. 1). Assuming that 40% of the ultrafiltration occurs as free-water transport, the median difference between Three-pore model and albumin dilution equation residual volumes were only -1 mL (-8 to 5.5) in 1.5% glucose dwells and 1 mL (-3 to 6) in 4.25% glucose dwells (Fig. 2A). Dilution-based calculations using creatinine overestimated residual volumes by 121 mL.
DYNAMICS AND ORIGIN IN PERITONEAL DIALYSIS
CROSS-OMIC PROFILING OF PROTEOME, METABOLOME, AND TRANSCRIPTOME REVEALS MOLECULE AND CLEARANCE DYNAMICS AND ORIGIN IN PERITONEAL DIALYSIS
Rebecca Herzog, Fabian Eibensteiner, Christoph Aufricht and Klaus Kratichwill
Medical University of Vienna, Austria

Background and Aims: Peritoneal dialysis (PD) effluent is not only a rich source of markers for therapy monitoring and investigation of deranged processes during PD it is also surprisingly underexplored and therefore poorly defined. Modern high performance mass spectrometry (MS) and sequencing methods allow monitoring of hundreds of analytes in parallel. For understanding PD transport dynamic and pathomechanisms and on a systems biology level, a multi-level omics approach is particularly attractive.

Method: Samples were obtained from stable patients chronically treated with PD at different time-points of standard 4h peritoneal equilibration tests (PETs). Effluent was collected after the pre-PET (overnight) dwell and at 4h, 1h and 4h dwells. Plasma samples were taken at the 2h PET time point. Effluent was separated into a cellular and cell-free component. Soluble proteins and metabolites in the cell-free compartment were processed using material-specific protocols and standardized LC-MS workflows. The cellular material was subjected to RNA sequencing. The Plasma-Proteome database was used for referencing plasma proteins and estimating plasma concentration. A bioinformatic workflow conjoined information from the datasets to reveal novel insights into the “PD-effluentome”, especially unravelling the origin of proteins and metabolites in PD effluent.

Results: Metabolomics enabled detecting of 207 unique metabolites in cell-free PD effluent. A mixed-effect ANOVA of all metabolites demonstrated dwell time-dependent concentration changes in 173 metabolites. Post-hoc testing revealed most metabolites to be changed between 1h and overnight time points, followed by 1h and overnight and 1h and 4h, respectively. We quantified 9,797 transcripts in PD-effluent cells and 2,729 proteins in PD effluent. 342 proteins were filtered from plasma, while 800 proteins were attributable to local origin or production. A quantitative analysis of the interaction proteome and cellular transcripts of ~1700 protein-transcript pairs showed clusters of proteins explained by over-expression in peritoneal cells compared to plasma concentrations.

Conclusion: Cross-omic profiling of PD effluent can be a valuable approach for revealing small molecule related changes during PD. The exploitation of PD effluent on multiple levels could improve the understanding of pathophysiological molecular processes and transport dynamics in the peritoneal cavity and their role in development of PD complications.

#4152
CROSS-OMICS PROFILING OF PROTEOME, METABOLOME, AND TRANSCRIPTOME REVEALS MOLECULE AND CLEARANCE DYNAMICS AND ORIGIN IN PERITONEAL DIALYSIS
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Conclusion: Cross-omic profiling of PD effluent can be a valuable approach for revealing small molecule related changes during PD. The exploitation of PD effluent on multiple levels could improve the understanding of pathophysiological molecular processes and transport dynamics in the peritoneal cavity and their role in development of PD complications.

#4202
FLUID OVERLOAD AT THE BEGINNING OF PERITONEAL DIALYSIS: A CROSS-SECTIONAL STUDY TO DETERMINE ITS ASSOCIATION WITH SERUM BIOMARKERS
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Background and Aims: Volume management in peritoneal dialysis (PD) patients is of major importance as fluid overload has been associated with cardiovascular and non-cardiovascular morbidity and mortality. Clinical examination itself has a poor diagnostic accuracy for minor deviations from normohydration, highlighting the need of additional tools. The aim of this study was to evaluate the association between serum biomarkers (CA-125 and NT-proBNP) and volume status, evaluated by clinical and bioimpedance analysis, at the initiation of PD technique.

Method: Single-center cross-sectional study including PD patients that started technique between 2017 and 2022. Demographic and clinical data were collected from the electronic records. Parameters evaluated were clinical examination, serum biomarkers, bioimpedance and dialysis adequacy.

Results: A total of 79 patients (51 male) were included with a mean age of 57±15 years. All of them started with CAPD and 52% were under icodextrin. Hypertension, cardiovascular disease and diabetes were present in 94%, 51% and 34%, respectively. The great majority were under renin-angiotensin-aldosterone system inhibitors (91%), beta-blockers (48%) and diuretic therapy (94%). Baseline PET showed that 77% were high or high-average transporters. Mean weekly Kt/V was 2.4±1.4. The mean residual renal function (RRF) and residual diuresis were 6.7±15 ml/min/1.73 m² and 1.6±0.8 L (4% anuric), respectively, and 11% had ultrafiltration failure. Median nPCR was 0.9 g/Kg/day (IQR 0.3). Median NT-proBNP and CA-125 were 1337 pg/mL (IQR 3401) and 14.6 U/mL (IQR 17.6), respectively. NT-proBNP was still associated with overhydration in a multivariable analysis, adjusted to diabetes, icodextrin use, RRF and CA-125 (p = 0.024).

Conclusion: Serum NT-proBNP and CA-125 seem to be good markers of overhydration at PD baseline. They were also associated with worse dialytic overload at the beginning of PD.
efficacy and ultrafiltration, lower residual renal function and an early need for peritoneal equilibration test results. The impact of this factor on peritoneal membrane function and PD technique survival has not been adequately investigated. The aim of our study was to disclosure the effect of prior abdominal surgical procedures on PD technique survival (main outcome), efficacy rates and also evaluate the risk of infectious complications (secondary outcomes).

Method: We performed a retrospective, longitudinal study, that included 155 PD patients followed at our unit, since September 2018 to September 2022. Two groups were created: G1 (without previous abdominal surgery) and G2 (with previous abdominal surgery). Demographic and clinical characteristics, such as age, gender, chronic kidney disease (CKD) etiology, time on PD program, dialytic efficacy and ultrafiltration, lower residual renal function and an early need for peritoneal equilibration test results were registered from our unit database. Statistical analyses were performed using SPSS statistics version 23.0. The statistical hypothesis tests performed using SPSS statistics version 23.0. The statistical hypothesis tests were considered significant.

Results: One-hundred and fifty-five patients (female: 50.9%) with a mean age of 55.4 ± 7 years were selected. The main CKD cause was glomerular diseases (n = 43, 27.7%), followed by uncertain etiology (n = 32, 20.6%) and autosomal dominant polycystic kidney disease (n = 21, 13.5%). G1 (n = 87; 56.1%) and G2 (n = 68; 43.9%) had similar distributions of gender (female: 50.6% vs 47.1%, p = 0.061), age (50.4± 9 vs 55.4± 10 years, p = 0.076) and dialysis vintage (27.9 vs 28.2 months, p = 0.081). In G1, 62.1% of patients were on continuous ambulatory peritoneal dialysis (vs 55.9% in G2). The majority of patients were high-average transporters in both groups (58.6% vs 54.4%, p = 0.066). Previous comorbidities were G1 (vs G2): arterial hypertension (95.4% vs. 98.5%, p = 0.87), diabetes (27.6% vs. 26.5%, p = 0.83), heart failure (25.3% vs. 26.5%, p = 0.64), peripheral arterial disease (28.7% vs 35.3%, p = 0.082), body mass index >30 kg/m2 (30.7% vs 29.4%, p = 0.072) and dyslipidemia (64.4% vs 64.7%, p = 0.91). In G1, Kt/V was inferior to 1.7 in 36.8% of patients (vs 66.2% in G2, p<0.001). Seven patients (8.1%) have reported more than one peritonitis during time in PD in group 1 (vs 32.4% in G2, p<0.001). We found no differences in PD technique survival between both groups. Transition to hemodialysis happened in 26.4% of patients in G1 (vs 26.5% in G2, p = 0.092). Mortality rate was similar in both groups (6.9% vs 10.3%, p = 0.063).

Conclusion: According to our results, prior abdominal surgical procedures do not appear to compromise technique survival in patients on PD. Although, abdominal surgical events places PD patients in a higher risk of infectious complications and lower efficacy rates. Thus, this group of patients deserve a more detailed evaluation before starting PD, in order to understand if they are good candidates for the technique, as this may not be the most advantageous for them in the long term.
Figure 1: Graph below summarize study recruitment and mortality. Overall patients and families were satisfied with program.

Results: 946 patients screened for the program. 237 were eligible (exclusion mostly due to lack of national insurance coverage or not meeting mobility/transport criteria). 121 patients refused to participate (mostly for feeling safer in the clinic setting or improper home environment), 40 patients were undecided, and 76 patients accepted and started AHHD. Age was 73±11 years. We had 32 males and 44 females. Mean follow up period were 7 months. 12 patients died and 2 patients returned to dialysis centre during follow up period. Only 15 out of the total 126 hospitalizations were related to dialysis (mostly due to volume overload and non-compliance with dialysis schedule and time). We had 55 patients with permcath and 21 with AV fistulas. We had 8 incidents of dialysis catheter malfunction (6 required tissue plasminogen activator installation in the house setting and only two needed catheter exchange (one had catheter related infection)). No reported significant access bleeding or hypotension episodes. We had 20 technical incidents during the study related to electricity or water supply failures. All incidents were resolved without much interruption of treatment. The program overall was cost effective and reduced cost by over 25% (mostly related to saving of ambulance cost). Patients and their families were very satisfied with the program overall. Conclusion: We present a unique successful program related to providing AHHD. Targeting certain dialysis population showed great care, safety, cost saving, better QOL and satisfaction.
TREATMENT PREFERENCES TO SERIOUS ILLNESS IN PATIENTS RECEIVING PERITONEAL DIALYSIS
Ching-I Cheng¹, Pei-Ni Chuang¹, Jen-Kuei Peng¹, Shu-Neng Chueh¹, Chun-Fu Lai¹, Hung-Bin Tsai¹, Chih-Kang Chang² and Jaw-Shiun Tsai*¹
¹National Taiwan University Hospital, Department of Nursing, Taipei, Taiwan, Rep. of China, ²National Taiwan University Hospital Hsin-Chu Branch, Department of Family Medicine, Hsin-Chu, Taiwan, Rep. of China, ³National Taiwan University Hospital, Department of Family Medicine, Taipei, Rep. of China, ⁴National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan, Rep. of China, and ⁵National Taiwan University Hospital, Department of Integrated Diagnostics & Therapeutics, Taipei, Taiwan, Rep. of China and ⁶National Taiwan University Hospital, Department of Family Medicine, Taipei, Taiwan, Rep. of China.

Background and Aims: People with end-stage kidney disease receiving maintenance dialysis are more likely to receive intensive pattern of end-of-life care than those with other severe illness. It’s important to understand the preferences to cardiopulmonary resuscitation (CPR) and other end-of-life care. However, no prior studies have investigated patients receiving peritoneal dialysis. This study aimed to explore the preference to CPR and patterns of end-of-life care in patient receiving peritoneal dialysis (PD), which had not been specifically investigated in the literature.

Method: This cross-sectional study of patients receiving PD was conducted in the National Taiwan University Hospital between Dec. 2021, and Mar. 2022. Patients were enrolled if they were 20 years or older, sufficiently fluent to complete surveys and cognitively able to provide written informed consent and had received maintenance peritoneal dialysis for at least 3 months. Enrollee were asked to the Chinese version of Physician Orders for Life-Sustaining Treatment questionnaire.

Results: Among 400 eligible patients, 364 (91%) responded to the questionnaire. The average age was 55.5 years; 50.3% were men. Among the 364 responders, 73.6% selected do not attempt resuscitation (DNR) and 26.4% preferred CPR. Multivariate logistic analysis revealed that age (OR = 0.96, 95% CI 0.94-0.98), male (OR = 2.44, 95% CI 1.45-4.1) and residual kidney Kt/V (OR = 2.45 95% CI 1.24-4.82) were associated with CPR. If they are facing on serious illness, 47.5% of participants prefer to “Focus on comfort”, 28.6% choose “try treatments, but do not suffer” and 23.9% request “live as long as possible”. Furthermore, 51.4% of participants selected “No artificial nutrient support” in the end of life and 87.1% select “comfort care” as their first priority. Paradoxically, only 13.5% of the patients who preferred CPR took “staying alive” as their first priority, while 71.9% focused on “comfort care”.

Conclusion: Around 75% of PD patients selected DNR when cardiopulmonary arrest. Age, gender, residual Kt/V were important factors associated with CPR preference. Most patients preferred supportive pattern of end-of-life care. Integrating patients’ treatment preference to serious illness and values and goals of end-of-life care in shared decision making is important for patients receiving dialysis.

IMPLEMENTATION OF AN INNOVATIVE ARTIFICIAL INTELLIGENCE CHAT ROBOT APPLICATION OF NURSING CARE IN PERITONEAL DIALYSIS
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¹National Taiwan University Hospital, Department of Nursing, Taipei, Taiwan, Rep. of China, ²National Taiwan University Hospital, Department of Integrated Diagnostics & Therapeutics, Taipei, Taiwan, Rep. of China and ³National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan, Rep. of China

Background and Aims: During the Covid-19 pandemic, this study used an innovative intelligent chatbot to investigate satisfaction. The higher score was associated with more agreement with innovative intelligent robot application. And chatbot satisfaction was scored with 1–5 points in which 5 points meant the highest satisfaction.

Method: During a period from May 1st to August 31st, 2021, we utilized questionnaire with the LIKER4 score before and 3 months after the implementation of chatbot to investigate satisfaction. The higher score was associated with more agreement with innovative intelligent robot application. And chatbot satisfaction was scored with 1–5 points in which 5 points meant the highest satisfaction.

Conclusion: We reported similar patient survival, but higher peritonitis rates and PD technique failure in the PDPotTx group, when compared to patients who started PD for other reasons. Considering these findings, taking precautions against peritonitis is more important for patients who started PD after KTx failure.
METHOD: In an observational study of 8113 prevalent PD patients treated with APD (n = 2692) or CAPD (n = 5421), PO4 levels together with demographic and clinical data, including dialysate to plasma ratio of creatinine at 240 min (D/PCr240min at peritoneal equilibration test) and body mass index (BMI), were recorded. During follow-up for a median of 1.99 years, 3619 patients died, and 988 patients underwent kidney transplantation (KT). We divided patients into 5 groups (P1 to P5) according to their baseline PO4 levels (first available measurement) with the following cut-off values for groups: up to 3.5, 3.5-4.5, 4.5-5.5, 5.5-6.5, and over 6.5 mg/dL, respectively. The association of baseline PO4 levels with all-cause and CV mortality risk was analyzed with a competing-risk regression model and KT as a competing risk.

RESULTS: Characteristics of patients classified into groups P1 (16%), P2 (33%), P3 (27%), P4 (13%), and P5 (9%) are presented in Table. P5-patients were in general younger, more often men, less often diabetic (DM), and had lower residual renal function, DM, and hypertension) was increased in P4- and P5-patients compared with P2-patients, sub-hazard ratio (sHR) of 1.14 (95% CI: 1.01-1.27) and sHR of 1.27 (95% CI: 1.10-1.46), respectively. Higher PO4 levels were not associated with significantly increased CV mortality risk for P4-

#5768

ASSOCIATION OF HIGH SERUM PHOSPHORUS WITH INCREASED MORTALITY RISK IN PATIENTS ON PERITONEAL DIALYSIS: RESULTS FROM COLOMBIA

Rafael Gomez1, Abdul Rashid Tony Qureshi2, Xiejia Li1, Joanna Stachowska-Pietka1, Malgorzata Debowska1, Jacek Waniewski1 and Bengt Lindholm2

1RTS San Fernando, Renal Unit, Cali, Colombia, 2Karolinska Institutet, Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden and 3Nalecz Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Poland

Background and Aims: Elevated levels of serum phosphorus (PO4) in patients with kidney failure are associated with complications such as cardiovascular (CV) disease, bone disease and impaired wound healing, and increased mortality in hemodialysis patients. A recent PDOPPS study (Lopes et al NDT 2023) showed that high PO4 is associated with increased mortality also in patients undergoing peritoneal dialysis (PD). We explored PO4 levels in a large cohort of patients undergoing chronic PD in Colombia to determine the association of PO4 levels with mortality.

Table 1: Demographic and clinical data of peritoneal dialysis patients, according to transplantation status.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>PD-postTx (n = 19, 21.3%)</th>
<th>PD-noTx (n = 70, 78.7%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Gender, n (%)</td>
<td>7 (36.8)</td>
<td>36 (51.4)</td>
<td>0.259</td>
</tr>
<tr>
<td>Age at PD initiation (Years) (Mean ± SD)</td>
<td>38.3 ± 12.4</td>
<td>48.9 ± 16.4</td>
<td>0.004</td>
</tr>
<tr>
<td>ESRD Etiology, n (%)</td>
<td>15 (78.9)</td>
<td>38 (54.3)</td>
<td>0.052</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5 (26.3)</td>
<td>17 (24.3)</td>
<td>0.091</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1 (5.3)</td>
<td>21 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>4 (21.1)</td>
<td>13 (18.6)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (21.1)</td>
<td>8 (11.4)</td>
<td></td>
</tr>
<tr>
<td>VUR+ON+PN</td>
<td>4 (21.1)</td>
<td>4 (5.7)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (5.3)</td>
<td>7 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>1 (5.3)</td>
<td>20 (28.6)</td>
<td>0.060</td>
</tr>
<tr>
<td>Weight, kg (Mean±SD)</td>
<td>67.0±14.0</td>
<td>71.2±15.4</td>
<td>0.305</td>
</tr>
<tr>
<td>APD, n (%)</td>
<td>15 (78.9)</td>
<td>38 (54.3)</td>
<td>0.052</td>
</tr>
<tr>
<td>Transtubular creatinine gradient</td>
<td>0.25 &lt; 0.50</td>
<td>0.62 &lt; 1.00</td>
<td>0.004</td>
</tr>
<tr>
<td>Duration Tx (Months) (Mean ± SD)</td>
<td>15.5±9.7</td>
<td>17.4±10.5</td>
<td>0.004</td>
</tr>
<tr>
<td>Complications, n (%)</td>
<td>1.01-1.27</td>
<td>1.27 (95% Cl: 1.10-1.46)</td>
<td></td>
</tr>
<tr>
<td>Number of peritonitis episode (Mean±SE)</td>
<td>1.63±0.38</td>
<td>0.5±0.13</td>
<td>0.015</td>
</tr>
<tr>
<td>Transfer to HD, n (%), n = 68</td>
<td>7 (36.8)</td>
<td>7 (10.0)</td>
<td>0.099</td>
</tr>
<tr>
<td>Reasons of PD failure, n (%)</td>
<td>0.604</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uf failure</td>
<td>5 (26.3)</td>
<td>44 (62.9)</td>
<td></td>
</tr>
<tr>
<td>Peritonitis</td>
<td>13 (68.4)</td>
<td>21 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Exit-site/ Tunnel infection</td>
<td>1 (5.3)</td>
<td>5 (7.2)</td>
<td></td>
</tr>
<tr>
<td>Catheter malfunction</td>
<td>1 (5.3)</td>
<td>3 (4.3)</td>
<td></td>
</tr>
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<td>7 (10.0)</td>
<td>0.099</td>
</tr>
<tr>
<td>Reasons of PD failure, n (%)</td>
<td>0.604</td>
<td></td>
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<tr>
<td>Uf failure</td>
<td>5 (26.3)</td>
<td>44 (62.9)</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>Catheter malfunction</td>
<td>1 (5.3)</td>
<td>3 (4.3)</td>
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</table>

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; ESRD, End Stage Renal Disease; HD, hemodialysis; ON, obstructive nephropaty; PD, peritoneal dialysis; PN, pyelonephritis; SD, standard deviation; Tx, transplantation; UF, ultrafiltration; VUR, vesicoureteral reflux.

Abstracts
patients, sHR of 1.10 (95% CI: 0.93-1.31), or for P5-patients, sHR = 1.14 (95% CI: 0.93-1.39) compared to P2-patients.

**Conclusion:** Among 8113 PD patients in Colombia, 49% had baseline PO4 > 4.5 mg/dL and 22% PO4 > 5.5 mg/dL. Baseline PO4 levels > 5.5 mg/dL (P4 and P5 groups) were associated with increased all-cause mortality. These results are in agreement with the results of the PDOPPS study and suggest that effective management of hyperphosphatemia is important to improve clinical outcomes in PD patients.

#4753

**TELEDIALYSIS: THE FIRST NORTHEAST ITALY EXPERIENCE OF TELEHEALTH IN PERITONEAL DIALYSIS PATIENTS**

Paolo Lentini¹, Giorgio Laudadio¹, Valeria Fuso¹, Claudia Benedetti¹, Antonio Previti¹, Sofia Andrighetto¹, Federica Vienna¹, Daniela Cremasco¹ and Giovanni Gambaro²

¹Azienda Ospedaliera AULSS7 Pedemontana, Nephrology and Dialysis Unit, Bassano del Grappa (VI), Italy and ²AOUVR, Nephrology, Verona, Italy

**Background and Aims:** During Covid19 epidemic, International Society of Peritoneal Dialysis recommend "People on PD should stay at home. Hospital visits should be minimized for only urgent indications. Consultations should otherwise be conducted by telehealth". In 2021 in Italy Government enforce plan to develop Telehealth and to create a new Nephrology home model to provide better oversight of care with remote monitoring. Telehealth has been used to manage patients with chronic kidney disease (CKD) and demonstrated equal outcomes in CKD care by either in-person or virtual visits. Telehealth also help facilitate patient education about home dialysis modalities and self-care, especially in peritoneal dialysis setting (PD). We report the first experience in the Northeast of Italy with Teledialysis, a combination of PD technique and new technology devices that we used together to overcome clinical, social and psychological barriers to PD.

**Method:** In our pilot study, we enrolled 12 consecutive Automated Peritoneal Dialysis (APD) patients from our Nephrology program in “San Bassiano Hospital”, Bassano del Grappa, VI, Italy. Teledialysis was perform with the combination of two systems:

1- A Web platform Sharesource (Baxter Renal care ®) that with a mod-M added to APD device supports remote patient management through secure communication with and allows details of the home dialysis treatment and provide to the clinician the ability to act on that assessment by updating the patient device setting to the cycler.

2- Totem eVISUS System (TesiSquare ®) that is a plug and play system consisting of two units: a) a transportable remote station at the patient’s home (Totem) equipped with high performance camera, touchscreen monitor, speaker microphone hand free and computers, internet routers for fixed and mobile phone, wireless access point and remote control to answer calls remotely and b) a Control Station (in our Hospital) that by a simple use of a mouse form our healthcare personnel can connect to one or more patients at the same time and check the Totem Camera. (Figure 1) We control day by day PD sessions by sharesource and we provide virtual support to our patients for medications of catheter exit-site and catheter exit-site monitoring and instructions for PD training; we also perform clinical evaluation status, we check PD effluent color and we aid patients and care givers for PD session management.

**Results:** During an observation period of 11 months we enrolled 12 consecutive patients (4m/8F) with an average age of 73 yrs; cognitive impairment, diabetes, hypertension, chronic heart failure and peripheral vascular disease (PVD) were common comorbidities (see Figure 2). We

![Figure 1: The Teledialysis System: 1) Sharesource for remote control; 2) Totem at home access point with remote control. 3) Central station in the hospital for virtual evaluation.](image-url)
perform 60 tele-dialysis sessions with an average duration of 26’ minutes. We don’t detect any exit Site Infection (ESI), Tunnel infection or Peritonitis in our population; none of our patients require urgently hospital or emergency room admission. Only once we suggest access to our department for fever and dyspnea and the patient require a one week hospitalization for acute bacterial pneumonia. (Table 1)

Conclusion: Our preliminary results shown that Tele-dialysis is a safe, reliable, flexible and effective system and is easy to use for our patients; we assert that technology really can help nephrologist to improve PD program and aid patients to overcome barriers to select PD and avoid fear of the failure. Tele-dialysis promote a real integration between Hospital and our territory by a new care pathway.

Table 1: Results from September 2021 to August 2022.

<table>
<thead>
<tr>
<th>Tele-dialysis Sessions (n)</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exit-Site Infections (n)</td>
<td>0</td>
</tr>
<tr>
<td>Tunnel Infections (n)</td>
<td>0</td>
</tr>
<tr>
<td>Peritonitis (n)</td>
<td>0</td>
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<tr>
<td>Emergency room Admissions (n)</td>
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</tr>
<tr>
<td>Hospitalization (n)</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 2: Characteristics of the patients.

**PERITONEAL DIALYSIS AND POSTOPERATIVE OUTCOMES IN CHILDREN AFTER CARDIAC SURGERY: A SINGLE-CENTER COHORT STUDY**

Gonçalo Pimenta¹, Rita Afonso², Ana Carlota Vida³, Rita Calca³, Isabel Graça³, Maria Estevens⁴, Patrícia Matias¹, Rui Anjos⁴ and Patricia Branco⁵

¹Hospital de Santa Cruz, Pediatric Cardiology, Carnaxide, Lisboa, Portugal, ²Centro Hospitalar Universitário do Algarve - Hospital de Faro, Nephrology, Faro, Portugal, ³Hospital Dr. Nélia Mendonça, Nephrology, Funchal, Madeira, Portugal and ⁴Hospital de Santa Cruz, Pediatric Cardiology, Carnaxide, Lisboa, Portugal

*Background and Aims:* Acute kidney injury (AKI) is a frequent complication in neonates and infants after congenital heart disease surgery, with great impact on morbidity and mortality. Peritoneal dialysis (PD) is the renal replacement therapy of choice, as it allows continuous gentle ultrafiltration with minimal impact on hemodynamic status. However, there is no standardized prescription. The present study aimed to describe our experience of using PD in the management of AKI after cardiac surgery in pediatric patients and the postoperative outcomes.

**Method:** Single-center cross-sectional study including 21 children undergoing cardiac surgery between 2017 and 2022, in a congenital heart disease reference center. Demographic and clinical data were collected from the electronic records.

**Results:** Of the 21 patients treated with PD, 11 were female. Mean age was 32 ± 45 days and median weight was 3.4 kg (IQR 0.5). All pregnancies had been full-term with a mean birth weight of 3.2 ± 0.3 kg. No congenital urinary tract anomalies had been previously documented. Previous history of AKI was present in 2 patients. Transposition of the great arteries was the most common surgical indication (52%). RACHS-1 score was >4 in 12 patients and median PRISM-IV score was 6.5% (IQR 6). Cardiopulmonary bypass was performed in 19 patients with a mean time of 181 ± 72 minutes and a mean aortic clamping time of 94 ± 29 minutes. All patients required inotropic support after cardiac surgery with ≥2 drugs, for 197 ± 136 hours. Median time with mechanical ventilation support was 126 hours (IQR 288) and median length of stay at the intensive care unit (ICU) was 9 days (IQR 15.3). The indications for PD initiation were anuria (66.7%), oliguria (23.8%) and fluid overload (9.5%). Median time between cardiac surgery and AKI diagnosis was 2.5 hours (IQR 8.8) and between AKI diagnosis and PD initiation was 1.8 hours (IQR 4.3). Median duration under dialysis was 2 days (IQR 3.5). Exchange volume of dialysate varied between 6 and 15 mL/kg at the beginning of PD. In 11 patients, this volume was progressively increased to a maximum of 60 mL/kg (minimum: 30 mL; maximum: 120 mL). Continuous veno-venous hemodialfiltration was required in 3 patients, mainly due to mechanical catheter dysfunction. Complications related to PD occurred in 5 patients: 1 patient developed peritonitis, 1 patient had mechanical catheter dysfunction and 3 patients had peri-catheter leak. Complete recovery of renal function was achieved in 14 patients. Longer time on PD was associated with lower weight before surgery (p = 0.04), longer time on mechanical ventilation and inotropic support (p < 0.001), and longer stay at the ICU (p < 0.001). Time on inotropic support could predict time on PD using a multiple regression model (adjusted R² = 59%, p = 0.003), adjusted to cardiopulmonary bypass time, time on mechanical ventilation support and weight before surgery (adjusted R² = 0.7, p = 0.005). Eight patients died during hospitalization, due to multiorgan failure (38%), cardiogenic shock (38%), disseminated intravascular coagulation (13%) and septic shock (13%). Longer cardiopulmonary bypass time was associated with in-hospital mortality (149 ± 53 vs 235 ± 46, p = 0.004). Both the time between AKI diagnosis and PD initiation and the time on PD were not associated with in-hospital mortality.

**Conclusion:** Our study suggests that PD is a safe and effective dialysis modality in the management of post-cardiac surgery AKI in pediatric population. Early identification of high-risk infants is important to implement preventive measures.

G. Pimenta*, R. Afonso*: Both authors contributed equally.
DEVELOPMENT OF A HOME DIALYSIS PATIENT SUPPORT SYSTEM WITH EXERCISE FUNCTION PART II: RESULTS OF A TRIAL OF ADDED EXERCISE FUNCTION
Akiko Okawa1,2, Natsumi Yamamoto1, Yuki Sekine3 and Tokuo Umeda
1Japan, 2Mie Prefectural College Of Nursing, Faculty of Nursing, Tsu, Japan and 3Japan

Background and Aims: In Japan, peritoneal dialysis patients are required to record daily dialysis information in continuous ambulatory peritoneal dialysis (CAPD) notes. However, as the CAPD notes are a list of numbers, it is difficult for medical staff to quickly understand the patient's physical condition. Although many people now use communications infrastructure, access to medical information on the Internet is restricted from the viewpoint of patient information security in medical institutions in Japan. Therefore, patient information outside the medical institution cannot be viewed on the system inside the medical institution. Therefore, we are developing a safe and securedialysissupportsystemtoconnectdialysispatients’ homes and medical institutions. We have developed a dialysis support system that can share the patient’s vital data, dialysis records, meal records, etc., between patients and medical institutions. Here, we added a function to support the exercise of dialysis patients, and present the results of a trial.

Method: The display and recording items of the previously developed system include vital data, and exchange start time as records necessary for peritoneal dialysis, dialysate concentration, drainage volume, fluid injection volume, drainage volume, drainage time, drainage confirmation, blood pressure, and blood sugar level. In addition to these items, we have added a new function to the system that can automatically input the patient’s exercise records from ergo-storage device. This added functionality links movement information from the ergo-storage device with relevant patient information in the previously developed system. It also enables medical staff to view and share the graphical data as visible information from within the facility. The patients exercise using the developed ergo-storage device, and the amount of exercise is stored in the charger. Patients can exercise with this ergo-storage device on both dialysis and non-dialysis days.

Results: To prevent erroneous input, the dialysis records could be entered automatically or selected using radio buttons. In addition, when confirming drainage, it was possible to transmit images to medical institutions. In the added exercise function, the strength of pedaling on the ergo-storage device, the number of rotations, etc., could be output in CSV format. The amount of exercise was sent to the previously developed system. In addition, the

Figure 1: Display of the developed dialysis support system with exercise function (patient side).

Figure 2:
system allowed storage of the electricity generated by rotating the pedals in the storage device. Therefore, the patients were motivated not only to exercise but also to continue to exercise. The accumulation of exercise data enabled the patients to understand changes over time, leading to self-management. Furthermore, exercise could be continued even on non-dialysis days. Medical institutions could also share not only the patient’s dialysis records, but also information on their amount of exercise, leading to improved patient care.

Conclusion: This developed system with new exercise function supported patients’ exercise and its continuation on both dialysis and non-dialysis days. The amount of exercise by the patient was stored as electricity, which could be used to charge the patient’s cell phone, etc. This increased the patients’ motivation to exercise. Furthermore, this information can be shared with medical institutions. This research was supported in part by Gakushin Kaken (JP20H03982).

#4062 PERITONEAL DIALYSIS CATHETER SURVIVAL: A TEN-YEAR SINGLE CENTER STUDY
Bárbara Beirão Rodrigues, Mariana Freitas, José Francisco, João Borges, Ana Beatriz Pereira, Ciria Sousa, Pedro Reis Pereira, Catarina Prata, Rui Castro and Teresa Pinto Ribeiro Morgado

Centro Hospitalar de Trás-os-Montes e Alto Douro, Nephrology, Vila Real, Portugal

Background and aims: Timely insertion and adequate management of peritoneal dialysis catheter (PDC) related complications are crucial for the success of Peritoneal Dialysis (PD). The aim of the present study was to review the peritoneal dialysis catheter outcomes at our center and evaluate variables influencing catheter survival.

Methods: We conducted a retrospective study including 146 patients who had their first PD catheter implanted between 1st of August 2012 and 31st of July 2022 in our institution. The primary endpoint was PD catheter failure, defined as removal of the PD catheter due to catheter-related complications. Kaplan-Meier curves were used to estimate catheter survival. Cox regression model was used to identify factors that were independently associated with catheter survival. All demographic and clinical characteristics of the patients and PD complications were included as covariates. A p value of less than 0.05 was considered statistically significant.

Results: The study population included 85 men and 61 women, aged 55.1 ± 16.7 years. Mean follow-up was 26.5 +/- 22.7 months. Diabetes was the most common etiology of the stage 5 chronic kidney disease (n = 41, 28%), followed by chronic glomerulonephritis (n = 30, 20.5%). Ninety patients (61.2%) had one or more comorbidities and seventeen (11.6%) had previous abdominal surgery. In 98 patients (60.1%), the PDC was inserted using a mini-laparotomy approach, whereas the laparoscopic method was used in 54 patients (33.1%).

Only 8 patients (4.9%) had their catheter placed percutaneously using the Seldinger technique. The total number of patients with one or more PD-related infectious complications during follow-up was 99 (67%): 51 patients (31%) had a single episode and 29 (17.8%) had multiple episodes of peritonitis; 34 patients (20.9%) had a single episode of PD catheter related exit site or tunnel infection, while 47 (28.8%) had more than 1 event. Sixty-six patients (45%) had PD-related mechanical complications, mostly due to outflow failure (19 patients with catheter migration, 11 with omental wrapping). The remaining non-infectious complications were hernia (n = 20, 13.7%), hemoperitoneum (n = 8, 5.5%), leakage (n = 4, 2.7%) and pleuroperitoneal shunt (n = 4, 2.7%).

Fourteen patients required intervention due to mechanical complications, namely repositioning of the catheter with fluoroscopic technique in 8 patients and surgical repositioning in 6. Removal of the catheter was required in 49 patients (33.6%). The leading cause of catheter removal was infection (n = 29, 59%): peritonitis in 28 patients and refractory tunnel infection in 1. Medical complications were also a significant factor, accounting for 40.8% of the removals (n = 20). Overall PD catheter survival rates over 12, 24 and 36 months were 80.2%, 72.4% and 61.6%, respectively. PD catheter-related non-infectious complications was the only independent variable significantly associated with catheter survival (Hazard ratio 2.573; 95% CI 1.426–4.645).

No significant association was observed between the PD catheter survival and other risk factors including age, diabetic status, comorbidities, previous abdominal surgeries, method of catheter insertion or infectious complications.

Conclusions: PDC non-infectious complications were the only independent factor significantly associated with catheter survival. Despite the significant number of infectious complications, including peritonitis, it was found that these complications did not result in a significant decrease in catheter survival. These findings highlight the crucial role of proper management of peritoneal dialysis catheter-related non-infectious complications for successful and long-term usage of PDC.

Figure 1: Kaplan-Meier curves for catheter longevity in patients with (green) and without (blue) peritoneal dialysis catheter related non-infectious complications.
Results: Techniquesurvival. (mechanical and infectious) within 90 days. Secondary outcomes included PD-L catheter placement. The primary outcomes were early complications whether the catheter was used during the first 15 days (PD-E) or 15 days after to October 2015). The patients were divided into two groups according to all patients treated with peritoneal dialysis for 18 months (from April 2014 year and four-month period (from April 2014 to August 2021), including Among the 36 patients included in the study, 14 started PD early (38.8%), while 22 started it 15 days after catheter placement (61.2%). The mean age between the two groups was not significantly different (41 ± 17 years vs 35 ± 16 years, p: not significant). There were no significant differences in the Charlson comorbidity index or the degree of autonomy. The incidence of infections was not significantly different between the two groups (13.6% in PD-L vs 21.4% in PD-E, p: not significant). The total number of mechanical complications was not significantly higher in the PD-E group compared to the PD-L group (42.8% vs 27.3%, respectively, p: not significant). Kaplan-Meier estimates of technique survival were comparable between the groups (log Rank: 1.908, p: 0.67). Our study showed no increase in the risk of complications associated with early use of the PD catheter and no difference in technique survival. PD can be used as first-line renal replacement therapy in the unplanned initiation of chronic dialysis.

Conclusion: Our study showed no increase in the risk of complications associated with early use of the PD catheter and no difference in technique survival. PD can be used as first-line renal replacement therapy in the unplanned initiation of chronic dialysis.

#2530
"HOME-MADE" REMOTE MANAGEMENT IN CAPD
Silvio Di Stante, Laurentia Lionte, Lucia Lucarelli, Loredana Magi, Sabrina Mambelli, Elena Manfredi, Elisa Mazzoli, Alessandra Ranocchi, Giovanni D’Onofrio, Angela Pia Rinaldi, Antonella Sebastianelli, Stefania Silvestrini and Marina Di Luca
UOC Nephrology and Dialysis, Azienda Ospedaliera “Ospedali Riuniti Marche Nord”, Fano, Italy

Background and Aims: Remote control of dialysis parameters has become an essential routine in the Centers that perform Peritoneal Dialysis. For patients in APD there are Cloud-based platforms or with VPN connection that allow daily monitoring and which have proved to be very useful for reducing hospital visits and treatment complications, especially during the recent pandemic. The same cannot be said of CAPD patients for whom the procedures are carried out manually, without electromedical devices, with a paper report of the parameters. Furthermore, to date, there are no dedicated applications able to communicate these important measurements to the Centres.

Method: In March 2021 we created a calculation table file, with limited data entry, divided by days, daily exchanges and monthly sheets. Patients and/or caregivers can insert loading and drainage volumes, type of bags used, blood pressure values, weight and diuresis at an agreed time. The system automatically calculates and graphically displays the total daily and monthly average ultrafiltration for each exchange, the daily balance as well as the average of all the aforementioned parameters for the entered period (Figure 1). There is also a graphic sheet with an annual summary of the average values (Figure 2). The file is uploaded online, subject to the patient’s consent, via a free file hosting service that allows modification and reading shared and protected by password between patients and Center operators.

Results: To date, 9 CAPD patients in our Center have been included in the program with good acceptance by patients and caregivers, who enter data based on their availability of time and regularly in anticipation of the monthly outpatient visit. The staff of the Centre, both Doctors and Nursing, access the file periodically, in case of need and in preparation for the visit. In this way, regular checks and evaluations of prescription compliance, ultrafiltration efficacy, maintenance within the expected ranges of weight, blood pressure and fluid balance of patients in CAPD are obtained, as is the case for patients in APD.

Conclusion: The creation of a shared file for monitoring the dialysis parameters of CAPD patients could be able to reduce the existing gap with those in APD, at least as regards the vital and dialysis parameters, since the functioning of the catheter in individual exchanges cannot be evaluated. A more extensive experience is needed, and is being studied, to confirm the usefulness of this approach which currently already guarantees a reduction in hospital admissions and integrates and structures the clinical information that can be obtained in the traditional way.
Figure 1:
Background and Aims: The evidence on the management of renal anaemia in peritoneal dialysis (PD) is much weaker than in hemodialysis (HD). Current guidelines establish the same haemoglobin (Hb) target for patients under erythropoietin stimulating agents (ESAs) in both dialysis techniques (PD, HD), although patients in PD are usually younger, more active and less comorbid. Unfortunately, there is not randomized controlled trials evaluating the efficacy and safety the effect of different Hb target on clinical outcomes. The aim of this study is to describe the current situation of anaemia prevalence, treatments, and achievement of clinical guidelines recommendations in this population.

Method: Retrospective nationwide multicenter study including patients from 19 PD units. All prevalent PD patients that were active in the technique in November 2019 for at least 3 months was included (to avoid COVID pandemic interferences). Exclusion criteria were a previous kidney transplant failure and being on PD due to a cardio-renal syndrome with a residual renal function over 20 ml/min/1.73 m². The nephrologists collected baseline data, demographics, comorbidities, and data related to anaemia management (ie, laboratory values, previously prescribed treatments, and subsequent adjustments) from electronic medical records. The European adaptation of KDIGO guidelines was the reference for iron and Hb limits, prescriptions and targets.

Results: A total of 343 patients (mean age 62.9 years, 61.2% male) were included. Regarding anaemia treatment prescription, 72.9% were receiving ESAs and 33.2% iron therapy (20.7% intravenously-IV and 12.5% orally). Eighty-two (32.8%) patients were receiving ESA without iron therapy, despite having an indication to do it according ERBP guidelines in 53 out of them. After knowing lab results, iron therapy was only started in 8 (15%) patients. Among ESA-treated patients, 58.8% had a normal control (Hb 10–12 g/dl). Seventeen patients had haemoglobin over 13 g/dl, and 12 of them continued receiving ESA after knowing lab results. Only three patients had persistent haemoglobin <10 g/dl. Seventy patients (2%) met criteria for ESA resistance (epoetin dose >300 IU/kg/week). Patients in the highest tertile of erythropoietin resistance index (ERI) (>6.3 UI/kg/week/g/dl) were more inflamed, had lower albumin levels and lower residual renal function.

Conclusion: Anaemia prevalence is high in this population and its management in PD Units could be improved according to the ERBP guidelines. The lack of iron therapy in patients who should have received it and the excessive tolerance to high Hb levels are the most relevant opportunities to improve compliance with clinical guidelines.

<table>
<thead>
<tr>
<th>Hb range (g/dl)</th>
<th>Absolute iron deficiency (%)</th>
<th>Functional iron deficiency (%)</th>
<th>No iron deficiency (%)</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Hb &gt;13</td>
<td>0</td>
<td>0</td>
<td>10.7</td>
<td>10.7</td>
</tr>
<tr>
<td>Hb between 12-13</td>
<td>1.7</td>
<td>2.6</td>
<td>19.3</td>
<td>23.6</td>
</tr>
<tr>
<td>Hb between 10-12</td>
<td>0.9</td>
<td>10.7</td>
<td>45.9</td>
<td>57.5</td>
</tr>
<tr>
<td>Hb &lt;10</td>
<td>0.4</td>
<td>1.3</td>
<td>6.4</td>
<td>8.2</td>
</tr>
<tr>
<td>Total</td>
<td>3.0</td>
<td>14.6</td>
<td>82.4</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Patient’s distribution of iron deficiency according to Hb ranges among those under ESA treatment.
INNOVATIVE ARTIFICIAL INTELLIGENCE EDUCATION TOOL IN PERITONEAL DIALYSIS PATIENTS

Woo-jean Lin1, Ching-I Cheng2, Jui-Hsin Hsu1, Hui-Ting Liu1, Yi-Tingchen2, Yu-Hsiang Chou3 and Chih-Kang Chiang2

Abstract

Background and Aims: Home self-care is an essential part of peritoneal dialysis. Adequate home self-care ability and how to prevent infection complication is very important for patients with PD. National Taiwan University Hospital peritoneal dialysis center began to introduce AI (artificial intelligence) health education tool-PD chatbot since May 2021. This chatbot can automatically reply and has a variety of interactive games. We used chatbot to educate patients how to deal with peritonitis and catheter-related infections. Using these interactive games could enhance patients’ understanding and help them to review the principles of peritoneal dialysis exchange and exit site care skills. Using chatbot, we could predict infection risks according to the patient’s adherence and make patients understand the possible risks and probability of non-compliance to achieve the purpose of strengthening cognition.

Method: We designed interactive games “Predict Peritonitis Risk” and “Predict Exit site Infection Risk”. The health education game was designed according to the expert experience and had been reviewed by 9 experts with practical experience in patients with hemodialysis and peritoneal dialysis, including 1 nephrologist and 8 senior dialysis nurses. We used technical evaluation form for training patients’ standard of peritoneal dialysis center. The user interface of the chatbot was designed based on the PD patients’ habits of dialysate exchange and exit site care. Through the interactive games and prediction of risks of infection, the patient was reminded of the key points of operating dialysate exchange and exit site care. It also could enhance self-care awareness and improve self-cognition and behavior. We utilized Likert 5-point score to investigate patients’ recognition of using interactive games and satisfaction.

Results: In November 2021, a total of 173 peritoneal dialysis patients were recruited. The percentage of male was 48%. Among these patients, 38.7% were 21–50 years old, 46.8% were 51–70 years old, and 10% did not comply with environmental preparations. Regarding the technical part of peritoneal dialysis exchange, 15% patients had the habit of occasional eating raw food, and 18% patients had constipation and diarrhea. In terms of the care of exit site, 21.4% patients did not watch out expired date of the medical materials, and 25% patients did not replace disinfection solution for more than 30 days. PD exit site infection risk notification and health education could correct patients’ poor habits at home. In 5-point scale, 90.8% patients scored more than 4 points about the item of “Overall Satisfaction with AI Interactive Games”.

Conclusion: Peritoneal dialysis is a long-term treatment. Through regular training and technical strengthening and reminders, the home exchange can be standardized and more reliable. Combining innovative AI health education with interactive games to educate peritonitis and catheter-related infections could allow patients to accept different health education models to improve learning and motivation of home care. As a result, techniques can be performed more accurate and standardized, and then we can reduce the infection-related complications of peritoneal dialysis.

PERITONEAL CLEARANCE OF TRACE ELEMENTS IN PERITONEAL DIALYSIS PATIENTS

Suleyman Koz1, Esin Oguz1,2 and Cagla Sayın1,2

Background and Aims: Both accumulations and deficiencies of trace elements (TE) could be seen in peritoneal dialysis (PD) patients. Peritoneal clearance remains major route of elimination for many solutes including TE, in PD patients. Imbalances of TE may have deleterious effects on the patients. Data on TE balances in PD patients are inadequate. Here, we present some data from a larger study. We aimed to analyze peritoneal clearance of Boron (B), Copper (Cu), Zinc (Zn), Selenium (Se), Strontium (Sr) and Molybdenum (Mo) in a cohort of PD patients.

Results: Data on plasma levels, clearances and daily loss of TE are shown in the Table 1. The clearances were ordered from smallest to largest as follows: Zn, Cu, Se, Sr, Mo, Ni, B. On the other hand, spent dialysate daily element losses were ordered from smallest to highest as follows: Cr, Ni, Se, Mo, Cu, Sr, Zn, B

Conclusion: Our study provides data on elimination of some trace elements, which may help to better understand the TE balance in PD patients. Data suggest that B has the highest and Zn the lowest peritoneal clearance values.

Table 1: Plasma levels, clearances and daily losses of trace elements.

<table>
<thead>
<tr>
<th>Element</th>
<th>PD (n = 8)</th>
<th>CG (n = 43)</th>
<th>Clearance (L/day)</th>
<th>Total daily peritoneal excretion (μg/day)</th>
<th>p (PD vs. CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B (μg/L)</td>
<td>131,8 (75,3-283,2)</td>
<td>141,1 (64,9-157,6)</td>
<td>8,50 (4,3-11,2)</td>
<td>115,8 (846,5-1559,5)</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Cr (μg/L)</td>
<td>#</td>
<td>#</td>
<td>#</td>
<td>#</td>
<td>#</td>
</tr>
<tr>
<td>Ni (μg/L)</td>
<td>0,3 (0,2-0,6)</td>
<td>0 (0-0,11)#</td>
<td>8,20 (4,5-10,8)</td>
<td>3,1 (2,1-5,1)</td>
<td>0,002</td>
</tr>
<tr>
<td>Cu (μg/L)</td>
<td>500,1 (109,5-824,1)</td>
<td>830,8 (659,5-1068,6)</td>
<td>0,28 (0,11-0,36)</td>
<td>124,4 (99,0-177,1)</td>
<td>0,021</td>
</tr>
<tr>
<td>Zn (μg/L)</td>
<td>878,7 (779,4-1661,6)</td>
<td>978,6 (722,4-2288,4)</td>
<td>0,21 (0,06-1,00)</td>
<td>276,1 (88,1-1048,5)</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Se (μg/L)</td>
<td>29,9 (10,4-51,5)</td>
<td>84,4 (58,9-106,8)</td>
<td>0,35 (0,18-0,93)</td>
<td>13,2 (9,1-25,7)</td>
<td>0,001</td>
</tr>
<tr>
<td>Sr (μg/L)</td>
<td>271,5 (18,9-315)</td>
<td>295,9 (263,5-314,1)</td>
<td>1,05 (0,84-6,3)</td>
<td>22,6 (148,0-368,4)</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Mo (μg/L)</td>
<td>4,4 (3,5-4,8)</td>
<td>0 (0-0,7)*</td>
<td>7,06 (6,18-8,68)</td>
<td>39,7 (27,8-59,1)</td>
<td>0,0001</td>
</tr>
</tbody>
</table>

All data are presented as median (interquartile range) PD, Peritoneal Dialysis Group; CG, Control Group;
# plasma levels were below limit of detection
& plasma levels were below limit of detection in 29 of the subjects
*plasma levels were below limit of detection in 25 of the subjects

B, Boron; Cr, Chromium; Ni, Nickel; Zn, Zinc; Se, Selenium; Sr, Strontium; Mo, Molybdenum

Conclusion: Peritoneal dialysis is a long-term treatment. Through regular training and technical strengthening and reminders, the home exchange can be standardized and more reliable. Combining innovative AI health education with interactive games to educate peritonitis and catheter-related infections could allow patients to accept different health education models to improve learning and motivation of home care. As a result, techniques can be performed more accurate and standardized, and then we can reduce the infection-related complications of peritoneal dialysis.
Background and Aims: Peritoneal dialysis (PD) is the incident kidney replacement therapy (KRT) for 16% of patients in Scotland. Conveying the healthcare-related burden associated with KRT is essential for informed patient choice but has not been characterised as comprehensively in PD as in haemodialysis (HD) or kidney transplantation. Knowledge of the patient journey and the cumulative impact of renal service interactions is key to practising patient-centred realistic medicine, and considering service configuration, resource deployment, and the targeting of carbon emission reductions necessary for addressing the climate emergency. This study therefore aimed to capture the nature and extent of kidney-related healthcare activity in the first year of PD therapy.

Method: This retrospective observational study included all incident adult patients on PD between 1st January 2015–31st December 2019 from two Scottish health boards servicing a population of 1.6 million people. Analysis was undertaken of prospectively recorded healthcare-related activity from the electronic patient record. Data pertaining to hospital admissions, scheduled and unscheduled outpatient clinic, and home visit activity was captured up to the first 365 days post commencement of PD, and censored by death or switch in KRT modality. Data concerning dialysis access activity, radiological activity and relevant infection episodes was also analysed. Carbon mapping of healthcare activity was estimated using patient postcode data and previously published carbon footprint estimations.

Results: PD was initiated in 112 patients over the study period. Four patients died and 63 patients (52%) transitioned to another KRT within 365 days of commencing PD (10 live donor kidney transplantation, 19 cadaveric kidney transplantation, 34 HD) and one patient recovered native function. The median duration from insertion of PD catheter to utilisation was 26 days (IQR 34). Mean distance travelled to renal unit was 23.7 miles. Over the first year, patients had a mean 36.4 days (SD 22.7) of face-to-face contact days with renal services. This included a mean of 1.5 (SD 1.6) hospital admissions, with a median 5 (IQR 10.8) in-patient days. Additionally, a mean of 2.5 (SD 2.5) unscheduled ambulatory assessments per patient; 4.7 (SD 6.2) telephone consultations; 14.9 (SD 8.96) face-to-face clinics with a PD nurse and 7 (SD 3.9) with a nephrologist, and 2.5 (SD 3.4) home visits occurred. Within these contact episodes there were on average 4.4 (SD 4.1) radiological investigations per patient (3.1 x-rays, 0.4 CTs, 0.4 ultrasounds, 0.1 MRIs); and 1.4 (SD 0.3) infection events (0.02 bloodstream infections, 0.2 urinary tract infections, 0.7 PD catheter site infections, and 0.5 PD peritonitis episodes). The estimated carbon footprint from patient contact with renal services was 803.6 kg CO2e/patient; this included 402.6 kg CO2e/patient for inpatient days, 54.6 kg CO2e/patient for unscheduled ambulatory assessment, 0.24 kg CO2e/patient for telephone consultations, 293.8 kg CO2e/patient for outpatient clinic activity and 17.6 kg CO2e/patient for home visits, and 34.8 kg CO2e/patient for radiological investigation and treatment of infection episodes.

Conclusion: Although PD is a home-based therapy patients should be aware of the frequency of attendance and admission days in the first year. KRT transition appeared common in this cohort, with similar proportions of transplantation and conversion to HD which prompts consideration of early vein mapping for arteriovenous haemodialysis in patients without prospect of early transplantation. Sixty-eight percent of the cohort experienced at least one infection episode necessitating anti-microbials, with implications for patient experience and anti-microbial stewardship. The length of time PD catheters remained in situ but not used was heterogeneous and merits further examination given the frequency of infection episodes and KRT transition. Estimates of carbon footprint relating to routine and unscheduled care indicate that carbon hotspots include patient travel and hospital admissions, and episodes of peritonitis; a full life cycle analysis is merited.
Table 1: Analysis of HD first versus PD first groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 135)</th>
<th>Previous HD (n = 22)</th>
<th>PD first (n = 113)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male), n (%)</td>
<td>86 (63.7)</td>
<td>14 (60.9)</td>
<td>72 (64.3)</td>
<td>0.756</td>
</tr>
<tr>
<td>Age at start of PD (years) (a)</td>
<td>52.9 ± 14.6</td>
<td>52.0 ± 15.5</td>
<td>53.0 ± 14.6</td>
<td>0.772</td>
</tr>
<tr>
<td>Time in PD (months) (a)</td>
<td>112.7 ± 44.2</td>
<td>97.7 ± 56.2</td>
<td>115.2 ± 41.6</td>
<td>0.107</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>88 (65.2)</td>
<td>11 (47.8)</td>
<td>77 (68.8)</td>
<td>0.055</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>54 (60)</td>
<td>10 (43.5)</td>
<td>44 (39.3)</td>
<td>0.709</td>
</tr>
<tr>
<td>Charleston Score (a)</td>
<td>4.4 ± 2.2</td>
<td>4.6 ± 2.3</td>
<td>4.3 ± 2.2</td>
<td>0.519</td>
</tr>
<tr>
<td>KtV at PD start (a)</td>
<td>2.7 ± 0.8</td>
<td>2.5 ± 0.7</td>
<td>2.7 ± 0.9</td>
<td>0.201</td>
</tr>
<tr>
<td>KtV at end of follow-up (a)</td>
<td>2.1 ± 0.6</td>
<td>1.9 ± 0.7</td>
<td>2.1 ± 0.6</td>
<td>0.250</td>
</tr>
<tr>
<td>Residual diuresis at PD start (mL/24h) (a)</td>
<td>1769 ± 955</td>
<td>1153 ± 920</td>
<td>1880 ± 924</td>
<td>0.007</td>
</tr>
<tr>
<td>Residual diuresis at end of follow-up (mL/24h) (a)</td>
<td>1175 ± 889</td>
<td>750 ± 1074</td>
<td>1252 ± 836</td>
<td>0.037</td>
</tr>
<tr>
<td>UF failure, n (%)</td>
<td>17 (14)</td>
<td>6 (30.1)</td>
<td>11 (10.9)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

PD adequacy

<table>
<thead>
<tr>
<th>Complications</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual peritonitis rate (a)</td>
<td>0.1 ± 0.2</td>
<td>0.1 ± 0.3</td>
<td>0.1 ± 0.2</td>
<td>0.855</td>
</tr>
<tr>
<td>Annual exit tunnel infections rate (a)</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.1</td>
<td>0.845</td>
</tr>
<tr>
<td>Annual tunnel infections rate (a)</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.890</td>
</tr>
<tr>
<td>Annual hospitalizations rate (a)</td>
<td>0.2 ± 0.5</td>
<td>0.2 ± 0.5</td>
<td>0.2 ± 0.5</td>
<td>0.955</td>
</tr>
</tbody>
</table>

Outcomes at end of follow-up, n (%)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total (n = 135)</th>
<th>Previous HD (n = 22)</th>
<th>PD first (n = 113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD maintenance</td>
<td>31 (23)</td>
<td>4 (17.4)</td>
<td>27 (24.1)</td>
</tr>
<tr>
<td>HD transfer</td>
<td>52 (38.5)</td>
<td>5 (21.7)</td>
<td>47 (42)</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>29 (21.5)</td>
<td>7 (30.4)</td>
<td>22 (19.6)</td>
</tr>
<tr>
<td>Death</td>
<td>20 (14.8)</td>
<td>7 (30.4)</td>
<td>13 (11.6)</td>
</tr>
<tr>
<td>Loss of follow-up</td>
<td>3 (2.2)</td>
<td>0 (0)</td>
<td>3 (2.7)</td>
</tr>
</tbody>
</table>

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INFLUENCE OF DIETARY INTAKE ON GASTROINTESTINAL SYMPTOMS AND INFLAMMATION MARKERS IN PERITONEAL DIALYSIS PATIENTS IN SLOVENIA

Mia Majer1, Bojan Knap2,3 and Nada Rotovnik Kozjek1,3,4

1Institute of Oncology, Department of Clinical Nutrition, Ljubljana, Slovenia, 2University Medical Center Ljubljana, Department of Nephrology, Ljubljana, Slovenia, 3Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia and 4Faculty of Health Sciences Izola, University of Primorska, Izola, Slovenia

Background and Aims: Gastrointestinal symptoms are prevalent in patients with end-stage renal disease. Gastrointestinal symptoms in such patients are related to gastric hypomotility, increased medication intake, uremia, and changes in diet. In addition GI symptoms and problems associated with bowel dysfunction are a common cause of technique failure and poor dialysis efficacy. The reason for presence of some gastrointestinal symptoms is also chronic inflammatory state. Inflammation can have many negative effects, including decreased appetite, accelerated protein skeletal muscle breakdown and hypercatabolism.

Method: 14 peritoneal dialysis patients were included in single Department of Nephrology in the University Medical Center in Ljubljana. All patients were interviewed by a dietitian and nutritional assessment was conducted. Gastrointestinal symptom Rating Scale (GSRS) with 7-grade Likert scale was used to evaluate the intensity of GI symptoms and Bristol Stool Form Scale (BSFS) to classify patient’s stool. The dietary intake of peritoneal dialysis patients was assessed using 7-day food diaries and analyzed with Prodi program (PRODI® 6.4 Expert program, Stuttgart, Deutschland). Body composition has been measured with bio impedance spectroscopy. Routine blood analysis was performed.

Results: Among 14 patients undergoing peritoneal dialysis, most of them were male (71.4%) with average age of 53.07 ± 12.32 years. Average energy intake of 14 patients was 21.05 ± 5.72 kcal/kg body weight per day, average protein intake was 0.87 ± 0.39 g/ kg body weight per day and average fiber intake was 13.75 ± 7.25 g per day. They were inadequate according to the dietary guidelines for peritoneal dialysis patients. Average dietary protein-fiber index was 6.86 ± 3.81 per day. Average dietary potassium intake was 1917.80 ± 790.08 mg per day which corresponds to the guidelines for peritoneal dialysis patients and average potassium serum value 4.45 ± 0.42 mmol/L. GSRS questionnaire showed peritoneal patients had minor to mild discomfort in abdominal pain, constipation and indigestion GI symptom cluster. Patients’ self-analysis of stool showed BSFS Types 3.23 ± 1.64 if BSFS Types 3–5 are defined as normal stools. Dietary protein intake strongly correlated with dietary energy intake (r = 0.76,
p = 0.003), dietary protein-fiber index strongly correlated with PRAL value (r = 0.70, p = 0.007) and dietary potassium moderately to strongly correlated with dietary fiber intake (r = 0.62, p = 0.025). Serum value of IL-6 strongly correlated with dietary potassium intake (r = 0.72, p = 0.006) and moderately to strongly correlated with dietary fiber intake (r = 0.6, p = 0.034). The correlation between dietary potassium intake and serum hsCRP was significant (p = 0.042). The correlation between Bristol stool consistency value and serum hsCRP was significant (p = 0.0255). The correlation between total GSRS score and serum value of albumin was significant (p = 0.0015). The correlation between total GSRS score and dietary protein-fiber index was significant (p = 0.0403).

Conclusion: Gastrointestinal diseases in peritoneal dialysis patients are comparatively understudied in the literature, despite having a significant impact on dialysis efficacy and the quality of life. Analysis of GSRS questionnaire showed that abdominal pain, constipation and indigestion caused minor to mild discomfort in PD patients. The analysis also showed that fiber intake, potassium intake and gastrointestinal symptoms are significantly associated with inflammation markers and are important contributing factors to chronic inflammatory state in these patients. Patients still lack the basic knowledge of nutrition, thus in the future nutritional consultations, innovative teaching techniques and help will be crucial to prevent the decline in nutritional status.

#4797
ASSOCIATION BETWEEN BLOOD PRESSURE AND SALT CONSUMPTION WITH FLUID STATUS USING BIOIMPEDANCE SPECTROSCOPY IN PERITONEAL DIALYSIS PATIENTS
Rita Silva, Pedro Castro, Marina Sofia Rodrigues Reis, Sofia Cerqueira, Catarina Romãozinho, Pedro Maia, Teresa Mendes and Rui Alves
Coimbra University Hospital, Nephrology, Portugal

Background and Aims: Control of extracellular volume in peritoneal dialysis (PD) patients requires both removal of sodium and water. Hypervolemia occurs more frequently in PD patients and is associated with greater morbidity and mortality. Dietary salt restriction (Na+ < 2g) is recommended in all PD patients. Most patients do not comply with this recommendation (prevalence difficult to assess). Bioimpedance spectroscopy (BIS) devices can help assess volume overload in patients receiving maintenance PD. The aim of our study was to determine the association between fluid status as measured using BIS to BP and salt consumption in continuous ambulatory peritoneal dialysis (CAPD) patients.

Method: We performed a retrospective, longitudinal study, that included 60 PD patients followed at our unit. Demographic and clinical characteristics, such as age, gender, chronic kidney disease (CKD) etiology, time on PD program, dialytic efficacy (Kt/V), peritoneal equilibration test results, BIS results and episodes of peritonitis were registered from our unit database. We measured total sodium removal and estimated daily sodium intake using dietary recall for one day, during the assessment of dialysis adequacy. Based on a 2017 study of 87 patients on PD that sought a correlation between effective daily sodium intake (memory recollection) and urinary + peritoneal sodium sieving. It allowed, through logistic regression, the creation of equations for patients with and without renal residual function (RRF) (Pearson’s 0.6).

- RRF(-) group, sodium intake (mg/d) = 19.3 × peritoneal sodium removal (mEq/d) + 211
- RRF(+) group, sodium intake (mg/d) = 15.4 × total sodium removal (mEq/d) + 609

Statistical analyses were performed using SPSS statistics version 23.0. The statistical hypothesis tests with p-value <0.05 were considered significant.

Results: Sixty patients (male: 60%) with a mean age of 55.9 ± 13.7 years were selected. Observation time on dialysis was 24.8 months ± 11.9 (min. 2, max. 63). The most common etiology of CKD was glomerular diseases (n = 16, 26.7%), followed by uncertain etiology (n = 11, 18.3%) and diabetic kidney disease (n = 9, 15%). In total, 71.7% of patients were on continuous ambulatory peritoneal dialysis (CAPD). Mean Kt/V was 2.2 ± 0.6 and the majority of patients were high-average transporters. Previous comorbidities were arterial hypertension (n = 60, 100%), diabetes (n = 16, 26.7%), heart failure (n = 13, 21.7%), body mass index <30 kg/m2 (n = 22, 36.7%) and dyslipidemia (n = 40, 66.7%). According to European Society of Cardiology we define three stages of hypertension: stage 1 (140–159/90–99 mmHg) with 15 patients (25%), stage 2 (160–179/100–109 mmHg) with 14 patients (23.3%) and stage 3 (≥180/≥110 mmHg) with 4 patients (6.7%). In total, we have 27 patients (45%) with hypertension under control. A statistically significant positive correlation was found between a status of overhydration (≥2 liters) with salt consumption (Na+ > 2g) (p = 0.01) and also of hypertension stages 2 and 3 (p = 0.03).

Conclusion: In PD patients, BIS is a reliable method for evaluating volume status. We found that stable CAPD patients with uncontrolled BP had higher overhydration and salt consumption compared to patients whose BP was controlled. Control of hypervolemia and blood pressure is associated with better cardiac condition. Thus, it is important to encourage patients on peritoneal dialysis to significantly restrict salt intake.

#3122
30-DAY COMPLICATIONS IN PERITONEAL DIALYSIS CATHETERS INSERTED PERCUTANEOUSLY VERSUS SURGICALLY IN A SECOND LEVEL HOSPITAL IN MERIDA, YUCATAN, MEXICO
Leticia Tapia and Naomi Alvarez
General Hospital Agustin O’Horan, Nephrology, Mérida, Mexico

Background and Aims: Peritoneal dialysis (PD) catheter insertion technique has an impact on the health outcomes and technical success in PD. The percutaneous technique allows for a bedside, minimally invasive and faster insertion without the need of using an operating room and general anesthesia. In 2021, Agarwal et. al reported that percutaneous insertion was associated with a 64% relative risk reduction (RRR) of early exit site infection and a 48% RRR of early peritonitis with no difference in terms of mechanical complications compared to the surgical technique [1]. The aim of our study was to describe the frequency of mechanical and infectious complications within the first 30 days of PD catheter insertion between the percutaneous and surgical technique.

Method: We conducted a descriptive and prospective study in our Hospital from January 1st to December 31st, 2022. Patients who were candidates for renal replacement therapy with PD and who had no previous history of abdominal surgery or only minor abdominal surgery, underwent percutaneous insertion of PD catheter by a nephrologist with a bedside blind technique, whereas patients with previous abdominal surgery underwent surgical insertion with a mini laparotomy. Informed consent and preoperative blood tests were obtained before the procedure in both techniques. Patient preparation for the percutaneous insertion included fasting the night before, colonic enema and the placement of a urinary catheter, patients received antimicrobial prophylaxis as well as analgesia and light sedation. Mechanical and infectious complications within the first 30 days after insertion of double cuff Tenckhoff catheters were registered.

Results: During the study period, 155 PD catheter insertions took place in our hospital, the majority of insertions were surgical (53.5% versus 46.4%) and happened in women (60.6%). The mean age of the population was 51.5 years and 70.3% of the participants were diabetic. Exit-site infection was significantly more frequent in the surgically placed PD catheters (10% versus 1%, p = 0.02), there was a tendency for more mechanical dysfunction in the surgical placement catheters (10.8% versus 1.3%, p = 0.07) and transfer to hemodialysis was more frequent in the surgical insertion group (10.8% versus 1.3%, p = 0.01). There was no difference between peritonitis in both groups and the frequency of uncomplicated PD catheters (catheter survival without any complication) was similar in both techniques.

Conclusion: Bedside PD catheter insertion by the nephrologist using a percutaneous technique can be an easy, timely, safe and adequate procedure with comparable success to the surgical insertion. It may have the advantage of more efficient control of infectious and mechanical complications. PD catheter survival without any complication was similar in both techniques.

REFERENCE
Table 1: Complications in PD catheters placed surgically versus percutaneously.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n = 155)</th>
<th>Surgical (n = 83)</th>
<th>Percutaneous (n = 72)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female (%)</td>
<td>94 (60.6)</td>
<td>57 (68.6)</td>
<td>37 (50.68)</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>109 (70.3)</td>
<td>57 (68.7)</td>
<td>52 (72.2)</td>
<td>0.63</td>
</tr>
<tr>
<td>Mechanical dysfunction (%)</td>
<td>16 (10.3)</td>
<td>12 (14.4)</td>
<td>4 (5.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>Exit-site infection (%)</td>
<td>9 (6)</td>
<td>8 (10)</td>
<td>1 (1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Peritonitis (%)</td>
<td>19 (12.2)</td>
<td>11 (13.2)</td>
<td>8 (10.9)</td>
<td>0.68</td>
</tr>
<tr>
<td>Uncomplicated catheter at 30 days (%)</td>
<td>115 (74.1)</td>
<td>57 (68.6)</td>
<td>58 (80.5)</td>
<td>0.12</td>
</tr>
<tr>
<td>Transfer to haemodialysis (%)</td>
<td>10 (6.4)</td>
<td>9 (10.8)</td>
<td>1 (1.3)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

#6292

**PSYCHOLOGICAL CHALLENGES OF THE PATIENT STARTING PERITONEAL DIALYSIS**

Marica Mulé1, Vincenzo Terlizzi2, Diana Bertoni3, Carla Bussi1, Anna Bertoni3, Francesco Scolari1, Valerio Vizzardi1 and Federico Alberici1

1Division of Nephrology and Dialysis, ASST Spedali Civili, Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Brescia, Italy and 2Psychology, Catholic University, Milan, Italy

**Background and Aims:** The start of peritoneal dialysis (PD) in patients affected by end stage renal disease (ESRD) may have a significant psychological impact. Aim of this study was to assess the most frequent reasons triggering the request of psychological referral in patients starting PD.

**Method:** A thematic analysis of the clinical diaries of the psychological support sessions of 15 consecutive patients requesting a psychological referral during the first 3 months of PD was performed from 2018 to 2021.

**Results:** Fifteen patients were enrolled, 6 women and 9 men. The median age was 59 (range 27–73) and the cause of the ESRD were glomerulonephritis (5/15), diabetic kidney disease (2/15), tubulo-interstitial (2/15), vascular nephropathy (1/15), other (5/15). The most frequent symptoms triggering the request for a psychological referral were insomnia and anxiety respectively in 12 and 15 cases. From the psychological assessments the most frequent causes of the patients’ symptoms have been identified as per follow:

- Difficulties in elaborating and accepting the chronic disease (why me?) in 15 Patients.
- Difficulties in accepting the esthetical impact of the peritoneal catheter in the summer how I do it? in 15 patients.
- The difficulties related to managing fluid restrictions in 15 patients.
- The limitations to traveling (what if something happens to me?) in 13 patients.
- The difficulties to comply to the dietetic restriction (things taste like cardboard; I always eat the same things) in 7 patients.
- The concerns related to the risks of developing peritonitis (fear of not doing the procedure correctly) in 5 patients.
- The anxiety of not being able to fulfil the tasks requested by the treatment (I can’t; I lack air when I have to start dialysis) in 6 patients.

**Conclusion:** This qualitative study performed in PD patients during the first 3 months of dialysis identified the most frequent causes triggering the request of a psychological referral. These findings may be of help for the physicians in order to identify which aspects need to be better discuss during the pre-dialysis counselling and stresses the importance of the availability of a psychological support in a PD unit.

#6717

**IS PERITONEAL DIALYSIS RELATED PERITONITIS A MAJOR RISK FACTOR FOR CARDIOVASCULAR EVENTS?**

Catarina Almeida, Maria Victoria Vaz Da Rocha Paes de Faria, Joana Pereira Dias, Daniela Lopes, Rute Carmo, João Carlos Fernandes, Maria Clara Almeida and Ana Marta Gomes

Centro Hospitalar Vila Nova de Gaia / Espinho, Nephrology, Portugal

**Background and Aims:** Cardiovascular (CV) disease remains the leading cause of death in peritoneal dialysis (PD) patients and traditional CV risk factors are unable to fully account for this high incidence. The aim of our study was to establish the incidence of CV events such as acute myocardial infarction (AMI) in the PD population and assess possible risk factors for its occurrence.

**Method:** We retrospectively studied patients on PD in our unit with a minimum 3-years dialysis vintage, between January 1st 2015 and April 30th 2022. Patients with previous CV disease were excluded. Demographic and clinical data were collected, such as traditional CV risk factors, AMI, peripheral artery disease, cerebrovascular events, as well as dialysis efficiency, hydration status obtained by Body Composition Monitor (Fresenius Medical Care) and PD-related infections before AMI or end of follow-up. Univariate analysis was performed and logistic regression was applied to access predictors of AMI.

**Results:** Of the 43 patients recruited, 53.5% were male, with a mean age of 56.4 ± 11.8 years. About 98% of patients were hypertensive, 21% were diabetic, 19% were obese, and 54% had dyslipidemia. Five (11.6%) patients had a CV event while on PD, 4 suffered AMI and 1 patient had an ischemic stroke. Patients’ characteristics are presented in Table 1. In the follow-up, peripheral arterial disease (p = 0.037), hyperphosphatemia (p = 0.035) and the cumulative number of peritonitis (p = 0.018) were associated with the occurrence of AMI. In our population we found a higher frequency of peritonitis in the year prior to the AMI (p = 0.024). In logistic regression, the cumulative number of peritonitis was a predictor of AMI (OR 4.918, CI 95%:1.093-22.132). In the mean follow-up time of 4.7 ± 1.4 years, the overall mortality was 21.7%, with CV disease accounting for 60% of the observed deaths. AMI and peritonitis were associated with higher mortality in PD patients (p = 0.016 and p = 0.009, respectively).

**Conclusion:** PD-related peritonitis was a predictor of AMI in these population. The risk is higher in the year following a peritonitis episode. This may be due to a chronic inflammatory state that persists after successful treatment of peritonitis which may predispose to enhanced CV risk. Similar to previous studies, we found that cumulative episodes of peritonitis were associated with increased mortality in PD population.
Table 1: Comparison between PD patients with and without AMI.

<table>
<thead>
<tr>
<th></th>
<th>AMI (4)</th>
<th>Non-AMI (39)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years - mean ± SD</td>
<td>60.8 ± 9.5</td>
<td>55.9 ± 12</td>
<td>ns</td>
</tr>
<tr>
<td>Male sex –N(%)</td>
<td>4(100.0)</td>
<td>19(48.7)</td>
<td>ns</td>
</tr>
<tr>
<td>CV risk factors –N(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4(100.0)</td>
<td>38(97.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1(25.0)</td>
<td>8(20.5)</td>
<td>ns</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>2(50.0)</td>
<td>21(53.8)</td>
<td>ns</td>
</tr>
<tr>
<td>Obesity</td>
<td>0(0.0)</td>
<td>8(20.5)</td>
<td>ns</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>0(0.0)</td>
<td>2(5.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Dialysis vintage, months – median (IQR)</td>
<td>61.6(53.8-80.8)</td>
<td>50.3(42.7-68.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Follow-up time, years- mean ± SD</td>
<td>5.4 ± 1.2</td>
<td>4.7 ± 1.4</td>
<td>ns</td>
</tr>
<tr>
<td>Peripheral arterial disease –N(%)</td>
<td>2(50.0)</td>
<td>2(5.1)</td>
<td>0.037</td>
</tr>
<tr>
<td>Cerebral vascular events –N(%)</td>
<td>0(0.0)</td>
<td>1(2.6)</td>
<td>ns</td>
</tr>
<tr>
<td>Hemoglobin g/dl- mean ± SD</td>
<td>11.8 ± 1.1</td>
<td>10.9 ± 1.3</td>
<td>ns</td>
</tr>
<tr>
<td>Phosphorus mg/dl- median (IQR)</td>
<td>6.6(6.0-7.3)</td>
<td>5.4(4.4-6.2)</td>
<td>0.035</td>
</tr>
<tr>
<td>Calcium mg/dl- mean ± SD</td>
<td>8.9 ± 0.6</td>
<td>8.7 ± 0.7</td>
<td>ns</td>
</tr>
<tr>
<td>PTH pg/ml- mean ± SD</td>
<td>713 ± 388</td>
<td>433 ± 252</td>
<td>ns</td>
</tr>
<tr>
<td>Albumin g/dl-mean ± SD</td>
<td>4.1 ± 0.4</td>
<td>3.8 ± 0.4</td>
<td>ns</td>
</tr>
<tr>
<td>Renal KT/V- mean ± SD</td>
<td>0.8 ± 0.7</td>
<td>0.5 ± 0.4</td>
<td>ns</td>
</tr>
<tr>
<td>Total KT/V-mean ± SD</td>
<td>2.1 ± 0.3</td>
<td>1.9 ± 0.3</td>
<td>ns</td>
</tr>
<tr>
<td>Over-hydration- mean ± SD</td>
<td>1.5 ± 1.0</td>
<td>1.5 ± 1.6</td>
<td>ns</td>
</tr>
<tr>
<td>Cumulative peritonitis number per patient -median (IQR)</td>
<td>2.5(2.0-3.8)</td>
<td>0.0(0.0-1.0)</td>
<td>0.018</td>
</tr>
<tr>
<td>Cumulative exit-site infection number per patient- median (IQR)</td>
<td>2.0(0.3-6.0)</td>
<td>1.0(0.0-3.0)</td>
<td>ns</td>
</tr>
</tbody>
</table>

#3563
VALIDATION OF AN M-HEALTH TECHNOLOGY TO SUPPORT PATIENTS UNDERGOING PERITONEAL DIALYSIS
Analayde Lima de Azevedo1, Juliana Gomes Ramalho de Oliveira2, Rodrigo Tavares Dantas2, Rayndrick Kelryn Assis Lima3, Geraldo Bezerra Da Silva Junior2 and Karla Maria Carneiro Rolim1

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Background and Aims: A global increase in the prevalence of chronic kidney disease (CKD) and, consequently, in the number of individuals submitted to renal replacement therapy (RRT) has been observed. In Brazil, there was an increase from 46,557 to 144,779 (>310%) in the number of people on dialysis between the years 2001 and 2020, respectively. Although peritoneal dialysis (PD) is a safe, low-cost and less aggressive dialysis method when compared to hemodialysis (HD) and can be performed at the home, HD remains the most common RRT type in Brazil (92.2%). This study aimed to validate a PD section incorporated into an existing m-Health application (app) called ‘Renal Health®’.

Method: This is a methodological study, with a quantitative and applied approach. For internal validation of the app usability, ten specialists/researchers in the study topic from the Nursing Nephrology participated in the study, hereafter referred to as ‘judges’, who carried out the validation process of the content to be inserted into the Renal Health® app. The validation instrument was sent to them electronically, organized according to a Likert scale following a four-degree gradation. Based on the specialists’ answers, the means of agreement were calculated, which ranged from –1 for a negative evaluation; 0 (zero) for a neither positive nor negative evaluation; and, +1 when the evaluation was positive. Data evaluation was done using descriptive statistics and the calculation of the content validity index (CVI). Each item of the validation instrument was analyzed in relation to these obtained averages, which, if they were less than 80%, would indicate the need for modifications. An evaluation instrument was created with 22 items arranged in three domains: objectives (4), structure and presentation (15), and relevance (3), aiming to reflect the app functionality, usability and appearance.

Results: Regarding the objectives related to the PD section, none of items received an “irrelevant” assessment and its CVI ranged from 0.90 to 1.0, with an overall CVI of 0.95. The sub-items with the highest scores were related to the text being compatible with the target audience and the PD section of the app having adequate information/content to guide the patients. Among the 15 sub-items related to the structure and presentation of the PD section, six showed 90% agreement among the judges and were distributed as follows: they indicated that the information directed to the object of interest was sufficient and adequate; stated that the colors applied to the text were relevant and facilitated its use; that the subtitles applied were adequate and helped the user to understand the image; confirmed that the amount of illustration was adequate for the content of the material; that the illustrations were clear and easy to understand and that they were relevant to the content of the material and elucidated the content. The other sub-items had a maximum CVI (1.0) and the

Figure 1: Initial prototype of the PD section of the Renal Health® application.
overall CVI for this domain was 0.95. Finally, regarding the relevance of the PD section, all sub-items showed 100% agreement among the participants, so that the overall CVI was 1.0. Regarding the qualitative analysis of the instrument, there was no disagreement between the judges and/or suggestions for changes in the PD section.

Conclusion: The present study allowed the validation of the PD section in the Renal Health® app, which showed good reliability and could promote the use of m-Health technology to support users undergoing this type of dialysis.

#3658
PERITONEAL INFLAMMATION INDUCES SYSTEMIC ERYPTOSIS IN PERITONEAL DIALYSIS-ASSOCIATED PERITONITIS
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Background and Aims: Eryptosis is stress-induced RBC (Red Blood Cell) death mechanism. Our preliminary data show that there is a significant increased of eryptosis during peritoneal dialysis-associated peritonitis. Furthermore, there is an elevation of local and systemic inflammatory mediators. The aim of this study was to evaluate the relationship between systemic eryptosis levels in peritonitis and specific peritonitis biomarkers in peritonitis effluent (PDE), such as Peritoneal White Blood cell count (pWBC), peritoneal NGAL (pNGAL) and peritoneal cytokines levels.

Method: We enrolled 22 PD patients with peritonitis and 17 healthy subjects. PD-related peritonitis was defined according to the Guidelines of the International Society of Peritoneal Dialysis. At the time of diagnosis, blood samples were collected for eryptosis and peritoneal effluent were taken to evaluate pWBC, pNGAL and cytokines. All eryptotic measurements were made in freshly isolated RBCs. PS avidly binds AnnexinV, which is thus employed to identify eryptotic cells. Thus, PS exposure at RBC surface was estimated from FITC-AnnexinV binding using flow cytometric analyses.

Results: 13/22 patients were treated with continuous ambulatory PD (CAPD) and 9 with automated PD (APD). The median length of PD treatment was 28.1 months and the range was: minimum: 3 – maximum: 124.9 months. The percentage of AnnexinV-binding RBCs was significantly higher in PD patients with peritonitis than in CTR (PD patients with peritonitis: 7.7; IQR 4.3-14.2, versus CTR: 0.7; IQR 0.7-1.3; p<0.001) (Figure 1). WBC, NGAL and cytokines levels in PDE are reported in Table 2. We observed important correlation between eryptosis levels and peritoneal biomarkers (Figure 2).

Conclusion: In conclusion, we investigated a potential connection between systemic eryptosis and peritoneal biomarkers involved in peritonitis. The presented results revealed that upregulated inflammatory markers could be the cause of high levels of systemic eryptosis during PD-related peritonitis.
#6690
THE ASSOCIATION BETWEEN SERUM CHEMERIN AND PERITONEAL MEMBRANE TRANSPORT FUNCTION IN INCIDENT PERITONEAL DIALYSIS PATIENTS: A PROSPECTIVE COHORT STUDY
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1Department of Nephrology, Institute of Nephrology, West China Hospital of Sichuan University, P.R. China and 2Department of Nephrology, The Third Affiliated Hospital of Chongming Medical University, P.R. China

Background and Aims: Some biomarkers in drained dialysate or peritoneal membrane have been found related to the dialysate/plasma ratio of creatinine at 4 h (D/P Cr) in patients undergoing peritoneal dialysis (PD). But so far, there is no report on serum markers. Some biomarkers are associated with cardiovascular diseases (CVDs). Chemerin is a multifunctional chemotactic adipokine which plays roles in inflammation, adipogenesis and metabolism. In this study, we intended to investigate the role of chemerin in the peritoneal membrane transport function and CVDs in incident PD patients.

Method: This prospective cohort study was conducted in our PD center. The patients underwent initial standardized peritoneal equilibration test (PET) after PD for 4–6 weeks. Level of serum chemerin was determined via enzyme-linked immunosorbsent assay (ELISA). The patients’ CVDs were recorded during the follow-up period.

Results: 151 eligible patients with a mean age of 46.59±13.52 years were enrolled. And the median duration of PD was 25.0 months. The median concentration of serum chemerin was 29.09 ng/mL. Baseline D/P Cr was found to be positively correlated with serum chemerin (r = 0.244, p = 0.003). The multivariate analyses revealed that serum chemerin (p = 0.002), age (p = 0.044), albumin (p = 0.000), and high-density lipoprotein (HDL) (p = 0.022) were independent factors of D/P Cr. The serum chemerin level was significantly higher in diabetes mellitus (DM) patients than that of patients without DM (36.45 vs 27.37 ng/mL, p = 0.000). And there was a significant statistical difference in CVDs between the high chemerin group (>29.09 ng/mL) and low chemerin group (<29.09 ng/mL) (42% vs 21%, p = 0.009).

Conclusion: Serum chemerin has a positive correlation with baseline D/P Cr in incident PD patients. It may be a biomarker that can predict the baseline transport function of peritoneal membrane. And serum chemerin may be a risk factor of CVDs for incident PD patients. Multicenter studies with a larger sample size are warranted in the future.

#5871
PERITONEAL DIALYSIS INFECTIONS IN MALTA: AN OVERVIEW OF THIRTEEN YEARS
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1Mater Dei Hospital, Malta, Nephrology, Malta and 2Mater Dei Hospital, Malta Infection Control & Sterile Services, Malta

Background and Aims: Peritoneal dialysis (PD)-related infections are still associated with an increased risk of morbidity and mortality. We describe an overview of PD peritonitis and catheter-related infection (CRI) rates in Malta over a period of thirteen years.

Method: All patients undergoing PD in Malta from 2008 to 2020 were included. Data from 2008 to 2012 was retrospective (shown as mean), whilst data from 2013 to 2020 was prospective. ISPD guidelines and definitions were followed.

Results: Study population sizes from 2008 to 2020 were as follows: 137 (2008-2012), 91, 80, 126, 117, 102, 103, 101, and 101 respectively. PD peritonitis rates from 2008 to 2020 were 0.38, 0.31, 0.35, 0.46, 0.43, 0.57, 0.54, 0.43, 0.39, 0.40, 0.46, 0.37, and 0.29 episodes/patient/year respectively. Gram-positive peritonitis episodes predominated, the majority of which were Staphylococcal infections. Methicillin-resistant Staphylococcus aureus (MRSA) rates have overall decreased from 0.03 episodes/patient in 2008–2012 to 0.01 episodes/patient in 2020, to no cases in 2016, 2017 and 2019. Coagulase-negative Staphylococcal (CNS) rates also decreased from 0.26 episodes/patient in 2013 to 0.03 in 2017, 0.11 in 2018, 0.04 in 2019, and 0.08 in 2020. With regards to Gram-negative peritonitis, Pseudomonas rates declined from 0.06 episodes/patient in 2008–2012 to 0.03 in 2018. No cases were recorded in 2016, 2019 and 2020. The rate of Escherichia coli-associated peritonitis was 0.03 episodes/patient/year in 2020, and no cases were found in 2016, 2017, 2018, and 2019. Fungal peritonitis rates varied from 0.03 in 2008–2012 to 0.01 episodes/patient/year in 2013, 2018, 2019 and 2020 with no cases being recorded in 2016 and 2017. CRI rates were as follows: 0.39 (2008-2012), 0.35, 0.91, 0.37, 0.38, 0.25, 0.50, 0.29, and 0.22 episodes/patient/year respectively. The incidence of Gram-negative infections from 2013 to 2020 was 49, 51, 52, 65, 58, 66, 48, 41% respectively, with an average rate of 54%. Gram-positive CRIs were mostly Staphylococcal, peaking in 2014 at 0.38 episodes/patient, down to 0.14 in 2019, and 0.10 in 2020. MRSA rates decreased from 0.15 episodes/patient/year to 0.04 in 2018, no cases in 2019, and 0.04 in 2020. CRI Pseudomonas rates have overall improved from 0.12 (2008-2012), to 0.06, 0.09, 0.09, 0.14, 0.03, 0.17, 0.06, 0.04 episodes/patient/year from 2013 to 2020.

Conclusion: The Maltese PD cohort has been achieving ISPD target requirements. Both PD peritonitis and catheter-related infection rates declined over the last thirteen years. There was no MRSA peritonitis in 2016, 2017 and 2019, no Pseudomonas peritonitis in 2016, 2019 and 2020, no E. coli in 2016,2017, 2018 and 2019 and no fungal PD peritonitis in 2016 and 2017. Overall CRIs were predominantly Gram-negative, but not in 2019 and 2020.

#4264
PERITONEAL DIALYSIS AFTER FAILED KIDNEY TRANSPLANT: A SUITABLE OPTION
Diogo Francisco, Andreia Carnevale, Gonçalo Ávila, Ana Rita Calça, Patricia Matias and Patricia Branco
Hospital de Santa Cruz, Centro Hospitalar Lisboa Ocidental, Nephrology Department, Carnaxide, Portugal

Background and Aims: Despite great advances in graft survival, kidney transplant (KT) recipients frequently return to dialysis. The aim of this study was to perform an analysis of peritoneal dialysis (PD) outcomes of patients with a failed KT.

Method: Single-center retrospective cohort study with end-stage renal disease (ESRD) patients who started PD from 1st January 2010 to 31st December 2017. Two groups were analyzed: patients who started PD with no previous renal replacement therapy (RRT) - PD first -, and patients who transitioned directly from a failed kidney transplant.

Results: Among 152 patients who started PD, 115 were PD first and 15 transitioned from KT. The population included 63.1% of male gender, with a mean age of 52.4 ± 15.5 years and had PD median vintage of 30 months (IQR 20,6). Patients who transitioned from KT were significantly younger (mean age 42.8 ± 14.3 vs 53.7 ± 15.3, p = 0.015) and had lower prevalence of diabetes mellitus (13.3% vs 40.0%, p = 0.044). In KT patients, glucocorticoids were continued until there was residual diuresis and non-glucocorticoid immunosuppression was maintained for a median of 180 days (± 176) after PD start. Nearly a third (30.0%) of patients had no hospitalizations and 35.5% had more than 2 hospital admissions. Annual hospitalization rate was higher in prior KT group (1.40 vs. 0.48, p = 0.002). Prior KT associated with higher annual peritonitis rate (0.70 vs. 0.20, p = 0.017). A higher number of MACE was also observed in prior KT group (33.3% vs. 7.9%, p = 0.004). Residual diuresis was significantly lower in the group with previous KT. Neither ultrafiltration failure (6.7% vs. 9.9%, p = 0.974), nor technique survival (death or hemodialysis transfer 53.3% vs. 54.8%, p = 0.917; logrank 0.354) were different between groups.

Conclusion: Although higher incidence of diabetes mellitus was observed in PD first group, no differences were identified in ultrafiltration failure rates between groups. Despite significantly lower diuresis in prior KT group, both groups had adequate dialysis efficacy (mean Kt/V>1.7) and similar technique survival. Higher peritonitis rate and MACE incidence was observed in prior KT group, possibly associated with maintenance immunosuppression. Nevertheless, PD is a valid choice for RRT after a failed KT and should be offered to these patients.
Table 1: Patients’ demographics, comorbidity and clinical events stratified for previous RRT.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Previous RRT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>KT (n = 15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at PD start (y), mean ± SD</td>
<td>52.4 ± 15.5</td>
<td>42.8 ± 14.3</td>
</tr>
<tr>
<td>Time under PD (y), median (IQR)</td>
<td>3.20 (3.21)</td>
<td>1.87 (2.75)</td>
</tr>
<tr>
<td>Time under RRT (y), median (IQR)</td>
<td>3.81 (3.12)</td>
<td>15.17 (8.03)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>82 (63.1)</td>
<td>6 (40.0)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>48 (36.9)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>88 (67.7)</td>
<td>9 (60.0)</td>
</tr>
<tr>
<td>Charlson score, n (%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>40 (30.8)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>3-6</td>
<td>64 (49.2)</td>
<td>6 (40.0)</td>
</tr>
<tr>
<td>More than 6</td>
<td>26 (20.0)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Annual hospitalization rate, median (IQR)</td>
<td>0.60 (1.34)</td>
<td>1.40 (1.18)</td>
</tr>
<tr>
<td>Annual peritonitis rate, median (IQR)</td>
<td>0.21 (0.64)</td>
<td>0.70 (1.01)</td>
</tr>
<tr>
<td>IOS, n (%)</td>
<td>57 (43.8)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Tunielitis, n (%)</td>
<td>25 (19.2)</td>
<td>4 (26.7)</td>
</tr>
<tr>
<td>MACE, n (%)</td>
<td>13 (10.0)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Peritoneal transport</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slow, n (%)</td>
<td>4 (3.1)</td>
<td>-</td>
</tr>
<tr>
<td>Intermediate-slow, n (%)</td>
<td>36 (27.7)</td>
<td>4 (26.7)</td>
</tr>
<tr>
<td>Intermediate-fast, n (%)</td>
<td>50 (38.5)</td>
<td>6 (40.0)</td>
</tr>
<tr>
<td>Fast, n (%)</td>
<td>12 (9.2)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Diuresis (at PD start), median (IQR)</td>
<td>1700 (1300)</td>
<td>750 (1260)</td>
</tr>
<tr>
<td>Diuresis (at end of follow up), median (IQR)</td>
<td>1150 (1275)</td>
<td>0 (200)</td>
</tr>
<tr>
<td>UF failure, n (%)</td>
<td>12 (9.2)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Kt/v (at PD start), mean ± SD</td>
<td>2.64 ± 0.84</td>
<td>2.24 ± 0.42</td>
</tr>
<tr>
<td>Drop out, n (%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PD maintenance</td>
<td>30 (23.1)</td>
<td>3 (20.0)</td>
</tr>
<tr>
<td>Haemodialysis transfer</td>
<td>55 (42.3)</td>
<td>6 (40.0)</td>
</tr>
<tr>
<td>KT</td>
<td>26 (2.0)</td>
<td>4 (26.7)</td>
</tr>
<tr>
<td>Death</td>
<td>16 (12.3)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Loss of follow up</td>
<td>3 (2.3)</td>
<td>-</td>
</tr>
<tr>
<td>Technique failure, n (%)</td>
<td>71 (54.6)</td>
<td>8 (53.3)</td>
</tr>
</tbody>
</table>

Figure 1: Technique survival stratified for previous RRT (logrank = 0.354). Solid line - prior KT group; Dashed line - DP first group.

#4752
EMERGENCY DEPARTMENT VISITS IN PERITONEAL DIALYSIS PATIENTS: A SINGLE CENTER STUDY DURING AN 8-YEAR PERIOD
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Background and Aims: Peritoneal dialysis patients may present to the emergency department (ED) with infectious, mechanical and metabolic complications of dialysis, as well as non-dialysis-related problems. We planned to retrospectively analyse ED visits in PD patients.

Method: Study included 189 PD patients followed between December 2014 and July 2022. Patients younger than 18 years and with less than 1-month follow-up were excluded. Demographic characteristics, co-morbidities, med-
Table 1: Laboratory data of the patients grouped by hospitalization status.

<table>
<thead>
<tr>
<th></th>
<th>Hospitalisation (+) (n = 92)</th>
<th>Hospitalisation (-) (n = 156)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte (x10^3/µL)</td>
<td>8800 (600-42000)</td>
<td>8500 (1170-31000)</td>
<td>0.133</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.0 (5-14)</td>
<td>10.0 (5.7-14.6)</td>
<td>0.085</td>
</tr>
<tr>
<td>Thromocyte (x10^7/µL)</td>
<td>233000 (15600-313000)</td>
<td>236000 (21900-671000)</td>
<td>0.336</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>7.0 (1.4-57.0)</td>
<td>8.2 (2.8-17)</td>
<td>0.515</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>134 (117-142)</td>
<td>135 (121-146)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>4.1 (2.4-6.9)</td>
<td>4.3 (2.6-7.5)</td>
<td>0.137</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>8.1 (5.0-13.0)</td>
<td>8.6 (4.0-11.0)</td>
<td>0.396</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>4.2 (1.7-13.0)</td>
<td>5.0 (2.0-10.0)</td>
<td>0.880</td>
</tr>
<tr>
<td>Magnesium (mg/dL)</td>
<td>1.8 (1.1-2.9)</td>
<td>2.0 (1-5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>2.9 (1.3-6.1)</td>
<td>3.4 (1.2-6.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>118 (67-403)</td>
<td>112 (69-565)</td>
<td>0.163</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>79 (1-357)</td>
<td>19 (2-290)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Procalcitonin (ng/mL)</td>
<td>1.0 (0.1-100)</td>
<td>0.3 (0.1-42.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.0 (4.0-8.1)</td>
<td>5.2 (3.0-13.5)</td>
<td>0.300</td>
</tr>
<tr>
<td>NT-Pro BNP (pg/mL)</td>
<td>21748 (6-350000)</td>
<td>2734 (150-350000)</td>
<td>0.452</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>110 (6-400)</td>
<td>120 (24-400)</td>
<td>0.037</td>
</tr>
</tbody>
</table>

Results: There were 32 (16.9%) female and 157 (83.1%) male patients. Patients were divided into two groups as those who applied to the ED (n = 109) or not (n = 80). Median age (47 (19-80) vs 52.5 (26-77) years, p = 0.389) and dialysis duration (41 (2-148) vs 20.5 (1-217) months, p = 0.390) were similar in both groups. Most common comorbidities were anaemia (103 (94.5%) vs 75 (93.8%), p = 1,000), hypertension (90 (82.6%) vs 64 (80%), p = 0.707) and diabetes mellitus (23 (21.9%) vs 17 (21.3%), p = 1,000). While mortality (39 (35.8%) vs. 16 (20%), p = 0.013) was significantly higher in patients presenting to ED, transfer to hemodialysis (29 (26.6%) vs 33 (41.3%), p = 0.008) and transplant (4 (3.7%) vs 12 (15%), p = 0.042) were lower. There were 248 ED admissions for 109 patients during follow-up. Ninety-two (37.1%) episodes required hospitalization, whereas 156 (62.9%) episodes were treated as outpatients. Mean hospital stay was 10.5 (1-103) days. Most common reasons for admission were abdominal pain, cloudy diuresis, nausea and/or vomiting in 111 episodes (44.8%), cardiovascular symptoms in 31 episodes (12.5%) and hypervolemia in 29 episodes (11.7%). Most common diagnoses were peritonitis in 61 (24.6%), hypervolemia in 32 (12.6%), and upper respiratory tract infection in 21 (8.5%) episodes. When patients were evaluated based on hospitalization status, mean patient age was higher in hospitalized patients (55 (17-84) vs 49 (15-87) years, p = 0.029), whereas residual renal function (RRF) was lower (150 (0-2500) vs 300 (0-9500) mL/day, p = 0.048). Laboratory data is shown in Table 1. In multivariate analysis, factors predicting hospitalization were CRP [0.991 (0.984-0.997), p = 0.003] and magnesium [5.315 (1.423-19.853), p = 0.013]. Patients presenting to ED were also evaluated based on mortality during follow-up and 39 (35.8%) out of 109 patients died. There was no difference in terms of patient age (p = 0.525), gender (p = 0.792), dialysis time (p = 0.536) or RRF (p = 0.377). However, number of ED admissions was significantly higher in patients who died (2.81±1.63 vs 1.99±1.26, p = 0.004) and the only factor predicting patient death was the number of ED admissions [1.603 (1.058-2.430) p = 0.026].

Conclusion: The most common symptoms associated with ED admissions were gastrointestinal and the most common diagnosis was peritonitis. In patients presenting to the ED, more than a third required hospitalization. Factors predicting hospitalization were high CRP and low magnesium levels. The number of admissions to the ED was the only factor that predicted death during follow-up.

#4983
THE UNEXPECTED BALANCE OF PROINFLAMMATORY CELLS IN PERITONEAL DIALYSIS PATIENTS
João Grilo1, Catarina Santos1, Andreia Monteiro2, Raquel Chorão1, Joana Coutinho1, Lígia Ribeiro1, Rui Filipe1 and Ernesto Rocha1
1Hospital Amato Lusitano, Nephrology, Castelo Branco, Portugal and 2Centro Hospitalar Universitário Covadiga Beira (CHUCB), Clinical Pathology, Covilhã, Portugal

Background and Aims: Chronic kidney disease (CKD) is a complex and heterogeneous disease and is increasingly becoming a global public health concern. It is characterized by a persistent inflammation state which appear to be caused by cytokines, growth factors and hormones. Peritoneal dialysis (PD) accounts for 9% of all kidney replacement therapy (KRT) and over time, some changes are expected to occur in the peritoneal membrane mainly due to exposure to PD solutions, infectious processes and non-infectious complications. This inflammatory process is poorly understood and needs further clarification, but Th17 cells and Th1 cells seem to be involved. Therefore, we aimed to quantify the frequency of peripheral immune cells and the concentration of IL-17A in peripheral blood (PB) and peritoneal effluent (PE) and compare to a healthy control group.

Method: In a cross-sectional study of 26 PD patients and 10 healthy, age and sex-matched controls we evaluated PB and PE frequencies of T lymphocytes, T CD4, T CD8 and Th1 cells by flow cytometry as well as IL-17 concentrations using enzyme-linked immunosorbent assay. Comparisons were performed between PD patients and controls and between the different groups of PD patients according to PD modality, number of exchanges, dialsate toxicity, extraneal use, infection and daily total volumes, type of peritoneal transport and volume indexes. Statistical analyses were performed using the SPSS statistics version 26.

Results: Table 1 summarizes the main characteristics of PD patients and controls. Overall, in comparison with the control group, the frequency of Th1 cells in PB of PD patients was significantly lower (P = 0.001). On the other hand, frequency of Th1 cells substantially expanded in the PE, as compared to the PB (P = 0.001). PD patients also presented lower Th17 cells frequencies (P = 0.061) and those prescribed Extraneal had the lowest frequencies of Th17 (P = 0.030). IL-17A concentration was significantly higher in PE vs PB of PD patients (P = 0.012). Finally, the frequency of total lymphocytes in high PD transporters was significantly higher in comparison with high-average transporters (P = 0.021).

Conclusion: In our cohort, PE presented high concentrations of proinflammatory cells and cytokines. Th1 cells rather than Th17 cells were increased, pointing to a predominant cytolytic activity but IL-17 was also increased. Treatment with Extraneal associated with a lower frequency of these cells, somehow counterbalancing the inflammatory milieu associated with high glucose concentrations.
#4452

ICODEXTRIN EFFICIENCY IN FLUID AND SODIUM REMOVAL REMAINS STABLE DURING LONG PERITONEAL DWELLS

Joanna Stachowska-Pietka1, Jacek Wanieowski1, Anna Olszowska2, Elvia Garcia-Lopez3, Zofia Wankowicz4 and Bengt Lindholm5

1Nalecz Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw, Poland. 2Military Institute of Medicine, Central Hospital of the Ministry of Public Defence, Warsaw, Poland and 3Karolinska Institute, Department of Clinical Science, Intervention and Technology, Division of Renal Medicine and Baxter Novum, Stockholm, Sweden

Background and Aims: Inadequate fluid and sodium removal has been shown to increase risk of overhydration and hypertension. In peritoneal dialysis, icodextrin-based solution provides sustained ultrafiltration, and therefore can be used for the long exchanges, especially in patients with fast solute transport rates in whom the effective ultrafiltration period is shortened. We investigated to which extent the efficiency of icodextrin in fluid and sodium removal is changing during 16-hour peritoneal dwells.

Method: Data on intraperitoneal volume, and concentrations of icodextrin and sodium in dialysate during 16 hours of peritoneal dwells with icodextrin-based solution were analysed in 11 clinically stable patients. Labeled serum albumin (RISA) was used as a volume marker and dialysate samples of 12 mL were collected at 8, 12, and 16 hours of peritoneal dwell. Residual volume was evaluated from marker dilution after 16 hours by rinsing peritoneal cavity with 2 L of fresh 1.36% glucose dialysis fluid. Ultrafiltration (UF) was calculated for each patient and each sampling time as the difference between drained and initially infused volume corrected for the sample volume. The total absorption of icodextrin-derived carbohydrates (AbsCHO) was calculated for each patient as the difference between initially infused and drained carbohydrates mass. The icodextrin ultrafiltration efficiency (UFE) was calculated for each sampling time as the ultrafiltration divided by the amount of icodextrin mass absorbed (AbsCHO). The efficiency of icodextrin in sodium removal (NaRE) was calculated for each sampling time as the sodium mass removed (difference between drained and initially infused sodium mass) divided by the corresponding icodextrin mass absorbed (AbsCHO). Correction for the residual volume and samples collections were applied for AbsCHO, UFE and NaRE calculations.

Results: After 16-hour dwell with icodextrin-based solution the ultrafiltration was positive in all except one patient, being on average (mean±SD) 669±369 mL. During the dwell, icodextrin was slowly absorbed from the peritoneal cavity, see Figure 1, left panel. At 16 hours, the mean cumulative CHO absorption (AbsCHO) reached 68.0±20.7 g (44±13% of initial CHO mass) while 56% of initial icodextrin mass infused still remained in dialysate, Figure 1, left panel. Icodextrin UF efficiency (UFE) calculated at 8, 12, and 16 hours remained stable (p = 0.6, ANOVA repeated measures) and was on average 9.9±5.8 mL/g, Figure 1, right panel. Moreover, icodextrin sodium removal efficiency (NaRE) also remained stable after 8 hours (p = 0.6, ANOVA repeated measures) and was on average 1.2±0.7 mmol/L/g, Figure 1, right panel. Conclusion: During 16 hours of peritoneal dialysis dwells with icodextrin-based solution, icodextrin was slowly absorbed with 56% of the osmotic agent remaining in the dialysate after 16 hours. The efficiency of icodextrin in terms

Table 1: Demographic and clinical characteristics of PD patients and controls.

<table>
<thead>
<tr>
<th></th>
<th>PD patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.7±16.3</td>
<td>43±11</td>
</tr>
<tr>
<td>Male/Female [n(%)]</td>
<td>18/8 (69/31%)</td>
<td>6/4 (60/40%)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m2)</td>
<td>27.6 ± 4.9</td>
<td>NA</td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>8 (30.8%)</td>
<td>NA</td>
</tr>
<tr>
<td>Primary cause of ESKD [n(%)]</td>
<td>7 (27%)</td>
<td>NA</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>4 (15%)</td>
<td>NA</td>
</tr>
<tr>
<td>Hypertensive nephrosclerosis</td>
<td>5 (19%)</td>
<td>NA</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>10 (39%)</td>
<td>NA</td>
</tr>
<tr>
<td>Other etiology</td>
<td>3274.2 ± 2558</td>
<td>NA</td>
</tr>
<tr>
<td>Referral to nephrology (days)</td>
<td>845.8 ± 658.1</td>
<td>NA</td>
</tr>
<tr>
<td>PD duration (days)</td>
<td>1.9</td>
<td>NA</td>
</tr>
<tr>
<td>PD modality [n(%)]</td>
<td>14 (54%)</td>
<td>NA</td>
</tr>
<tr>
<td>CAPD</td>
<td>12 (46%)</td>
<td>NA</td>
</tr>
<tr>
<td>APD</td>
<td>11</td>
<td>NA</td>
</tr>
<tr>
<td>Peritoneal membrane transport characteristics (PET)</td>
<td>4.4 ± 1.2</td>
<td>NA</td>
</tr>
<tr>
<td>Low</td>
<td>0 (0%)</td>
<td>NA</td>
</tr>
<tr>
<td>Low-average</td>
<td>7 (27%)</td>
<td>NA</td>
</tr>
<tr>
<td>High-average</td>
<td>14 (54%)</td>
<td>NA</td>
</tr>
<tr>
<td>High</td>
<td>5 (19%)</td>
<td>NA</td>
</tr>
<tr>
<td>Number of cycles</td>
<td>2(8%)</td>
<td>NA</td>
</tr>
<tr>
<td>Dialysis solution tonicity</td>
<td>16 (62%)</td>
<td>NA</td>
</tr>
<tr>
<td>&gt; 1 hypertonic solution cycle</td>
<td>6 (23%)</td>
<td>NA</td>
</tr>
<tr>
<td>&gt; 3 hypertonic solution cycle</td>
<td>2 (8%)</td>
<td>NA</td>
</tr>
<tr>
<td>Extraneal solution</td>
<td>11 (65%)</td>
<td>NA</td>
</tr>
<tr>
<td>PD Plus</td>
<td>6 (23%)</td>
<td>NA</td>
</tr>
<tr>
<td>Total solution volume (mL/24h)</td>
<td>9365.4 ± 4739.1</td>
<td>NA</td>
</tr>
<tr>
<td>Infusion volume (mL/24h)</td>
<td>1896.2 ± 417.1</td>
<td>NA</td>
</tr>
<tr>
<td>Residual diuresis (mL/24h)</td>
<td>1007.9 ± 700.8</td>
<td>NA</td>
</tr>
<tr>
<td>Ultrafiltration rate (mL/24h)</td>
<td>906.9 ± 560.7</td>
<td>NA</td>
</tr>
<tr>
<td>Residual diuresis + Ultrafiltration rate (mL/24h)</td>
<td>1914.8 ± 731.7</td>
<td>NA</td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.9 ± 0.5</td>
<td>NA</td>
</tr>
<tr>
<td>Previous history of peritonitis in the last 6 months [n(%)]</td>
<td>6 (23%)</td>
<td>NA</td>
</tr>
<tr>
<td>Laboratory parameters</td>
<td>7.4 ± 2.4</td>
<td>8.4 ± 2.6</td>
</tr>
<tr>
<td>Blood leukocyte counts (x103 cells/μL)</td>
<td>4.4 ± 5.1</td>
<td>0.4 ± 0.3</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>7.9 ± 2.9</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>PE leukocyte counts (cells/μL)</td>
<td>12.5 ± 16</td>
<td>NA</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD or number (n). Statistically significant differences (p < 0.050) are identified in bold; ESKD, End-stage kidney disease; PD, Peritoneal dialysis; PE, peritoneal effluent; NA, not applicable.
of fluid (UCE) and sodium (NaRE) removal remained stable and did not subside from 8 to 16 hours of the dwell.

**3478**

**THE EFFECT ON NET ULTRAFILTRATION WHEN TRANSFERRING PATIENTS FROM NOCTURNAL INTERVAL (NIPD) TO CONTINUOUS CYCLING PERITONEAL DIALYSIS (CCPD)**

Marios Theodoridis1, Stylianos Panagoutsos2, Nikos Margaritis3, Triantafyllia Bounta4, Efthimia Mourvati5, Christos Tsalikidis1, Evaggelia Charitaki2 and Elias Thodis2

1University Hospital of Alexandroupolis, Nephrology, Alexandroupolis, Greece, 2University Hospital of Alexandroupolis, Nephrology, Alexandroupolis, Greece and 3University Hospital of Alexandroupolis, Surgery, Alexandroupolis, Greece

**Background and Aims:** Peritoneal Dialysis (P.D.) Adequacy includes a variety of targets such as the sufficient uremic toxins removal (Kt/V), patients’ euvolemia, acid-base and electrolyte balance etc.. Based on incremental PD prescription NIPD is often a reasonable modality choice when there is adequate Residual Renal Function (RRF). Eventually due to RRF decrease patients need to increase their PD adequacy by adding a solution during the day i.e Icodextrin (CCPD). The aim of this study was to evaluate the alteration of Cyclers’ ultrafiltration (UF) as well as Total Ultrafiltration (sum of Cycler ultrafiltration and the UF of the initial drainage) when transferring patients from NIPD to CCPD.

**Method:** This is a single center retrospective study of 16 patients (m = 9, f = 7). These patients were transferred from NIPD to CCPD due to inadequate PD adequacy. The patients’ mean age was 53.±19 years, their mean PD duration was 74.±25.7 months and their mean Peritoneal Solute Transfer Rate (PSTR-D/Pcr) was 0.69±0.12. We evaluated small solute clearance targets (Kt/V – ttotal, p:peritoneal, r:renal), RRF (eGFR, Vurine), Cycler ultrafiltration, the UF of the initial drainage and the sum of them (Total UF) on three consecutive days before the initiation of CCPD and three consecutive days after the initiation. The patients’ cycler treatment program remain constant and all of them received an initial day volume of 1000 ml with Icodextrin.

**Results:** We compared the alterations with Paired t-Test (normal distribution) We found a statistically significant improvement of the peritoneal fraction of Kt/V when applying CCPD (p = 0.01), on the other hand we found a statistically significant decrease from Cycler’s UF (p<0.05) as well as from Total UF (p<0.05) without any statistically significant increase in urine’s volume. Additionally, from the regression analysis there was statistically significant correlation between PSTR and ΔUF(UFNIPD–UFCCPD) showing that the faster the transporter the greater the ultrafiltration loss (p = 0.035, R = 0.58).

**Conclusion:** Transferring patients with adequacy problems from NIPD to CCPD improves small solute clearances but in some cases the risk for total ultrafiltration decrease is important and may lead to overhydration. It is necessary to contact perspective studies with hydration status evaluation ie Bioimpedance Spectroscopy.

**3849**

**PERITONEAL DIALYSIS CATHETER LOCK: PREVENTING RELAPSES**

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Hospital Universitario Virgen de las Nieves, Nefrología, Granada, Spain

**Background and Aims:** The incidence of peritonitis has markedly decreased in the last decades, nevertheless it remains one of the main causes of catheter removal and subsequent dialysis modality change. In the long-term severe peritonitis and relapses can lead to peritoneal membrane failure. Some bacteria can form biofilms in the peritoneal catheter lumen granting them resistance against antibiotics and thus being one of the causes for infection recurrences. To find a viable way to avoid or/and eradicate the bacterial biofilm in the peritoneal catheters given the importance of infections.

**Method:** We present the experience in our peritoneal dialysis unit in the coadjuvant treatment of peritoneal dialysis-associated peritonitis with peritoneal catheter locks in the past few years. We used two kinds of peritoneal catheter lock depending on the isolated germ and divided them in two groups. Group I for the gram-positive staphylococcus group and Group II for gram-negative germs, specifically pseudomon. We reported 12 cases from which 10 were the first episode of gram-positive staphylococcus (epidermidis and Aureus) peritonitis. For the treatment we locked the catheter with 350mg of daptomycin in 7ml of saline solution once a week without using the catheter for 12 hours. For the other 2 cases of pseudomona peritonitis we locked the catheter with taurodilone/urokinase during the exchange with icodextrin twice a week with a 12 hours dwell time until 9 locks were archived.

**Results:** We treated 12 patients (Table 1). Peritonitis was resolved without recurrences in 9 of 10 patients in group I. In one case were a Methicillin-resistant *Staphylococcus aureus* was involved there was no response to the treatment and the peritoneal catheter was removed. In Group II both patients resolved their peritoneal infection without recurrences.

**Conclusion:** In our study peritoneal catheter locking seems to avoid the biofilm and reduce the peritoneal infection recurrences.

**Table 1:**

<table>
<thead>
<tr>
<th>p = 16</th>
<th>NIPD</th>
<th>CCPD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>KT/V-tnipd – KT/V-tccpd</td>
<td>1.99±0.67</td>
<td>2.33±1</td>
<td>0.103</td>
</tr>
<tr>
<td>KT/V-nipd – KT/V-ccpd</td>
<td>1.03±0.27</td>
<td>1.42±0.33</td>
<td>0.01</td>
</tr>
<tr>
<td>KT/Vr-nipd – KT/Vr-ccpd</td>
<td>1.02±0.44</td>
<td>0.97±0.66</td>
<td>0.657</td>
</tr>
<tr>
<td>Vurine/nipd–Vurine/ccpd (ml)</td>
<td>1413.57±700.3</td>
<td>1271±605.6</td>
<td>0.31</td>
</tr>
<tr>
<td>eGFRnipd–eGFRccpd (ml/min)</td>
<td>5.9±3.14</td>
<td>4.8±2.4</td>
<td>0.12</td>
</tr>
<tr>
<td>UFNIPD – UFCCPD: from cycler (ml)</td>
<td>698.88±239.02</td>
<td>267.92±338.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>UFNIPD – UFCCPD: Total (ml)</td>
<td>698.88±239.02</td>
<td>371.78±205.37</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table 1:

<table>
<thead>
<tr>
<th>PATIENT</th>
<th>GERM</th>
<th>DAYS WITH POSITIVE CELL COUNT</th>
<th>NEED FOR HOSPITAL ADMISSION</th>
<th>RECURRENCE</th>
<th>LOCK</th>
<th>INTRAPERITONEAL ANTIBIOTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MRSA</td>
<td>8</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>CEFAZOLIN</td>
</tr>
<tr>
<td>2</td>
<td>MRSA</td>
<td>8</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>CEFAZOLIN</td>
</tr>
<tr>
<td>3</td>
<td>MRSA</td>
<td>6</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>CEFAZOLIN</td>
</tr>
<tr>
<td>4</td>
<td>MRSA</td>
<td>4</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>CEFAZOLIN</td>
</tr>
<tr>
<td>5</td>
<td>S. EPIDERMIDIS MS</td>
<td>4</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>CEFAZOLIN</td>
</tr>
<tr>
<td>6</td>
<td>MRSA</td>
<td>10</td>
<td>SI</td>
<td>SI</td>
<td>DAPTOMYCIN</td>
<td>CLOXACILLIN</td>
</tr>
<tr>
<td>7</td>
<td>MRSA</td>
<td>16</td>
<td>SI</td>
<td>SI</td>
<td>DAPTOMYCIN</td>
<td>CLOXACILLIN</td>
</tr>
<tr>
<td>8</td>
<td>MRSA</td>
<td>12</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>VANCOMYCIN</td>
</tr>
<tr>
<td>9</td>
<td>MRSA</td>
<td>9</td>
<td>SI</td>
<td>SI</td>
<td>DAPTOMYCIN</td>
<td>CEFAZOLIN</td>
</tr>
<tr>
<td>10</td>
<td>MRSA</td>
<td>6</td>
<td>NO</td>
<td>NO</td>
<td>DAPTOMYCIN</td>
<td>MEROPEMEN</td>
</tr>
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<td>11</td>
<td>PSEUDOMONA AERUGINOSA</td>
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<td>SI</td>
<td>SI</td>
<td>TAUROLOK/ UROKINASE</td>
<td>+GENTAMICIN</td>
</tr>
<tr>
<td>12</td>
<td>PSEUDOMONA AERUGINOSA</td>
<td>14</td>
<td>NO</td>
<td>NO</td>
<td>TAUROLOK/ UROKINASE</td>
<td>GENTAMICIN + MEROPEMEN</td>
</tr>
</tbody>
</table>

#4383

WHEN SHOULD WE TRY TREATMENT FOR PERITONEAL SCLEROSIS?

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Background and Aims: Although it is very important to detect patients at increased risk of developing encapsulating peritonitis (EPS), there are not established predictors which would promote early diagnosis and treatment of EPS ensuring sustainability of peritoneal dialysis (PD). D-Dimers are considered a significant test in evaluation of peritoneal fibrinolysis activity and Ca 125 is used as an alternative marker for assessing the integrity of peritoneal membrane.[1] We examined prospectively a combination of these surrogate markers both in serum and effluent dialysate at the beginning of the study. In a cohort of 39 PD patients D-Dimers, Ca 125 and CRP along with a complete biochemical profile were tested both in serum and overnight effluent dialysate at the beginning of the study. In 9 patients, who presented with recurrent gastrointestinal symptoms, such as mild nausea, incidence of gastric discomfort or sense of bloating, CT imaging was performed for evaluation of potent EPS and thickening of the bowel wall was measured. The latter group of nine patients received tamoxifene for a period of approximately one year and both serum/effluent biomarkers and CT imaging were repeated at the end of this period.

Results: In Table 1 characteristics of patients are shown. At the beginning of the study CRP was the only biomarker that was different between the group with or without gastrointestinal symptoms (4±6mg/dl vs 0.8±1.1mg/dl, p = 0.04).

In patients, who received tamoxifene gastrointestinal symptoms improved. In these patients follow up with CT imaging demonstrated amelioration of bowel wall thickening compared to the beginning (3±1.2mm vs 2.1±0.4mm), which was not statistically significant. Moreover, Ca 125 in dialysate decreased (60.4±7.4 U/ml vs 27±2.7 U/ml, p = 0.04). No side effects were recorded. Five patients are still on PD, 3 patients died from unrelated causes and 1 was transferred to hemodialysis.

Conclusion: In this study neither D-Dimers, a test for the assessment of the peritoneal fibrinolysis activity, nor Ca 125 an alternative marker for assessing the integrity of peritoneal membrane helped us to distinguish patients at risk for EPS. In fact Ca 125 levels in the effluent were higher in the treated group just before initiation of treatment, although in some references it is proposed that it is minimized.[1,2] Clinical evaluation along with radiologic findings led us to the decision to treat patients with tamoxifene, which exerts a protective effect on the peritoneal membrane during both early and late stages of fibrotic disorders.[3] Despite the small number of patients in this study, bowel wall thickening showed a tendency to decrease and symptoms improved.

REFERENCES


#6822

ANALYSIS OF IRON STATUS AND ITS INFLUENCING FACTORS IN INITIAL PERITONEAL DIALYSIS PATIENTS

Yuhao Peng and Zhong Hui

P.R. China

Background and Aims: Iron deficiency (ID) is an important cause of poor response to anemia treatment in dialysis patients. The initial status of iron metabolism in uremic patients when they enter peritoneal dialysis (PD) may affect the strategy of iron therapy. Therefore, we investigated and analyzed the initial iron indicator levels and ID in patients with end-stage renal disease undergoing continuous ambulatory peritoneal dialysis (CAPD), and discussed the possible influencing factors of ID and iron supplementation treatment strategies.

Method: The clinical data of patients who underwent PD for 1–3 months in West China Hospital, Sichuan University from January, 2011 to January, 2018 were collected. The clinical data including patients’ characteristics, medication (oral iron supplement and erythropoietin), iron indicators [ferritin, serum
iron, serum iron saturation (TSAT) and transferrin), hemoglobin (HB), serum albumin (Alb), blood lipids, C-reactive protein and IL-6, β2-microglobulin, electrolytes and other biochemical indicators, as well as PD-related parameters. ID or relative ID was defined as ferritin \(< 100 \text{ ng/mL}\) or TSAT \(< 20\%\) and absolute ID was defined as ferritin \(< 100 \text{ ng/mL}\) or TSAT \(< 20\%\) and absolute ID was defined as ferritin \(< 100 \text{ ng/mL}\) or TSAT \(< 20\%\). Person correlation and Spearman correlation were used for normal distribution and non-normal distribution measurement data, respectively. Kendall correlation was used for categorical variables. Multivariate linear regression was used to analyze the independent influencing factors of ferritin and transferrin saturation. Binary logistic regression was used to analyze the independent influencing factors of ID.

**Results:** A total of 633 adult patients with stable condition and complete iron metabolism data were enrolled. The mean age was 45.7±14.0 years (18-91 years). There were 397 males (61.1%) and 100 patients (15.8%) with diabetes. The mean HB level was 95.4±18.4g/L, the ferritin level was 277.9±278.1ng/mL, the TSAT 29.9±12.9%, and the transferrin level 1.89±0.4 g/L. Among them, 487 (76.9%) used oral iron therapy and 412 (65.1%) used erythropoietin. 156 (58.8%) had HB less than 100g/L, and 156 (44.2%) had ID. There were 32.2% patients with ferritin \(< 100 \text{ ng/mL}\) and 23.4% patients with TSAT \(< 20\%\). Among patients who used oral iron therapy, 16.2% had absolute ID and 39.6% relative ID. There was no correlation between ID and diabetes, cardiovascular disease, gender, age, Alb, high-sensitivity CRP, IL-6, most of electrolytes, β2 microglobulin, blood leukocyte count, dialysate serum creatinine ratio at 4 hours, D/P Cr (4h), and there was no correlation between ID and eGFR (\(r = 0.057\)). Serum magnesium level (\(r = -0.014, p < 0.001\)), body surface area (\(r = -0.112, p = 0.005\)) and triglyceride (\(r = -0.086, p = 0.03\)) were negatively correlated with ID. Transferrin level (\(r = 0.427, p < 0.001\)) and platelet count (\(r = 0.169, p < 0.001\)) were positively correlated with ID. Multiple linear regression analysis with serum magnesium, body surface area, triglyceride, platelet count and eGFR input showed that triglyceride (\(p = 0.001\)), body surface area (\(p = 0.05\)) and platelet count (\(p = 0.001\)) were independently correlated with ferritin. With transferrin saturation as the dependent variable, showed that only platelet count (\(p < 0.001\)) was independently associated with transferrin saturation. Binary logistic regression analysis model (dependent variable being presence of ID = 1) showed that body surface area (\(\beta = -1.055, p = 0.042\)), triglyceride (\(\beta = -0.295, p = 0.014\)), serum magnesium (\(\beta = 0.997, p = 0.040\)) and platelet count (\(\beta = -0.006, p = 0.014\), \(p < 0.001\)) were independently associated with ID.

**Conclusion:** ID is common in new PD patients in our hospital, with a ferritin level of less than 100 ng/mL in one-third of patients. Platelet counts were higher in ID patients. People with larger body surface area and higher triglyceride levels may have more iron stores. Our study showed new PD patients should pay attention to iron supplementation before and after PD catheterization. Intravenous iron supplementation should be considered in time for those who still have ID after oral iron supplementation. In addition, increased platelet count may predict the occurrence of ID anemia.

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**#6918 PATIENT AND TECHNIQUE SURVIVAL ON PERITONEAL DIALYSIS: A RETROSPECTIVE STUDY**

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**Background and Aims:** Peritoneal dialysis (PD) is a well-established replacement therapy for patients with end-stage kidney disease (ESKD). Despite innovations in PD fluid composition, PD patients experience a high morbidity rate. In particular, patients on PD have a high likelihood to switch from PD to HD due to catheter malfunction, peritonitis and ultrafiltration failure. A considerable number of risk factors are associated with a high risk of death, almost comparable with patients receiving hemodialysis (HD). This study aimed to analyze the outcome of patients receiving PD.

**Method:** A single center-retrospective study was conducted at the University Hospital of Modena. We collected data from patients who started PD from 1996 to 2021. Data were extracted from electronic healthcare records. Subjects aged \(< 18\) years were excluded. Patients with pre-existing abdominal wall defects (i.e., hernia), low-back pain, obesity and active working life were treated by automated peritoneal dialysis (APD). Kt/V was performed at least 5 times per year. Low depeurative efficacy, ultrafiltration failure and severe abdominal pathology were causes of permanent transition from HD to PD. Baseline characteristics were described using mean and standard deviation (SD), or frequencies. The chi-square or Fisher's test, and student's t-test were used to compare categorical and continuous variables between groups. For survival analysis were used Kaplan-Meier and Cox regression methods. A P value of \(< 0.05\) was considered statistically significant. All statistical analyses were performed using SPSS® statistical software.

**Results:** During the observational period, 497 patients on PD were enrolled in the study. Mean age was 63.5 (±15.6) years. Most of them were male (61%). Overall, 62.1% of the patients had at least 3 comorbidities beyond ESKD. Patients were affected by hypertension (70.4%), dyslipidemia (56.9%), cardiovascular disease (53.5%), hyperuricemia (41.6%) and diabetes (15.7%). Only 20.3% of the patients were on therapy with renin-angiotensin system inhibitors. PD was commenced at eGFR of 7±2.1 ml/min and CAPD (65.1%) was the modality of choice at the start of PD. The mean follow-up was 2.9 (±2.4) years. At end of the follow-up, 204 (41%) switched from PD to HD, 137 (27%) died, 92 (18.5%) underwent kidney transplantation and 64 (12.9%) were alive. On average, the switch from PD to home HD occurred after 3.3±2.7 years. The likelihood of transition from PD to HD for this group of patients was 10.7%, 30.3% 52.3%, and 70.3% at 1-, 3-, 5-, and 7 years, respectively (Fig. 1A). Patients who switched to HD were more frequently affected by diabetes (\(p = 0.02\)), hyperuricemia (\(p < 0.001\)) and hypercholesterolemia (\(p = 0.001\)) than those who remained in DP. Overall, males anticipated of 1.1 years the transition to HD compared to the females (\(p = 0.006\)). All-cause mortality in DP patients was 100.3 per 1000 person-years. In patients aged \(< 75\) years, mortality accounted for 242.1 per 1000 person-years. Cumulative all-cause 1-, 3-, 5-, and 7-year mortality accounted for 8.8%, 26%, 40.4% and 55.1%.
In the present study all IPD group patients started PD with increment cessation of PD, whichever occurs first.

**Results:**

In the present study all IPD group patients started PD with increment cessation of PD, whichever occurs first.

**Background and Aims:** At its start, Peritoneal dialysis (PD) was implemented only in advanced renal disease with a myriad of symptoms and signs. However, many subsequent literatures have highlighted possible benefits of early rather than late start of PD. Nevertheless, when to start PD has been a matter of controversy. This debate has created a new era of starting dialysis early during the course of the disease, in a small dose that was termed ‘incremental’ dialysis. By this modality, the dose of PD, is low at the initiation of RRT, and could be progressively increased over time in parallel with the reduction of RKF. Although incremental dialysis is growing worldwide, there has been no substantial agreement on the benefits of this approach. Moreover, the few available observational studies have compared incremental versus full-dose PD, with controversial results. On the other hand, studies comparing incremental dialysis with the conservative management for non-symptomatic ESRD patients are mostly deficient in the published literature. The present work is a retrospective, case-control, longitudinal study, aimed to evaluate the adequacy of incremental peritoneal dialysis as a modality of renal replacement therapy in ESRD patients, and whether it adds superior benefits over the conservative and the standard peritoneal dialysis (STPD) management.

**Method:** Data were collected retrospectively from Complesso Integrato Columbus Policlinico Gemelli, nephrology and dialysis unit archives. The study comprising three groups: first included 23 patients who were managed with one exchange to achieve the target Kt/V, a mean CrCl of less than 3.6±0.8 ml/min/1.73 m² failed to reach adequacy even with two exchanges a day and needed to be transferred to full dose while those with a mean CrCl in between the above values could only achieve Kt/V above 1.7 with two exchanges per day.

**Conclusion:** Incremental peritoneal dialysis, a rapidly growing new modality, is superior to the conservative treatment in patients with end-stage renal disease that can be adequately applied to patients with a GFR of 4 ml/min or more without adding the burden of full dose dialysis.

**References:**

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**Absaracts**

**Abstracts**

**#5231**

**INCREMENTAL PERITONEAL DIALYSIS VERSUS CONSERVATIVE MANAGEMENT IN PATIENTS WITH ESRD**

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**Background and Aims:** At its start, Peritoneal dialysis (PD) was implemented only in advanced renal disease with a myriad of symptoms and signs. However, many subsequent literatures have highlighted possible benefits of early rather than late start of PD. Nevertheless, when to start PD has been a matter of controversy. This debate has created a new era of starting dialysis early during the course of the disease, in a small dose that was termed ‘incremental’ dialysis. By this modality, the dose of PD, is low at the initiation of RRT, and could be progressively increased over time in parallel with the reduction of RKF. Although incremental dialysis is growing worldwide, there has been no substantial agreement on the benefits of this approach. Moreover, the few available observational studies have compared incremental versus full-dose PD, with controversial results. On the other hand, studies comparing incremental dialysis with the conservative management for non-symptomatic ESRD patients are mostly deficient in the published literature. The present work is a retrospective, case-control, longitudinal study, aimed to evaluate the adequacy of incremental peritoneal dialysis as a modality of renal replacement therapy in ESRD patients, and whether it adds superior benefits over the conservative and the standard peritoneal dialysis (STPD) management.

**Method:** Data were collected retrospectively from Complesso Integrato Columbus Policlinico Gemelli, nephrology and dialysis unit archives. The study comprising three groups: first included 23 patients who were treated with IPD and second group included 30 patients who were managed with the standard dose of PD (STPD), and a third group include 19 ESRD patients who had GFR values of < 15 ml/min/173 m² failed to reach dialysis adequacy even with two exchanges a day and needed to be transferred to full dose while those with a mean CrCl in between the above values could only achieve Kt/V above 1.7 with two exchanges per day.

**Conclusion:** Incremental peritoneal dialysis, a rapidly growing new modality, is superior to the conservative treatment in patients with end-stage renal disease that can be adequately applied to patients with a GFR of 4 ml/min or more without adding the burden of full dose dialysis.

**#6297**

**LAPAROSCOPIC VERSUS OPEN-SURGERY CATHETER PLACEMENT IN PERITONEAL DIALYSIS PATIENTS: A META-ANALYSIS OF OUTCOMES**

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**Background and Aims:** The peritoneal dialysis catheter (PDC) can be placed either through the laparoscopic technique, percutaneous technique or surgical procedures. The utilization of these PDC placement procedures is based on successful placement and reduced risk of development of complications. The main objective of this study was to compare the complications associated with laparoscopic vs. open-surgery PDC placement procedure.

**Method:** Literature for this review was obtained from all databases; to studies published in the period between 1998 and 2019 using Stata Version 12.

**Results:** The results showed significant difference in catheter malfunction between the laparoscopic and open-surgery group (relative risk [RR] = 0.58; 95% CI: 0.42–0.8; P = 0.031). Furthermore, there was no significant statistical difference in dialysate leakage (RR = 0.77; 95% CI: 0.51–1.17, P = 0.116) peritonitis (RR = 0.8; 95% CI: 0.6–1.06, P = 0.349) and exit-site infection (RR = 0.84; 95% CI: 0.65–1.09, P = 0.834) between the laparoscopic and open-surgery PDC placement groups.

**Conclusion:** The laparoscopic PDC placement procedure was superior to open surgery in regards to catheter malfunction. Additionally, the choice of treatment procedure should put in consideration factors such as cost and comfortability of the patient.

**Abstracts**

**Figure 1:** Kaplan-Meier analysis showing technique (A) and patient survival (B) stratified by patient age.
Figure 1: Selection strategy for studies to be included in meta-analysis.

REFERENCES
Figure 2: Relative ratio of dialysate leakages between laparoscopic and open-surgery PDC placement technique.
Figure 3: Relative ratio of catheter malfunction between laparoscopic and open surgery PDC placement techniques.
Figure 4: Relative ratio of peritonitis between laparoscopic and open-surgery PDC placement techniques.
Figure 5: Relative ratio of exit-site infection between laparoscopic and open-surgery PDC placement techniques.
Figure 6: Funnel plot from all studies comparing dialysate leakage between laparoscopic and open-surgery PDC placement techniques.

Figure 7: Funnel plot from all studies comparing catheter malfunction between laparoscopic and open-surgery PDC placement techniques.
Figure 8: Funnel plot from all studies comparing peritonitis between laparoscopic and open-surgery PDC placement techniques.

Figure 9: Funnel plot from all studies comparing exit-site infection between laparoscopic and open-surgery PDC placement techniques.
Table 1:

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Year of publication</th>
<th>Study design</th>
<th>Study period</th>
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<th>Age (years)</th>
<th>Comparison</th>
<th>Outcomes</th>
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<td>Tuncer, Yardimsever, and Ersoy</td>
<td>Turkey</td>
<td>2003</td>
<td>Prospective, non-randomized</td>
<td>March 1998–Oct 2001</td>
<td>42</td>
<td>46.9 ± 8.8</td>
<td>Laparoscopic omental fixation vs open surgical placement</td>
<td>Complications</td>
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<td>Open and laparoscopic secure placement</td>
<td>Complications</td>
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<td>Prospective randomized</td>
<td>Dec 2002 – Oct 2006</td>
<td>77</td>
<td>54.4 ± 16.5</td>
<td>Open surgery with Laparoscopic assisted placement</td>
<td>Positive findings of complications</td>
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<td>Wright et al.,</td>
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<td>1999</td>
<td>Prospective randomized</td>
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<td>45</td>
<td>49.3 ± 20.2</td>
<td>Laparoscopic and open peritoneal dialysis</td>
<td>Complications of catheter insertion</td>
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<td>Prabhakar et al.,</td>
<td>USA</td>
<td>2019</td>
<td>Retrospective, non-randomized</td>
<td>May 2005 – March 2018</td>
<td>173</td>
<td>58.3 ± 1.1</td>
<td>Laparoscopic and open CAPD placement</td>
<td>Complications (infection, malposition and malfunction)</td>
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<td>Atapour et al.,</td>
<td>Iran</td>
<td>2011</td>
<td>Randomized clinical trial</td>
<td>2009 - 2010</td>
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<td>55.1 ± 17.2</td>
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<td>Netherlands</td>
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<td>Randomized controlled trial</td>
<td>March 2010-March 2016</td>
<td>90</td>
<td>63.6 ± 21.3</td>
<td>Open versus laparoscopic placement</td>
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<td>Basic and advanced laparoscopic versus open dissection</td>
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<td>Australia</td>
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<td>Retrospective cohort</td>
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<td>Finland</td>
<td>1998</td>
<td>Retrospective cohort</td>
<td>June 1994-March 1997</td>
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<td>51.1 ± 1.1</td>
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<td>Catheter related complications</td>
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<td>Sun et al.,</td>
<td>New Zealand</td>
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<td>Retrospective cohort</td>
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<td>Peritoneoscopic versus surgical</td>
<td>Perioperative outcomes</td>
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Table 2: Harbord test assessing the presence of small study effects in 14 studies comparing dialysate leakage between laparoscopic and open-surgery PDC placement procedure.

<table>
<thead>
<tr>
<th>Z/sqrt(V)</th>
<th>Coef.</th>
<th>Std. Err.</th>
<th>t</th>
<th>P &gt;</th>
<th>95% Conf. Interval</th>
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<td>-1.32</td>
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<td>1.094247</td>
<td>1.08</td>
<td>0.302</td>
<td>-1.204196 3.564121</td>
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Test of H0: no small-study effects P = 0.302
Table 3: Harbord test assessing the presence of small study effects in 14 studies comparing catheter malfunction between laparoscopic and open-surgery PDC placement procedure.

| Z/sqrt(V) | Coef.          | Std. Err. | t    | P>|t| [95% Conf. Interval] |
|-----------|----------------|-----------|------|--------------------------|
| sqrt(V)   | -1.350746      | .9195935  | -1.47| 0.168 -3.354368 .652876  |
| bias      | 1.083912       | 1.333848  | 0.81 | 0.432 -1.822292 3.990117 |
| Test of H0: no small-study effects | effects | P = 0.432 |

Table 4: Harbord test assessing the presence of small study effects in 12 studies comparing dialysate leakage between laparoscopic and open-surgery PDC placement procedure.

| Z/sqrt(V) | Coef.          | Std. Err. | t    | P>|t| [95% Conf. Interval] |
|-----------|----------------|-----------|------|--------------------------|
| sqrt(V)   | .0531265       | .771228   | 0.07 | 0.946 -1.665277 1.77153  |
| bias      | -.5625115      | 1.290941  | 0.44 | 0.672 -3.438908 2.313885 |
| Test of H0: no small-study effects | effects | P = 0.672 |

Table 5: Harbord test assessing the presence of small study effects in 11 studies comparing dialysate leakage between laparoscopic and open-surgery PDC placement procedure.

| Z/sqrt(V) | Coef.          | Std. Err. | t    | P>|t| [95% Conf. Interval] |
|-----------|----------------|-----------|------|--------------------------|
| sqrt(V)   | .2393408       | .3787949  | 0.63 | 0.543 -1.6175528 1.096234 |
| bias      | -.9076283      | .6999336  | 1.30 | 0.227 -2.490988 2.6757315 |
| Test of H0: no small-study effects | effects | P = 0.227 |

#5367

CLINICAL SIGNIFICANCE OF NORMO-HYDRATION STATE IN PERITONEAL DIALYSIS PATIENTS

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3 University of Debrecen, Faculty of Medicine, Institute of Cardiology, Debrecen, Hungary,
4 University of Debrecen, Faculty of Medicine, Institute of Infectology, Debrecen, Hungary and
5 University of Debrecen, Faculty of Medicine, Institute of Internal Medicine, Department of Nephrology, Debrecen, Hungary

Background and Aims: The assessment of fluid status in dialysis patients is of paramount importance. Managing persistent volume overload and instability during dialysis is a significant challenge, with concomitant symptomatic and asymptomatic intradialytic hypotension (IDH) that results in dialysis-induced myocardial ischemia (cardiac stunning) and long patient recovery times. Our aim was to estimate the status of hydration in our peritoneal dialysis population by body composition monitoring (BCM) device to modify our pharmaceutical and dialysis policy and to evaluate echocardiographic parameters of the RV functions in patients with end-stage renal disease (ESRD) undergoing PD.

Method: We used a Fresenius Body Composition Monitor (BCM), a whole-body bioimpedance spectroscopy (50 frequencies, 5–1,000 kHz), to assess the body composition of 15 patients on peritoneal dialysis in our centre. We measured body weight, 24 h diuresis and performed a BCM session. Analysed results of echocardiography focused on RV (tricuspid annular plane systolic excursion (TAPSE). As per statistics, comparisons between 2 groups done by students t test, Mann Whitney U test or Wilcoxon test. Correlation between data was done by Pearson or spearman correlation. And lastly categorical variables were assessed by fisher’s exact, and Chi squared test.

Results: Average age was 47 years old (SD 9.45 t-test p = 0.1154). Gender distribution was 54.3% of our patients were female. 8.6% of our patients were anuric, 91.4% had residual urine (more than 1 litre). TAPSE value were average 23.17 mm (±4.5). We measured over-hydration in 8 cases by BCM that followed dialysis policy modification. In 8 PD patients we measured more than 2 L volume overload (VO) with BCM followed by dialysis policy modification (fluid intake restriction, diuretic dose increasing, frequent solution exchange).

Conclusion: Our data raised the importance of regular echocardiography to identify it. More attention should be focused on improving BP and volume control and identifying treatment strategies that effectively lower further deterioration in PD patients. One way of doing this is monitoring with BCM. With this clinician can manage persistent overload in CAPD patients, to better modify the dialysis regime, restrict fluid intake and use diuretics, to all in all preserve LV and RV function, and to prevent deterioration of the peritoneal membrane, and most importantly improve their survival.

Figure 1: Septum thickness in Echocardiography and hydration status among CAPD patients: volume overload can lead to thicker septum.
Figure 2: Ejection fraction and hydration status among CAPD patients: hyperhydration often associated with weaker cardiac function.

Figure 3: TAPSE and hydration status: Hyperhydration correlate with lower ejection fraction and elevated calculated right ventricle pressure in CAPD patients, but this is not significantly blue dots represents patients' observations, red line demonstrates empirical trends.
**Figure 4:** Distribution of HF in PD and in HD/predialytic group. Ejection fraction categories were classified as HFrEF: left ventricular (LV) EF ≤ 40%; HF with mildly reduced EF (HFrEF): LVEF 41–49%; HFpEF: LVEF > 50% Values of Ejection fraction and TAPSE in CAPD patients due to volume overload.

<table>
<thead>
<tr>
<th>Table 1: Study population, laboratory results.</th>
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<tr>
<td><strong>CAPD</strong></td>
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<tr>
<td>Number of pts (n)</td>
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<tr>
<td>Male, n (%)</td>
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<tr>
<td>Body weight (kg) (SD)</td>
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<td>Residual diuresis (ml/24hrs) (IQR)</td>
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<td>Total calcium (mmol/L) (median IQR)</td>
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<td>Phosphorus (mmol/L)</td>
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<td>Hemoglobin (g/L) (SD)</td>
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<td>Albumin (g/L) (IQR)</td>
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<tr>
<td>CRP (median IQR)</td>
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<td>Creatinine (SD)</td>
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IQR: interquartile range

## PERITONEAL DIALYSIS COMPLICATIONS IN PEDIATRICS: A TUNISIAN EXPERIENCE

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**Background and Aims:** Peritoneal dialysis (PD) is the preferred chronic dialysis modality for children suffering from chronic end-stage renal failure (CKD). But, it presents different infectious and non-infectious complications, causes of important morbidity and mortality. In this study, we aimed to describe the different infectious and mechanical complications observed in children on PD and to investigate the risk factors for the occurrence of different infectious and mechanical complications.

**Method:** In this study, we retrospectively collected the records of 99 patients who were treated with PD within the last eleven years (2010-2020) in the department of pediatrics of the University Hospital Charles Nicolle of Tunis. Analysis examining possible risk factors were performed using parametric and non-parametric tests and multivariate logistic regression in multivariate analysis.

**Results:** Ninety-nine children were on PD. All our patients were on automated PD. The sex ratio was 1.02. The overall duration of the PD was 390 years with an average of 2.93 years: 1.92 years. The average age at the beginning of PD was 9.75 ± 4.67 years. Sixty-nine patients had infectious complications, of which 65 patients had 120 episodes of peritonitis (IP) with a rate of 0.41 episodes per patient-year, 10 patients had exit-site infection and 3 patients had a tunnel infection. Mechanical complications were noted in 63 patients with a catheter revision rate of 1 per 38 patient-months. We noted an hernia in six patients, hemoperitoneum in seven patients, pancreatitis in three patients and no cases of hydrothorax. Analysis of PD complications risk revealed the following factors: poor adherence to treatment (p = 0.018 and p = 0.011) and weight less than 15 Kg (p = 0.041, p = 0.02) for infectious complications and IP respectively, comorbidity (p = 0.005) for mechanical complications, comorbidity (p = 0.008) and history of PI (p = 0.46) for catheter revision.

**Conclusion:** Ongoing educational programs for doctors, nurses and caregivers are needed to limit infectious complications. A collaboration between the pediatric nephrologist and the pediatric surgeon is recommended to improve catheter insertion techniques and prevent mechanical complications.

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## KIDNEY TRANSPLANTATION

E1 - EXPERIMENTAL, IMMUNE-TOLERANCE & XENOGENIC TRANSPLANTS

#3823

CAN HLA MOLECULAR MISMATCH GUIDE CLINICAL DECISION IN PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE STUDY

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De novo donor specific antibodies

Figure 1: Association between molecular mismatches calculated with PIRCHE, HLA EMMA, and HLA-A, -B, -Cw, -DRB1, -DQB1 antigen mismatches and de novo donor specific antibodies. Showing odds ratio and 95% confidence interval.

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Background and Aims: Optimizing graft survival and diminishing anti-HLA sensitization are essential in paediatric kidney transplant recipients (KTRs) facing multiple retransplantations. Improved pretransplant risk stratification and donor selection using in silico molecular HLA matching could enhance personalized immunosuppression and improve outcomes. HLA EMMA is a new in silico method to predict B cell epitope mismatches, and its clinical applicability needs confirmation in paediatric transplantation. We investigated the association of HLA B cell epitope (HLA EMMA) and predicted HLA T cell epitope (PIRCHIE) mismatches with de novo donor specific antibodies (dnDSA), anti-HLA antibodies, rejection, and graft survival.

Method: We retrospectively analysed 49 consecutive paediatric KTRs aged 1 to 16 transplanted from 2009-2020 at a single Danish centre. The centre has a long tradition of steroid-free kidney transplantations in immunologically uncomplicated recipients, and 80% of the KTRs did not receive steroids. Donors and recipients were all high-resolution HLA typed, and HLA EMMA (v 1.00) and PIRCHIE (v 3.3.60) predicted the molecular mismatches. KTRs were screened with mixed and single bead antigen kits after the transplantation. Logistic regression analyses were performed to explore the association of molecular mismatches and dnDSA, sensitization, graft loss, and rejection.

Results: The median age of the KTRs was 11 years (IQR 8), with a median follow-up time of 5 years (IQR 5). 11.36% developed dnDSA (60% class II, 40% class I and II) within a median of 3.91 years (IQR 2.28; range: 2.22-9.20); 57.45% had detectable anti-HLA antibodies during follow-up. Six KTRs lost their graft. None of the graft losses were related to alloimmunity, and 5-year death censored (one KTR died) graft survival was 88%. The cumulative incidence of rejection was 4% (95% CI: -1.5; 5.5) after one year and 10% (95% CI: 1.6; 18.7) after five years. The mean PIRCHIE score was 368.47 (95% CI: -1.6; 18.7) after five years. The mean HLA EMMA class I mismatch was 30.02 (95% CI: 1.6; 18.7) after five years. The mean PIRCHIE score was 368.47 (95% CI: 1.6; 18.7) after five years. The mean HLA EMMA class I mismatch was 30.02 (95% CI: 1.6; 18.7) after five years. The mean HLA EMMA class II mismatch was 30.02 (95% CI: 1.6; 18.7) after five years. We found no association between PIRCHIE or HLA EMMA with dnDSA, sensitization, graft loss, or rejection in the logistic regression models. We did see a trend towards an increased odds ratio in PIRCHIE predicting dnDSA (odds ratio: 1.31 (95% CI: 0.96; 1.80)) (Figure 1).

Conclusion: We did not find evidence to support the inclusion of the prediction of molecular mismatches in our clinical practice. The role of molecular mismatches in a clinical setting has yet to be established.
transplantation, higher levels of intra-renal MPO+ neutrophils were found upon cold storage using UW compared to cold storage using HTK.

Conclusion: The inflammatory process during chronic kidney rejection is T-cell driven and may involve the IL17C cascade. The early phase is dominated by neutrophils with enhanced intra-renal expression of CXCL1 and CXCL2. Furthermore, the polarization of the T-cell driven immune response may change depending on the time point after transplantation.

REFERENCES

#6727
INFLAMMATORY INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY ARE ASSOCIATED WITH HIGHER EXPRESSION OF INTRAGRAFT GRANZYME-B+ AND PHOSPHOSMAD-3+ PROTEIN
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Background and Aims: Inflammatory interstitial fibrosis and tubular atrophy (i-IF/TA) is a prominent histological lesion reported in late biopsy and poorly associated with graft survival. Cytotoxic T cell secrets Granzyme-B, which cleaves cytoskeleton protein, and activates pro-IL-1β, and TGF-β into their active form, leading to inflammation, fibrosis, and the apoptosis in target cell. The association of Granzyme-B+ cytotoxic T cell and phospho-SMAD-3 expression has been not explored in i-IF/TA in depth. Therefore, in this study, we aimed to determine the circulating and intragraft profiles of Granzyme-B+ cytotoxic T cell together with fibrosis pathway mediator p-SMAD-3 expression in renal transplant recipients (RTRs) patients with biopsy proven i-IF/TA.

Method: The circulating frequency of CD3+CD8+Granzyme-B+ cytotoxic T (CTLc) was measured by the flowcytometry; serum and PBMCs culture supernatants Granzyme-B and proinflammatory cytokines TGF-β, IL-1β level by the ELISA. Intragraft Granzyme-B mRNA transcript expression by the RT-PCR and Granzyme-B+, pSMAD-3+ Cell was analyzed by the immunohistochemistry techniques. Independent T-test for continuous variables and Pearson correlation was applied for the different variables.

Results: The circulating frequency of cytotoxic-T cell (CD3+CD8+Granzyme-B+) in SGF vs i-IF/TA was (27.96±4.86 vs 23.19±3.85%, p = 0.011), CD3+ T cell was (66.08±6.8 vs 65.18±9.35%; p = 0.68), CD3+CD8+ T cell was (37.29±4.11 vs 34.68±5.43%; p = 0.28). Serum Granzyme-B level was in SGF vs IF/TA was (100.82±22.41 vs 130.32±46.60, p = 0.038 pg/ml), serum TGF-β level was (367.50±31.50 vs 318.81±48.39, p = 0.005), IL-1β level was (49.14±17.03 vs 63.69±23.13, p = 0.076). Intragraft Granzyme-B mRNA transcript expression in SGF vs i-IF/TA was (1.01±0.048 vs 2.10±1.02-fold; p<0.001). Granzyme-B+ cell/mm² count was (0.40±0.69 vs 2.20±1.27; p = 0.001). The intragraft phosphorylated SMAD-3+ cell was (3.70±1.82 vs 6.73±3.21; p = 0.008). Fig. 1. The intragraft Granzyme-B+ cell count was positively correlated with pSMAD-3+ cell (r = 0.315, p = 0.047). The frequency of circulating CTLc was negatively correlated with urine proteinuria (r = -0.51, p<0.001), serum creatinine (r = -0.28, p = 0.037) and eGFR (r = -0.28, p = 0.037). While urine proteinuria was positively correlated with serum Granzyme-B level (r = 0.343, p = 0.001), intragraft Granzyme-B mRNA transcript expression (r = 0.38, p<0.001).

Conclusions: Higher intragraft Granzyme-B+ Cytotoxic T-cell and phosphoSMAD-3 positive cells are associated with i-IF/TA in RTRs.

#6062
EFFECT OF KIDNEY TRANSPLANTATION ON ARTERIOULAR MOLECULAR PATHWAYS IN CHILDREN WITH PRECEDING PERITONEAL DIALYSIS
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Background and Aims: Patients on peritoneal dialysis suffer from progressive peritoneal membrane transformation and accelerated vascular disease, underlying molecular machineries have recently been described. Molecular effects
of kidney transplantation (KTx) on vascular and peritoneal pathophysiology following PD are hardly understood.

Method: Fat surrounded omental arterioles (i.e. not directly exposed to PD fluids) from age-matched (median 6.5 years) children with chronic kidney disease (CKD5, n = 8), 5 children on PD [neutral pH, low glucose degradation product content, median PD duration 22 (5,50) months] and 6 children, who underwent successful KTx 4-5 weeks after a median 22 (12, 36) months of PD were analyzed by digital histomorphometry. Following microdissection from fat tissue, arterioles underwent transcriptomic and proteome analyses, followed by Gene Set Enrichment Analysis (GSEA), weighted gene co-expression network analysis (WGCNA), gene ontology (GO) and protein interaction analysis (string-db.org). Key pathways were validated in independent, matched cohorts by quantitative immunohistochemistry (n = 15/group) and in vitro.

Results: 5000 most variable arteriolar transcripts (cut off p-value < 0.05 and |r| ≥ 0.9) were grouped into 23 modules by WGCNA, of which 8 significantly differed between CKD5, PD and KTx. Seven were specifically related to KTx and one module to PD. Four out of seven KTx specific modules resulted in significant GO terms summarized as fatty acid biosynthesis, negative regulation of RNA metabolism, cell cycle arrest, and apoptosis. The PD specific module was associated with muscle cell proliferation, detoxification and complement activation (with thrombospondin as most interconnected gene). Multi-omics analysis of KTx vs. PD demonstrated concordant upregulation of lipid and fatty acid biosynthesis with the hub gene fatty acid synthase (FASN) and downregulation of positive cell cycle regulation. In independent, matched cohorts, arteriolar abundance of thrombospondin and terminal complex component were higher in children on PD, arterioles from children after KTx had levels comparable to arterioles from children with CKD5. Key drivers of fibrotic process, arteriolar TGF-β and pSMAD2/3, were also higher in PD arterioles compared to CKD5 and persistently high after KTx. Arteriolar cell cycle arrest marker p16 and apoptosis marker cleaved Casp3 were higher after KTx as compared to PD and CKD5. FASN was abundant in intima and media layers of all arterioles, and three-fold higher after KTx then in children with PD and CKD5, respectively. Neutral lipids (oil red staining) were present in all three groups, more abundant in the media than in the intima, and two-fold increased in the media of children after KTx compared to children on PD (p = 0.018) and with CKD5 (p = 0.002). In vitro, methylprednisolone and tacrolimus, but not mycophenolate mofetil increased FASN abundance and activity in human umbilical arterial endothelial and vascular smooth muscle cells compared to media controls.

Conclusion: We for the first time comprehensively describe molecular pathways activated after KTx in children following a standard immunosuppressive regime. After KTx, arteriolar fatty acid biosynthesis, apoptosis and cell cycle arrest markers are increased as compared to arterioles from children with PD and CKD5; profibrotic pathways induced by PD are persistently activated.

#3687 KIDNEY TRANSCRIPTOME VARIES BETWEEN DONOR TYPES, WITH A DIFFERENTIAL RESPONSE TO ISCHEMIC PRECONDITIONING

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Background and Aims: The prevention/attenuation of graft ischemic injury is a challenge in kidney transplantation. We developed two rat models to investigate the impact of mesenchymal stromal cells (MSCs) in the ischemic preconditioning of kidneys from Donors after Circulatory Death (DCD) and Donors after Brain Death (DBD).

Method: Under general anesthesia, rats underwent iv injection of saline (S-groups) or 1.5 10⁶ MSCs (MSC-groups) followed by either DBD (6hr of brain death) or DCD (6hr of anesthesia and 20min warm ischemia) models, resulting in 4 groups (S-DBD, S-DCD, MSC-DBD, MSC-DCD). Kidneys were then pre-conditioned after IGLI flush. One kidney was directly fixed and the other one immersed for 14 hours in IGLI at 4°C. Serum samples were collected before treatment (baseline) and at the time of kidney collection. Urine samples were collected by bladder puncture at the time of kidney collection. Renal function was evaluated. Kidney histology was assessed by PAS staining and KIM1 immunostaining. Total RNA was extracted from S-DCD vs S-DBD kidneys for RNAseq.

Results: BUN was increased after 6h of anesthesia (DCD) or brain death (DBD) (p < 0.01). SGR increased in both S-DBD and MSC-DBD but was lower in MSC-treated rats (MSC-DBD 0.5±0.2mg/dL vs S-DBD 0.7±0.1mg/dL; p = 0.037). Urinary KIM1 was lower in MSC-treated DBD (S-DBD 10±4.5 vs MSC-DBD 7±1.7; p = 0.03). Acute Tubular Injury (ATI) and KIM1 expression were higher in S-DBD (ATI: S-DBD 65±24% of surface vs S-DCD 39±27% of surface (p = 0.03) and KIM1: S-DBD 0.39±0.24% of surface vs S-DCD 0.10±0.09% of surface (p = 0.0002)). In MSC groups, there was a significant extension in both extension and KIM expression. RNAseq showed that proinflammatory and proapoptotic pathways were upregulated in DBD, whereas transmembrane transport and metabolic pathways were downregulated, compared to DCD.

Conclusion: The RNA profiles of the kidneys are different upon donor types, which may impact the response to MSC-based ischemic preconditioning.
CD40-TRAF6 signaling inhibition blocks trained immunity and promotes allograft tolerance.

A: TNF and IL-6 production in RPMI-, HKCA- and HKCA+TRAF6i-trained PBMCs upon LPS restimulation (n=9). Mean ± SEM.

B: H3K4me3 intensity in RPMI-, HKCA and HKCA+TRAF6i-trained monocytes for genomic regions with significantly altered H3K4me3 intensity in HKCA- versus RPMI-treated monocytes (Fold Change (FC) > 2 or < 0.5, FDR < 0.1) (n=3).

C: Metabolic parameters in RPMI-, HKCA and HKCA+TRAF6i-trained PBMCs 6 days post-stimulation, normalized to RPMI-trained PBMCs (n=5).

D: FOXP3 expression in CD4+ T cells after 7-day MLR with RPMI-, HKCA- or HKCA+TRAF6i-trained monocytes (n=3). Mean ± SEM.

E: Graft survival in PBS, CTLA4- Ig, TRAF6i-NB and CTLA4- Ig+TRAF6i-NB treated mice upon heterotopic heart transplantation. (n=6/group).

\*p < 0.05, \**p < 0.01, \***p < 0.001. Paired One-way ANOVA with Dunnett’s post-test (A, C, D) or Kaplan Meier with log-rank test (E).
#5108
SUSTAINED IL-6 SECRETION CAN LEAD TO AN AMPLIFIED INFLAMMATORY RESPONSE, MEDIATED BY THE ACTIVATION OF STAT3 AND NFKB VIA THE IL-6 AMPLIFIER LOOP
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Background and Aims: Organ transplants are the preferred treatment for end-stage organ failure. Potent and specific immunosuppressive agents have significantly decreased acute allograft rejection following renal transplantation. A significant barrier to long-term kidney allograft outcomes is chronic antibody-mediated rejection (CABMR). Chronic inflammation is a major cause of late graft loss that is mediated by soluble mediators released by immune and non-immune cells. IL-6 is a crucial cytokine that plays a central role in developing chronic inflammation. Non-immune cells, such as fibroblasts, have recently been identified as mediating chronic allograft rejection by activating the IL-6 amplifier loop (IL-6 + IL-17). Our Aim of the study:- to study the effect of IL-6 + IL-17 on secretion of IL-6 in the culture supernatant of fibroblasts derived from renal biopsy of chronic antibody mediated rejection (CABMR) patients; -to see the effect of anti-IL-6 (Tocilizumab) and anti-IL-17 on the secretion of IL-6 from the fibroblasts derived from kidney tissue of chronic antibody mediated rejection (CABMR) patients; and -to elucidate the pro-inflammatory pathway leading to increased IL-6 secretion by induction of Amplifier loop.

Method: Fibroblasts from grafted kidney from CABMR patients (n = 6) were cultured and stimulated with IL-6 (20ng/μl), IL-17(50ng/μl), IL-6 plus IL-17 for 24 hours. Levels of IL-6, MCP-1 and CCL20 were estimated in culture supernatants by ELISA as marker of IL-6 amplifier loop activation. mRNA expression of IL-6, MCP1, CCL20, and SOCS3 genes were measured in the stimulated fibroblasts. Stimulated Renal fibroblast cells from CABMR patients were lysed with Lysis buffer and subjected to SDS–PAGE and western blotting with anti-phospho-STAT3 and anti-phospho-NFkB p65. Additionally, IL-6, MCP1, and CCL20 levels were measured in Healthy control (n = 10), CABMR (n = 20), and non-CABMR (n = 30) patients.

Results: IL-6 and IL-17 synergistically induced more IL-6, CCL-20 & MCP-1 production from fibroblasts in culture supernatant. Gene expression analysis of IL-6, MCP1, and CCL20 was significantly higher with synergistic activation of IL-6 and IL-17 as compared to either IL-6 or IL-17 alone, while SOCS3 gene expression was downregulated. Our results also suggested that IL-6 Amplifier loop activation induces the NFkB and STAT3 signalling pathway activation in the non-immune cells like fibroblast derived from CABMR patients. Additionally, concentrations of IL-6, CCL-20 & MCP-1 in sera were significantly higher in CABMR patients compared to non-CABMR patients (p<0.001). There was a significant reduction in IL-6 concentration in culture supernatant with IL-6 and IL-17 inhibitor together and mRNA expression of IL-6, CCL20 and MCP-1 was significantly reduced while SOCS3 gene expression was upregulated.

Conclusion: In humans after kidney transplantation, IL-6 amplifier activation plays an active role in chronic rejection responses. Inhibition of IL-6 with Anti-IL-6 (Tocilizumab) and inhibition of IL-17 with Anti-IL-17 together reduces markers of tissue injury (IL-6, MCP1, CCL20) and rejection of allografts. so, IL-6 amplifier may be a therapeutic target for Chronic transplant rejection.

REFERENCES
#2556

**BIOLOGICAL EFFECTS OF A SHORT PERIOD OF NORMOTHERMIC MACHINE PERFUSION IN MARGINAL KIDNEYS: RESULTS OF A PROTEOMICS ANALYSIS**

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**Background and Aims:** Renal normothermic machine perfusion (NMP) is an organ preservation method based on the circulation of a warm (35–37°C) perfusion solution through the renal vasculature to deliver oxygen and nutrients. However, the biological effects of this technique on the marginal kidneys are uncertain. We consequently used mass spectrometry to define the proteomic profile of kidney tissue and urine from eight organs, considered unsuitable for transplantation, reconditioned for 120 min using a Kidney Assist device.

**Method:** Biopsies were taken during the pre-implantation histological evaluation (T-1), at the start of back table preparation (T0), and after 60 and 120 min of perfusion (T60, T120). Urine was collected at T0, T30, T60, and T120. Multiple algorithms, support vector machine (SVM) learning and partial least squares discriminant analysis (PLS-DA) were used to select the most discriminative proteins during NMP.

**Results:** Statistical analysis revealed the upregulation of 169 proteins and the downregulation of 196 in kidney tissue during NMP. Machine learning algorithms recognized the top 50 most discriminative proteins, five of which were concomitantly upregulated (LXN, ETFB, NUDT3, CYCS and UQCRBC1) and six downregulated (CFHR3, C1S, CFI, KNG1, SERPINC1, and F9) in the kidney and urine after NMP. Functional analysis showed that the most upregulated proteins were involved in the oxidative phosphorylation system and ATP synthesis, whereas the downregulated proteins were involved in the complement system and coagulation cascade. Results were, then, validated by classical and highly conservative biomolecular lab techniques.

**Conclusion:** Our proteomic analysis revealed that even brief periods of NMP induce substantial metabolic and biochemical changes in marginal organs, which supports the use of this promising technique in the clinic.

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**E2 - EPIDEMIOLOGY & OUTCOME**

#5733

**NIERKEUZE.NL: A WEB-BASED APPLICATION TO SUPPORT THE SHARED DECISION PROCESS FOR KIDNEY REPLACEMENT THERAPY BASED ON OUTCOME DATA IN THE NETHERLANDS**

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**Background and Aims:** Access to individualized, evidence-based prognostics is needed to facilitate decision making about the clinical implications of whether to opt for kidney transplantation or long-term dialysis. We aim to implement a data-driven support tool (Nierkeuze.nl) that incorporates basic patient characteristics and treatment options.

**Method:** Consecutive patients (N = 14,275) above 18 years of age with end-stage renal disease (ESRD) who were eligible candidates for their first kidney transplantation and started renal replacement therapy between 2000 and 2019 were included from the national registries RENINE and NOTR. SF-12 quality of life data was obtained from RENINE and a local transplant database. Several algorithms were developed to predict waiting time, short- and long-term patient survival, graft survival, and quality of life according to factors that are known at ESRD. Probabilities of 3- and 5-year mortality were calculated using two-stage distinct Cox regression: 1) waitlist-mortality according to median time on the waiting list, 2) mortality after transplantation in remaining follow-up. Product and complement rules defined the final probabilities. No mortality on the waiting list was assumed for living donor transplants. Missing data were imputed. Model performance was evaluated by internally validated C-statistics and calibration plots.

**Results:** We included 4,889 deceased donor transplants, of which 990 were within the Eurotransplant Senior allocation Program (ESP), and 6,251 living donor transplants. Discrimination varied for patient survival models (C-stats: 0.68 deceased-ETKAS-TX; 0.58 for deceased-ESP-TX; 0.74 for living-TX; 0.64 for waitlisted-candidates). Survival models achieved good calibration by visual inspection across the range of predicted probabilities. Figure 1 illustrates a clear 5-year survival benefit of transplantation (living and deceased donor groups) compared with wait-listed candidates for a 65-year-old male with glomerulonephritis. Other developed algorithms of the support tool will be presented with an overview of the first experiences in the kidney failure clinic.

**Conclusion:** Nierkeuze.nl depicts the influence of anticipated waiting time, patient characteristics, kidney allocation program, and donor type on survival outcome of the different treatment options. Incorporating this individualized quantitative outcome information may provide valuable support for an informed choice by patients and potential living donors.
#2984

**ACHIEVED BLOOD PRESSURE AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH ADVANCED STAGE CHRONIC KIDNEY DISEASE**

Ehab Al-Sodany, Karolina Szummer, Franz Peter Barany, Olof Heimbürger and Marie Evans

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**Background and Aims:** In patients with severely decreased eGFR (stage 4-5 CKD), efficacy of treating patients to a lower blood pressure (BP) target is uncertain. The Systolic blood Pressure Intervention Trial (SPRINT) demonstrated lower rates of a composite cardiovascular (CVD) endpoint and death in the intensive treatment group with a target systolic blood pressure (SBP) of <120 mmHg. This study has influenced guidelines; the updated 2021 Kidney Disease Improving Global Outcomes (KDIGO) now suggest lowering the SBP to < 120 mmHg, if tolerated. In this study we set out to investigate the association between SBP and CVD in a large cohort of nephrology-referred patients with CKD stage 3-5.

**Method:** We included patients ≥18 years participating in the Swedish Renal Registry (SRR-CKD) who had a first registered eGFR <60 ml/min/1.73 m² 2006-2017 with at least one recorded BP measurement and two outpatient visits within one year. We excluded individuals with a recorded SBP <100 mmHg or prior kidney failure replacement treatment. After the initial one-year observation period, we followed patients until the primary or death event occurred or until the end of the study period.

**Figure 1: Unadjusted association between systolic blood pressure and risk of MACE.**
secondary outcome was attained, or until December 31, 2017. The achieved average systolic BP, measured during routine out-patient care using any standard electronic or manual blood pressure device, was categorized into a priori defined categories. To align with SPRINT, the primary endpoint was Major Cardiovascular Events (MACE) defined as the composite of first myocardial infarction (MI), non-MI acute coronary syndrome, stroke, heart failure, or death attributable to CVD. The secondary endpoints were the individual components of the primary composite endpoint, all-cause death, or a composite of the primary endpoint and death. Demographics, body mass index, underlying kidney disease, and laboratory values at the start of follow-up were obtained from the SRR-CqD. Information on comorbidity, including Charlson comorbidity index was gathered from a linkage with the National Patient Registry; medications were obtained from the National Prescribed drug register. The primary endpoint and secondary endpoints were assessed by cause-specific Cox proportional hazards regression, adjusting for age, sex, history of CVD, Charlson comorbidity, plasma albumin, phosphate, diuretics, RAASi, betablockers, eGFR, and diastolic blood pressure. Missing data were handled through multiple imputation.

Results: In total 15,668 patients with a median eGFR 23 ml/min/1.73 m², mean age 71 years and 33% women were followed over a period of 2.8 years (IQR 1.4–5.0). There were 6359 patients (41%) experiencing the primary outcome; 2601 (11%) with a coronary artery event, 1427 (9%) MI, 1345 (9%) cerebrovascular event, and 5,480 (35%) patients died. The unadjusted analysis showed a J-shaped relationship between SBP and the primary outcome, with the lowest risk of events in patients with SBP around 125 mmHg (Figure 1). In multivariable models, there was a higher risk of experiencing the primary outcome if the average SBP was >150 mmHg (HR 1.09; 95% CI 1.0–1.19), the highest risk being in those with SBP above 160 mmHg (HR 1.40 with 95% CI 1.28–1.53) as compared to those with SBP 130–140 mmHg (Figure 2). We observed 30% lower risk of MI when the SBP was 100–120 mmHg after adjustments (HR 0.70 (95% CI 0.56–0.88) as compared to 130–140, and higher risk of MI at SBP >160 mmHg (1.78; 1.49–2.12) with 11% higher risk of MI with every 10 mmHg increase in SBP (HR 1.11; 1.07–1.14). The other cardiovascular endpoints, including all-cause mortality showed a similar pattern as the primary composite endpoint.

Conclusion: In patients with advanced stage CKD, SBP <120 mmHg is associated with lower risk of MI, but with lower risk of other cardiovascular outcomes or all-cause mortality. A SBP >140 mmHg was associated with higher risk of most cardiovascular events including cardiovascular mortality and all-cause mortality.
immunosuppression therapy enables KT to patients with high immunological risk and avoid prolonged time on the waiting list.

#3852
INCIDENCE AND SEVERITY OF COVID-19 IN RELATION TO ANTI-RBD IgG ANTIBODY LEVEL AFTER COVID-19 VACCINATION IN KIDNEY TRANSPLANT RECIPIENTS
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Background and Aims: Kidney transplant recipients (KTRs) remain at increased risk for severe COVID-19 after vaccination, most likely due to an impaired immune response. However, the exact clinical impact of this impaired response remains unclear. Therefore we analysed the relationship between antibody levels after vaccination and the occurrence and severity of COVID-19 in a large cohort of KTRs.

Method: All KTRs, living in the Netherlands, who received COVID-19 vaccination were invited to participate in this observational cohort study. At approximately 28 days after the 2nd vaccination blood samples were obtained by a home-based finger-prick method and analysed for IgG antibodies against the receptor-binding domain of the SARS-CoV-2 spike protein (anti-RBD IgG). Participants were classified as either seronegative or seropositive using an anti-RBD IgG threshold of 50 BAU/mL. Participants who previously experienced COVID-19 were excluded. Primary endpoint was the incidence of COVID-19 from the moment the blood sample for anti-RBD IgG measurement was obtained until 6 months thereafter. Multivariable Cox and logistic regression analyses were performed to analyse which factors affected the occurrence and the severity (i.e. hospitalization and/or death) of COVID-19.

Results: In total 12,159 KTRs were approached of whom 3,828 agreed to participate. In 2,885 subjects successful antibody measurement was performed after the 2nd COVID-19 vaccination. Among those, 1,578 (54.7%) became seropositive, whereas 1,307 (45.3%) remained seronegative. During a follow-up of 6 months, seropositivity was associated with a lower risk for COVID-19 incidence, also after adjusting for age, sex, socio-economic status and adherence to COVID-19 restrictions (HR 0.48 (0.27-0.86), p = 0.01). COVID-19 was also significantly less severe in seropositive as compared to seronegative participants (OR 0.14 (0.03-0.67), p = 0.01). When studied on a continuous scale, we observed a log-linear relationship between antibody level and risk for COVID-19 incidence (HR 0.52 (0.31-0.89) per tenfold higher anti-RBD IgG antibody level, p = 0.02). A threshold above which optimal protection was offered could not be detected. A similar association was found for COVID-19 severity.

Conclusion: In conclusion, antibody level after COVID-19 vaccination is associated in a log-linear relationship with the occurrence and severity of COVID-19 in KTRs. Therefore higher antibody levels, and not only reaching seropositivity, should be the aim of COVID-19 vaccination in KTRs. Immunosuppressed patients who have no or low antibody levels after vaccination should be offered repeat vaccinations, whether or not via alternative vaccination strategies, or passive immunization.

#4150
INTERNATIONAL COMPARISON AND TIME TRENDS OF FIRST KIDNEY TRANSPLANT RECIPIENT CHARACTERISTICS ACROSS EUROPE: A STUDY FROM THE ERA REGISTRY
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Background and Aims: Large international differences exist in the kidney transplantation (KT) rate across Europe. Countries might transplant a different group of end-stage kidney disease (ESKD) patients, but up to now an overview of recipient characteristics in first kidney transplant recipients in the different European countries is lacking. Therefore, the aim of this study was to give an overview as well as time trends in age, sex and primary renal disease (PRD) distribution of first kidney transplant recipients in Europe.

Method: The European Renal Association (ERA) Registry database was used to obtain data on adult patients receiving their first KT between 2010 and 2019 from 12 European countries. The numbers and percentages of recipients in each age, sex and PRD group were calculated by country, donor type and year. The first KT rate was calculated by dividing the number of first KT’s by the adult general population counts and multiplied by one million.

Results: In total, 99,543 patients received a first KT between 2010 and 2019 for all countries combined. The percentage of recipients aged 65 years and older varied greatly between countries, with Bosnia and Herzegovina having the lowest percentage (1%), and the Netherlands, Spain and Norway having the highest percentages (>25%). Similar results were found for deceased donor first KT, but for living donor first KT Spain was no longer among the countries with the highest percentage of recipients aged 65 years and older. The percentage of female recipients ranged between 33% in Austria and 38% in the Netherlands for total first KT, between 33% in Austria and 38% in Denmark for deceased donor first KT and between 30% in Austria and 39% in the United Kingdom for living donor first KT. When comparing the distribution of PRDs, Bosnia and Herzegovina had a relative high percentage of recipients with glomerulonephritis (35%), while Finland had a high percentage of recipients with diabetes mellitus (29%) and the Netherlands and Norway a high percentage of recipients with hypertension / renal vascular diseases (17% and 22% respectively). This distribution was similar for deceased and living donor first KT recipients. Over time, the most prominent change regarding the recipient characteristics was observed for the age of the recipient, with an increasing proportion of recipients aged 65 years and older from 18% in 2010 to 28% in 2019 for all countries combined, and with a similar trend observed in most countries.

Conclusion: We observed large differences in the recipient characteristics at first KT between European countries and over time, especially for the recipient age and PRD. These new insights in the distribution of recipient characteristics in the first KT population could elucidate which ESKD patients receive a KT.

#5465
RACE-FREE eGFR EQUATION IN KIDNEY RECIPIENTS: A DEVELOPMENT AND VALIDATION STUDY
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Background and Aims: To assess the performances of the current eGFR equations, including the race-free CKD-EPI-2021, in the kidney transplant population, and compare these performances to a race-free kidney-recipient-specific (KRS) GFR equation.

Method: We included adult kidney recipients transplanted between 01/01/2000 and 01/01/2017 in 16 academic cohorts in Europe, the USA and Australia comprising 14 transplant centres and three clinical trials. Measured GFRs (mGFR) were assessed using 51Cr-EDTA, 99mTc-DTPA, inulin, iothalamate or iohexol clearance, according to the local practice. A KRS GFR equation was developed using additive and multiplicative stepwise linear regressions and its performance was compared to those of the current GFR equations. The performances were assessed with the P30 and the correct classification of chronic kidney disease (CKD) stage metrics.

Results: The study included 15,489 patients, having 50,466 GFR values both measured and estimated by creatinine-based equations. Among the current GFR equations, race-free CKD-EPI-2021 equation showed the lowest performance compared with MDRD and CKD-EPI-2009 equations. We then built a race-free KRS GFR equation based on an additive model including creatinine, age, and sex. We showed that using race did not increase the performance of the equation. We found that the race-free KRS GFR equation showed significantly improved performance compared with the race-free CKD-EPI-2021 equation and performed well in the external validation cohorts (P30 ranging from 73.0% to 91.3%). Finally, we showed that the race-free KRS GFR equation performed well in a series of kidney transplant recipient subpopulations stratified by race, sex, age, body mass index, donor type, therapeutics, creatinine and GFR measurement methods and timing. Based on these results we developed an online application that estimates GFR
Based on recipient age, sex and creatinine: https://transplant-prediction-system.shinyapps.io/eGFR_equation_KTX/

Conclusion: Using multiple, international cohorts of kidney recipients, we developed and validated a new race-free KRS GFR equation that demonstrated high accuracy and outperformed the race-free CKD-EPI-2021 equation developed in individuals with native kidneys.

#4624

DO WOMEN HAVE LESS ACCESS TO THE KIDNEY TRANSPLANTATION WAITING LIST THAN MEN IN FRANCE?
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Background and Aims: Studies performed in several countries and in some French regions showed that women have less access to kidney transplantation waiting list (KTWL) than men. The aim of this study is to analyse women’s access to the kidney transplantation waiting list at the national level and in all French regions.

Method: This is a retrospective cohort study using the French National Renal Epidemiology registry (REIN). All incident patients initiated dialysis from 2017 to 2019 and aged between 18 and 85 were included. Patients were followed three years from the dialysis start. Our outcome of interest was the registration on the KTWL 1 and 3 years following dialysis initiation. We performed Cox proportional hazard models, adjusted on age, comorbidities and neighbourhood deprivation level using European Deprivation Index (EDI), at national level and in all French regions. The sex/age and sex/EDI interactions were studied.

Results: 29 395 patients started dialysis in 2017-2019. 35% were women. 40% of female and 34% of male patients lived in most deprived areas. Men were more comorbid than women at dialysis start. At the national level, women had less access to the KTWL compared to men one (adjHR: 0.91; IC95: [0.87 – 0.96]) and three years (adjHR: 0.87 [0.84 – 0.91]) after dialysis start. There was no significant sex/EDI interaction but a significant sex/age interaction. Therefore, the analyses were stratified by age (<60 and > 60 years old). Only women aged more than 60 had less access to the KTWL at one year (adjHR: 0.76 [0.71 – 0.82]) and three years (adjHR: 0.75 [0.71 – 0.81]). At regional level, the same trends were found in Nouvelle Aquitaine and Pays de Loire one-year after dialysis start and two more regions (Bourgogne-Franche-Comté and Île-de-France) 3 years after dialysis start.

Conclusion: This study shows that women have less access to KT WL one and three years after dialysis start at the national level and in some regions. This disparity is found to be present especially among patients aged beyond 60 years. A qualitative study is planned to better understand this sex based disparity.

#6327

ACCEPT OR DECLINE? A STATISTICAL APPROACH TO AID DECISION MAKING
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Background and Aims: The clinician-patient decision of whether to accept or decline an offered deceased donor kidney is one of the most complex in transplantation. Though many attempts have been made to risk stratify based on donor and recipient characteristics as well as other methods, reliance on clinical intuition remains high. We used a novel statistical modelling technique to better understand potential outcomes for patients following acceptance or decline of a deceased donor organ offer in the UK.

Method: We obtained UKTR data held by NHS Blood and Transplant (NHSBT) on adult patients listed for kidney transplantation in the UK, deceased donor kidney offers and post-transplant outcomes. Multivariable models to demonstrate 5-year transplant survival (a composite of graft and patient survival) for patients from the point of offering and post-transplant survival were developed using a Cox proportional hazard techniques. Waiting time to a “better” offer was modelled using a micro-simulation approach for patients and donors with different profiles, incorporating the points system from the current UK kidney offering scheme. Rates of patients arriving on the waiting list, leaving the list and being transplanted were obtained to facilitate this, as well as characteristics of waitlisted patients and organ donors. Simulations were then run to ascertain potential outcomes from the point of offer for an index patient for scenarios characterised by offers from donors with differing profiles.

Results: Figure 1 demonstrates the outcomes of an index patient if they accept an organ offer from a donor with the demonstrated characteristics compared with potential outcomes if the next offer is accepted. Figure 2 uses the same techniques but demonstrates outcomes if a kidney from a donor with ‘worse’ characteristics is offered.

Conclusion: This study demonstrates a novel method to help visualise potential outcomes for patients listed for deceased donor kidney transplantation. Though many attempts have been made to risk stratify based on donor and recipient characteristics as well as other methods, reliance on clinical intuition remains high. We used a novel statistical modelling technique to better understand potential outcomes for patients following acceptance or decline of a deceased donor organ offer in the UK.
KIDNEY TRANSPLANTATION IN PATIENTS WITH AA AMYLOIDOSIS: A FRENCH MULTI-CENTER MATCHED COHORT STUDY IN THE ERA OF BIOTHERAPIES

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Background and Aims: Outcomes of kidney transplantation for patients with renal AA amyloidosis are uncertain, with reports of poor survival and high
Figure 1: Kaplan-Meier estimates of patient survival (A) and death-censored graft survival (B) in AA amyloidosis patients and in controls. Tables represent patients at risk in each group. Statistical difference was assessed with the Log-rank test.

Figure 2: allograft recurrence. However, recent advances in biotherapies, especially anti-IL-1 treatments, may have improved patients’ outcome in the transplantation setting.

Method: We conducted a retrospective multicenter matched cohort study in 26 French centers reporting all patients with AA amyloidosis who received a kidney transplant between 2008 and 2018, and compared them to matched control patients (ratio 1:2 controls) who received a kidney transplant for other causes.

Results: Eighty-six AA amyloidosis transplants and 157 control transplants were included. Median age was 49.4 years (interquartile range 39.7-61.1), and the main cause of amyloidosis was Familial Mediterranean Fever (37 cases, 43%). Sixteen (18.6%) patients received a biotherapy after transplantation. At 5 years, patient survival was 85.5% (95% confidence interval 77.8-94.0) and 86.2% (80.5-92.2) for cases and controls, respectively (p = 0.5). Death censored graft survival was 78.2% (78.2-93.5) and 91.7% (87.0-96.6), respectively (p = 0.05). Histologically proven AA amyloidosis recurrence was found in 5 patients (5.8%). 55.8% of amyloid patients had at least one infection requiring hospitalization and 27.9% an episode of acute graft rejection. In this group, multivariable analysis showed that CRP concentration at time of transplantation was associated with patient survival (HR 1.01, p = 0.01).

Conclusion: In this recent cohort, patient survival was comparable to controls and recurrence rates were lower than previously reported. Provided the underlying inflammatory disease is well controlled, patients with AA amyloidosis may be transplanted with similar patient and graft outcomes than that of matched controls.

#6440 C1Q-BINDING ANTI-HLA DONOR-SPECIFIC ANTIBODIES AND LONG-TERM KIDNEY GRAFT OUTCOMES
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Background and Aims: Immunological response mediated by anti-HLA donor specific antibodies plays an important role in renal allograft injury in kidney transplant recipients. Several characteristics of donor-specific antibodies such as HLA class, specificity, mean fluorescence intensity, IgG
subclass and C1q-binding capacity can be assessed. The aim of this study was to determine the impact of circulating anti-HLA donor-specific and their characteristics, including C1q-binding capacity, on long-term kidney graft outcomes.

**Method:** One hundred eight patients from our transplant center, who underwent kidney allograft biopsy within three to twenty-four months after renal transplantation from brain-dead deceased donor between 2018 and 2020, were included in the study. At the time of biopsy patients' sera were collected and stored for analysis. Samples were tested for anti-HLA donor-specific antibodies and their characteristics. Antibodies with mean fluorescence intensity > 500 were considered positive.

**Results:** Median time of follow-up of patients was thirty-nine months. Out of nineteen patients with detected donor-specific antibodies, ten patients were identified with immunodominant donor-specific antibodies with C1q-binding capacity (out of them, six patients had anti-HLA donor-specific antibodies detected also before transplantation). C1q-binding antibodies were IgG1 (six patients), IgG3 (three patients) and IgG1 + IgG3 (one patient). Presence at the time of biopsy of donor-specific antibodies and their C1q-binding capacity were independent predictors (HR = 5.13, p < 0.001 and HR = 14.64, p < 0.001; respectively) of inferior kidney graft outcomes (composite of 30% reduction from eGFR at biopsy or death-censored graft loss).

**Conclusion:** Detection of donor-specific antibodies and their C1q-binding capacity might provide prognostic information in post-transplant monitoring in kidney transplant recipients.

#4617

**THE IMPACT OF DONOR NEPHRECTOMY ON THE ELDERLY LIVING KIDNEY DONORS**

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**Background and Aims:** Because of the serious cadaveric donor shortage, the number of living donor kidney transplantation (LDKT) is increasing. To increase the living donor (LD) source, elderly LDs are indicated for the donor nephrectomy. However, the safety of the LDs ≥ 70 years is still remained to be investigated.

**Method:** Between January 2008 and December 2020, a total 1226 LDs for LDKT was included in this retrospective cohort study. LDs were stratified into 3 groups based on age; 244 LDs aged 30–49 years, 803 LDs aged 50–69 years, 179 LDs aged 70–89 years. To investigate the safety of donor nephrectomy in the LDs ≥ 70 years, operative outcomes, the estimated glomerular filtration rate (eGFR) changes, end stage renal disease (ESRD), and mortality were investigated among 3 groups. eGFR changes were analyzed using mixed linear models. The contributing factors for the recovery in the eGFR from the nadir eGFR were analyzed using multivariate linear regression analysis adjusted for mixed linear models. Mortality rates were analyzed using Cox regression models.

**Results:** In the LD characteristics, significant difference was identified in sex. In the operative outcomes, significant difference was not identified in operative duration, blood loss, and complications among 3 groups. In the mixed linear models adjusted for sex, eGFRs of LDs aged 70–89 years were significantly lower at any time points after donor nephrectomy than those in 2 other groups (Figure 1). The eGFR after donor nephrectomy recovers with time in 3 groups. The recoveries in the eGFR from the nadir eGFR were similar among 3 groups. The recoveries in the eGFR were independently affected by the hypertension ($P = 0.008$), smoking history ($P < 0.001$), and body mass index ($P = 0.011$) at donor nephrectomy. Donor age was not the independent factor. The mortality rate of LDs aged 70-89 years was significantly higher than those in 2 other groups (Figure 2). However, during the observational period, ESRD was not identified among 3 groups.

**Conclusion:** eGFR changes and mortality rate were significantly low in LDs aged 70–89 years. However, the recoveries in the eGFR from the nadir eGFR were similar among 3 groups. ESRD was not identified among 3 groups. These results implied that LDs aged 70–89 years might undergo donor nephrectomy safely and complete their lives without ESRD after donor nephrectomy.
Background and Aims: Kidney transplant recipients (KTRs) were advised to tightly adhere to government recommendations to curb the spread of SARS-CoV-2 because of a high risk of morbidity and mortality and decreased immunogenicity after vaccination. The aim of this study was to analyze the change in adherence to preventive measures after vaccination and awareness of antibody response, and to evaluate the effectiveness of these measures.

Method: Questionnaires were sent to 3531 KTRs enrolled in the Dutch RECOVAC studies, retrospectively asking for adherence to nine preventive measures on a 5-point Likert scale before and after SARS-CoV-2 vaccination and after awareness of antibody response. Blood samples were collected 28 days after the second vaccination. Antibody response was categorized as non-responder (≤50 BAU/mL), low-responder (>50 ≤300 BAU/mL) or high-responder (>300 BAU/mL), and shared with participants as a correlate of protection. Adherence before and after vaccination were compared by the Wilcoxon signed rank sum test. Logistic regression analysis was performed to estimate the association between antibody response and adherence, and adherence on acquiring SARS-CoV-2 infection.

Results: In 2939 KTRs (83%) who completed the first questionnaire on adherence to preventive measures, adherence was higher before than after SARS-CoV-2 vaccination (4.56, IQR 4.11-4.78 and 4.22, IQR 3.67-4.67, p < .001) (Figure 1). Adherence after awareness of antibody response was analyzed in 2399 KTRs (82%) of whom also blood samples were available, containing 949 non-responders, 500 low-responders and 950 high-responders. Compared to non-responders, low- and high-responders reported lower adherence (Figure 2). Higher adherence was associated with lower infection rates before and after vaccination (OR 0.67 [0.51-0.91], p = 0.008 and OR 0.48 [0.28–0.86], p = 0.010).

Conclusion: To the best of our knowledge, we are the first to show that KTRs became less adherent to social isolation and other preventive measures after vaccination against COVID-19. Adherence decreased in KTRs who were aware of a subsequent antibody response compared to those without. Moreover, preventive measures in this vulnerable group are effective, regardless of vaccination status.
HUMORAL RESPONSE TO SARS-COV-2 AFTER FIVE SUCCESSIVE DOSES OF mRNA VACCINE AND PASSIVE IMMUNIZATION THERAPY IN STABLE KIDNEY TRANSPLANTATION PATIENTS

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Background and Aims: The poor humoral response after vaccination against SARS-CoV-2 in kidney transplant recipients (KT) led to the approval of new doses, the fifth being the last administered, and to the development of drugs for passive immunization. Our aim is to analyze the humoral immune response and the evolution of the anti spike (antiS) antibody titer after 5 doses of mRNA vaccine against SARS-CoV-2 and the administration of pre-exposure prophylaxis.

Method: We performed a prospective cohort study of stable KT patients from our center who received 5 doses of an mRNA vaccine from March 2021 to December 2022. KT recipients with less than 6 months after transplantation and with active oncological or hematologic disease were excluded. We determined antiS titers (Abbott SARS-CoV-2 IgG chemiluminescent microparticle immunoassay) at baseline and one month after the second, third, fourth and fifth doses. We consider seroconversion if antiS titer was greater than 260 BAU/mL. We compared humoral response after 2, 3, 4 and 5 doses.

Results: We included 18 KT. Mean age was 59.8 years and 72.2% were male. The median time from KT to the first vaccine dose was 45 months, between the second and third 4 months and 6 months between the third and fourth and fourth and fifth doses. Seroconversion rate was 72% after the fourth and fifth doses. We consider seroconversion if antiS titer was greater than 260 BAU/mL. We compared humoral response after 2, 3, 4 and 5 doses. Seroconversion rate was 11.1% after 2 doses, 50% after 3 doses, 72% after the fourth, and 94.4% after the fifth (p < 0.001). One TR did not develop antibodies after 5 doses. Two KT that had not seroconverted after the fourth also received passive immunization (tixagevimab-cilgavimab), maintaining high antiS titers 3 and 5 months after administration. The KT who seroconverted after 2 doses doubled the antiS titer after the third (1070 vs. 2168 BAU/mL; p = 0.180), in those who seroconverted after 3 doses it increased by 380% after the fourth (802 vs. 2896 BAU/mL; p = 0.028) and in those who seroconverted after 4 doses, the antiS titer increased by 60% (1067 vs. 1762 BAU/mL; p = 0.213). No patients had neither acute rejection nor serious adverse effects.

Conclusion: Successful doses of vaccination increased the development and titer of antibodies against SARS-CoV-2 in KT. However the administration of new doses is necessary, especially bivalent vaccines, which increase protection against new variants of the virus. We should identify those patients who do not generate an adequate humoral response in order to offer them other prevention strategies.

Impact of Mental Illness on Post-transplantation Outcomes in New Zealand: The Asset-Mh Data Linkage Study

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Background and Aims: People with severe mental illness are 6 times more likely to develop kidney disease. Mental illness is overrepresented in the kidney failure population. Up to 40% of dialysis patients are affected by depression and anxiety. There is limited understanding of the extent and impact of mental illness on transplant outcomes. We aimed to evaluate the impact mental illness has upon post-transplant outcomes, including graft failure and death in kidney transplant recipients in New Zealand.

Method: We included all incident kidney transplant recipients in New Zealand, 2006-2019 from the ASSET linked data platform, including Australian and New Zealand Dialysis and Transplant Registry, and national health registries (eg. hospitalisations, prescriptions and mental health services). Presence of mental illness was ascertained based on past use of medications (antipsychotics and antidepressants) and mental health services (community/residential support and inpatient) occurring at least twice over a year. Follow-up was from transplantation until death, graft failure or 31st Dec 2019. We used Cox models to evaluate risk of graft failure or death for mental health users compared to non-mental health users, adjusting for age, sex, calendar year and prior dialysis time.

Results: We included 1,796 kidney transplant recipients, where 457 (25%) had mental illness comorbidity. Overall, 228 (13%) used medication for mental illness (25 antipsychotics; 203 antidepressants) and 340 (19%) used mental health services (327 community/residential support; 14 inpatient). There were 111 recipients (6%) who had used medications and services for mental illness. There were 42 (9%) graft failures and 34 (7%) deaths among those with mental illness compared to 137 (10%) graft failures and 125 (9%) deaths among those without mental illness. Those with mental illness had the same risk of graft failure compared to others (p = 0.17), regardless of whether they used antipsychotics (HR: 1.52, 95%CI: 0.93-2.48, p = 0.09) or received community/residential support (HR: 1.19, 95%CI: 0.78-1.81, p = 0.42). There were no graft failures among those using antipsychotics or receiving inpatient care. Risk of death increased 3-fold (HR: 3.24, 95%CI: 1.51-6.99, p < 0.01) in those using antipsychotics compared to those without mental illness, but was not increased among those using antidepressants (HR: 0.90, 95%CI: 0.47-1.72, p = 0.74). There was weak evidence for an increased risk of death among those receiving community/residential support (HR: 1.57, 95%CI: 0.99-2.49, p = 0.06) compared to those without mental illness. Risk of death was not significantly associated with those receiving inpatient care (HR: 3.00, 95%CI:0.72-12.42, p = 0.13), although event rates were low. For composite of graft failure or death, those with mental illness had the same risk as those without (p > 0.10), regardless of receiving antipsychotics (HR: 1.77, 95%CI: 0.83-3.75) or antidepressants (HR: 1.23, 95%CI: 0.84-1.82), or community/residential support (HR: 1.37, 95%CI: 1.00-1.87) or inpatient care (HR: 1.41, 95%CI: 0.35-5.71).

Conclusion: Mental illness comorbidity is common in this setting, with one in ten transplant recipients in New Zealand receiving psychiatric treatment. Antipsychotic use was associated with three times the risk of death. Otherwise, those with mental illness had comparable post-transplant outcomes. There is opportunity for more collaborative psychiatric and transplant services to promote better patient outcomes and reduce post-transplant mortality.
**Abstracts**

**KIDNEY TRANSPLANT, CHRONIC KIDNEY DISEASE, ON DIALYSIS AND LIVING WITH A PREVALENCE OF POST-COVID-19 CONDITION IN PATIENTS WITH #4473

1Dongguk University Ilsan Hospital, Rep. of South Korea and 2Asan medical center, Rep. of South Korea

**MELLITUS**

**TAKING TACROLIMUS WITH POST-TRANSPLANTATION DIABETES**

Jiyun Jung1, Jaeun Lee2, Jae Yoon Park1 and Hyosang Kim2

1Dongguk University Ilsan Hospital, Rep. of South Korea and 2Asan medical center, Rep. of South Korea

**EFFECTS OF METFORMIN IN KIDNEY TRANSPLANT RECIPIENTS TAKING TACROLIMUS WITH POST-TRANSPLANTATION DIABETES MELLITUS**

Jiyun Jung1, Jaeun Lee2, Jae Yoon Park1 and Hyosang Kim2

1Dongguk University Ilsan Hospital, Rep. of South Korea and 2Asan medical center, Rep. of South Korea

**Background and Aims:** Tacrolimus is a pivotal maintenance immunosuppressive drug in kidney transplantation (KT). Although diabetogenic property of tacrolimus is still an inevitable concern, it can reduce the risk of acute rejection and improve graft survival compared to cyclosporine. Metformin, despite limited randomized controlled trial, has been found to be safe and effective in patients with post-transplantation diabetes mellitus (PTDM). We aimed to investigate the effect of metformin on acute rejection and graft survival in kidney transplant recipients taking tacrolimus.

**Method:** 442 PTDM patients who were prescribed tacrolimus between 2000 and 2018 were collected. We conducted propensity score matching between the metformin and non-metformin group and evaluated the effects of metformin on the occurrence of T-cell mediated rejection (TCMR) and antibody-mediated rejection (ABMR), and graft survival with Cox proportional hazard model.

**Results:** During the average follow up of 8.7 years, 90 patients were diagnosed as PTDM within one year after KT. Among 442 patients taking tacrolimus, 297 patients were treated with metformin for the average of 4.4 years. After 1:1 matching, cumulative incidences of TCMR (p = 0.008) and graft failure (p = 0.005) in the metformin group was lower than the non-metformin group, while no significant difference was observed in ABMR. Metformin use was associated with a reduced risk of TCMR (HR 0.43, 95% CI 0.21-0.88, p = 0.021) and graft failure (HR 0.39, 95% CI 0.19-0.79, p = 0.009). There was no significant difference in t (tubulitis), i (interstitial inflammation), and v (endarteritis) scores of TCMR between the metformin and the non-metformin group.

**Conclusion:** Our study demonstrates that combination therapy with metformin and tacrolimus in kidney transplant recipients with PTDM is associated with a lower risk of acute rejection and graft failure.

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**Figure 1:** Risk of graft failure, death and composite of both for those with mental illness compared to those without mental illness (left panels = unadjusted, right panels = adjusted estimates).

*p < 0.05**

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**#3629**

**EFFECTS OF METFORMIN IN KIDNEY TRANSPLANT RECIPIENTS TAKING TACROLIMUS WITH POST-TRANSPLANTATION DIABETES MELLITUS**

Jiyun Jung1, Jaeun Lee2, Jae Yoon Park1 and Hyosang Kim2

1Dongguk University Ilsan Hospital, Rep. of South Korea and 2Asan medical center, Rep. of South Korea

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**Conclusion:** Our study demonstrates that combination therapy with metformin and tacrolimus in kidney transplant recipients with PTDM is associated with a lower risk of acute rejection and graft failure.

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**#4473**

**PREVALENCE OF POST-COVID-19 CONDITION IN PATIENTS WITH CHRONIC KIDNEY DISEASE, ON DIALYSIS AND LIVING WITH A KIDNEY TRANSPLANT**

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**Background and Aims:** The prevalence of post-COVID-19 condition (PCC) is estimated to be 13% in healthy individuals. We analyzed the prevalence and disease burden of PCC in patients with chronic kidney disease (CKD) G4/5, dialysis patients and kidney transplant recipients (KTR).

**Method:** Patients participated in the RECOVAC study, in which SARS-CoV-2 antibodies were measured in CKD G4/5, dialysis patients and KTR after the second and third COVID-19 vaccination in the Netherlands. A questionnaire was sent to 4868 participants one year after initial vaccination asking for the presence of long-lasting symptoms after diagnosis in COVID-19 positive patients, or since the start of the pandemic in COVID-19 negative patients. PCC was defined according to the WHO clinical case definition. Blood samples at one month after the second and third vaccination were analysed with anti-RBD IgG ELISA. COVID-19 diagnosis was assessed by questionnaire and antibody analysis. Logistic regression analysis was used to compare the presence of one or more long-lasting symptoms between COVID-19 positive and negative patients. In COVID-19 positive patients, we likewise identified predictors of PCC by backward selection and estimated the association between log-transformed antibody levels and PCC.

**Results:** 2747 patients were included, of which 222 patients with CKD G4/5, 390 dialysis patients and 2135 KTR. PCC was present in 25%, 16%, and 21% of CKD G4/5 patients, dialysis patients and KTR with high or very...
high symptom burden in 57%, 61% and 71%, respectively. In COVID-19 negative patients, long-lasting symptoms were present in 15%, 13% and 18%, respectively. COVID-19 positive patients (n = 1004) were at higher odds of having one or more long-lasting symptoms compared with COVID-19 negative patients (n = 1743) (OR: 1.33 [1.09–1.61], p = .005). Predictors of PCC were chronic lung disease (adjusted OR 2.04 [1.18–3.50], p = .01) and hospital/ICU admission (adjusted OR 5.03 [3.22-7.86], p < .001). Log anti-RBD IgG antibody level was negatively associated with PCC (adjusted OR: 0.79 [0.66–0.94], p = .008).

Conclusion: Patients with CKD G4/5, dialysis patients and KTR are at risk for PCC with a high symptom burden, especially if antibody levels after COVID-19 vaccination are low.

#5999

GRADES II-III INTRA-ABDOMINAL HYPERTENSION INCREASE THE RISK OF GRAFT LOSS OR DEATH AFTER KIDNEY TRANSPLANTATION

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1Hospital Clínico Universitario de Valladolid, Nephrology, Valladolid, Spain, 2Hospital Río Carrión, Nephrology, Palencia, Spain and 3Complejo Asistencial de Zamora, Zamora, Spain

Background and Aims: Intra-abdominal hypertension (IAH) is common among post-surgical, critically ill and kidney transplant patients, and is associated with acute kidney injury and increased morbidity and mortality. We aimed to describe the medium-term effect of IAH on graft and patient survival after deceased-donor kidney transplantation.

Method: 192 consecutive patients who received a cadaveric renal allograft transplant at our hospital were included in this study. IAP was measured every 8h for at least the first 72h after surgery using the urinary bladder technique, and an average value was obtained. Patients were followed up for 24 months or until a composite outcome (defined as graft loss or recipient death) occurred. Clinical, anthropometric, and analytical data was extracted from our hospital’s database. Statistical analysis was performed using IBM SPSS Statistics 22. The study was approved by the local ethics committee.

Results: 192 patients were included. Relevant clinical and anthropometric data are summarized in Table 1. Patients with grades II or III IAH were more frequently male, had longer dialysis vintage, received more frequently hemodialysis as renal replacement therapy and suffered delayed graft function, graft loss or death more repeatedly. In Kaplan-Meier analysis, grade II IAH or higher were associated with lower composite-outcome free survival (Log-Rank: 8.053; p = 0.018) (Figure 1).

Conclusion: Grade II-III IAH appear to be a risk factor for graft loss or recipient death in our sample of deceased donor kidney transplant recipients. Monitoring of intra-abdominal hypertension could provide useful information to identify patients at higher risk of post-transplant complications.

Table 1: Clinical and anthropometric data.

<table>
<thead>
<tr>
<th></th>
<th>No IAH</th>
<th>Grade 1 IAH</th>
<th>Grade 2-3 IAH</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>99</td>
<td>79</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>62 (49-70)</td>
<td>62 (53-69)</td>
<td>63 (54-68)</td>
<td>0.715</td>
</tr>
<tr>
<td>Male sex, n(%)</td>
<td>51 (51.5)</td>
<td>60 (75.9)</td>
<td>13 (92.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis vintage, months</td>
<td>15 (8-28)</td>
<td>19 (10-37)</td>
<td>31 (28-47)</td>
<td>0.047</td>
</tr>
<tr>
<td>PD as RRT, n(%)</td>
<td>45 (45.5)</td>
<td>28 (35.4)</td>
<td>2 (14.3)</td>
<td>0.057</td>
</tr>
<tr>
<td>First KT, n(%)</td>
<td>86 (86.9)</td>
<td>66 (83.5)</td>
<td>11 (78.6)</td>
<td>0.654</td>
</tr>
<tr>
<td>HTN, n(%)</td>
<td>87 (87.9)</td>
<td>72 (91.1)</td>
<td>12 (85.7)</td>
<td>0.721</td>
</tr>
<tr>
<td>Diabetes, n(%)</td>
<td>16 (16.2)</td>
<td>13 (16.5)</td>
<td>4 (28.6)</td>
<td>0.502</td>
</tr>
<tr>
<td>Age (D), years</td>
<td>59 (48-71)</td>
<td>63 (54-72)</td>
<td>68 (50-75)</td>
<td>0.127</td>
</tr>
<tr>
<td>Male sex (D), n(%)</td>
<td>61 (61.6)</td>
<td>53 (67.1)</td>
<td>12 (85.7)</td>
<td>0.194</td>
</tr>
<tr>
<td>KDPI, %</td>
<td>73 (52-96)</td>
<td>79 (59-96)</td>
<td>93 (52-97)</td>
<td>0.236</td>
</tr>
<tr>
<td>CIT, hours</td>
<td>17 (14-19)</td>
<td>17 (14-19)</td>
<td>16 (14-18)</td>
<td>0.896</td>
</tr>
<tr>
<td>HLA mismatches, number</td>
<td>5 (4-5)</td>
<td>4 (3-5)</td>
<td>4 (3-5)</td>
<td>0.029</td>
</tr>
<tr>
<td>DGF, n(%)</td>
<td>18 (18.6)</td>
<td>22 (28.6)</td>
<td>10 (71.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>72h mean IAP, mmHg</td>
<td>10±1.4</td>
<td>13.7±1.1</td>
<td>18.2±1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Composite outcome, n (%)</td>
<td>12 (12.1)</td>
<td>9 (11.4)</td>
<td>5 (35.7)</td>
<td>0.042</td>
</tr>
</tbody>
</table>

CIT, cold ischemia time; D, donor; DGF, delayed graft function; HLA, human leukocyte antigen; HTN, hypertension; IAH, intra-abdominal hypertension; KDPI, kidney donor profile index; KT, kidney transplantation, PD, peritoneal dialysis; RRT, renal replacement therapy.

Figure 1: Composite outcome-free survival according to IAH grade.
#6019

DEVELOPMENT, APPLICATION, AND VALIDATION OF A HISTOLOGICAL CLASSIFICATION AUTOMATION SYSTEM FOR KIDNEY ALLOGRAFT PRECISION DIAGNOSTICS

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2Néphrologie-Immunologie Clinique, Hôpital Bretonneau, CHU Tours, Tours, France, Tours, France, 3KTD-Innov Consortium, France and 4Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA, Los Angeles, United States of America

Background and Aims: The Banff histological classification is the gold standard for allograft rejection diagnostics but has become considerably more complex over the past three decades, leading to misclassifications. We aimed to develop an automated rejection classification system and demonstrate its ability to improve rejection diagnoses.

Method: We built a consortium consisting of pathologists, physicians, and developers to translate all Banff classification rules until the latest version published in 2019 into an algorithm, further embedded in an application which automatically assigns diagnoses. We then tested the Banff Automation System's ability to reclassify rejection diagnoses on 4,409 kidney transplant biopsies from 3,054 adult and pediatric patients, from multicenter cohorts and clinical trials, totaling 20 transplant referral centers in Europe and North America. The impact of diagnostic reclassifications on graft survival was evaluated.

Results: We devised a system that generates automatic reports with diagnoses and a decision tree. In the adult kidney transplant biopsies, the Banff Automation System reclassified 83 of 279 (29.75%) antibody-mediated rejection (AMR) cases and 57 of 105 (54.29%) T-cell mediated rejection (TCMR) cases, while 237 of 3,239 (7.32%) biopsies with non-rejection-related diagnoses were reclassified as rejection. The rejection reclassification rates were 8 of 26 (30.77%) and 12 of 39 (30.77%) for AMR and TCMR, respectively, in the pediatric cohort. Finally, we found that the non-rejection diagnoses according to the pathologists which were reclassified as rejections by the Banff Automation System had similar outcomes as those of confirmed rejection cases.

Conclusion: We built the first comprehensive Banff Automation System and confirmed its ability to reclassify rejection diagnoses. This decision support system might help for training and standardizing diagnoses in routine care and clinical trials.

Figure 1: Sankey diagram representing diagnostic reclassifications by the Banff Automation System.

#4089

SARCOPENIA AS A PREDICTOR OF MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: Sarcopenia is a risk factor for adverse outcomes in older adults and dialysis patients, but this has yet to be confirmed in kidney transplant recipients. This study aimed to investigate the association of sarcopenia with all-cause mortality in kidney transplant recipients.

Method: In this single-center prospective cohort study, kidney transplant recipients were evaluated at baseline muscle mass, muscle strength, and physical performance using a hand dynamometer, 10-m walk test, and bioelectrical impedance analysis, respectively. Sarcopenia was defined according to the Asia Working Group for Sarcopenia 2019 criteria. Propensity score matching was used to reduce bias between the sarcopenia and non-sarcopenia groups, adjusted for three potential confounding variables including age, sex, and body mass index. After a 5-year follow-up, patient survival was assessed by the Kaplan-Meier method and Cox proportional hazards model in the matched cohort.

Results: Out of 212 patients (median age, 54 years; median transplant vintage, 79 months) enrolled in this study, patients who had sarcopenia at baseline was 33 (16%). After 1:1 propensity score matching, a matched cohort with 62 patients was generated. In the matched cohort, the overall incidence density rates of mortality were 48.8 and 6.75 per 1000 person-years in the sarcopenia and non-sarcopenia groups, respectively. The survival curves estimated using the Kaplan-Meier method indicated that the sarcopenia group was significantly lower cumulative survival than the non-sarcopenia group (log-rank test, p = 0.025). Moreover, the sarcopenia group had a significantly higher mortality risk than the non-sarcopenia group (hazard ratio = 7.59, 95% confidence interval = 1.93–61.7).

Conclusion: Sarcopenia was a significant predictor of mortality in kidney transplant recipients.
#5950
MAJOR HLA ALLELE AND HAPLOTYPE FREQUENCIES IN THE MALTESE KIDNEY TRANSPLANT REGISTRY
Sarah Micallef and Jesmar Buttigieg
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**Background and Aims:** The human leukocyte antigens (HLA) are the most diverse and polymorphic genes in the human genome and matching them is of vital importance for maximising the survival of kidney transplants. The Maltese archipelago consists of three inhabited islands in the Mediterranean Sea, with a total population of just over half a million people. HLA polymorphisms in Malta have never been described. The aim of this study was to investigate allelic frequencies and determine the most common haplotypes for major HLA Class I and Class II groups in the Maltese kidney transplant registry. This will hopefully facilitate organ sharing with other European countries and improve the HLA matching for kidney transplant recipients.

**Method:** All patients of Maltese ethnicity on the national kidney transplant list between 2018 and 2022 were analysed retrospectively. HLA typing is routinely performed at medium to high resolution using polymerase chain reaction sequence specific oligonucleotide probes and Luminex technology at the HLA-A, HLA-B, HLA-C, HLA-DR, HLA-DQ and HLA-DP loci. Allele and haplotype frequencies were calculated by direct counting and simple percentages.

**Results:** A total of 191 patient samples were analysed yielding the following allele types: 16 HLA-A, 31 HLA-B, 17 HLA-C, 15 HLA-DRB1, 6 HLA-DP, 7 HLA-DQ, 5 HLA-DRB3, one HLA-DRB4 and one HLA DRB5. The most frequent allele groups for the HLA-A locus were HLA-A*02 (30.9%), HLA-A*24 (12.0%) and HLA-A*01 (11.8%) whilst for the HLA-B locus these were HLA-B*35 (16.2%), HLA-B*18 (11.5%) and HLA-B*51 (7.1%). The most prevalent allele groups for the HLA-DRB1 locus were HLA-DRB1*11 (24.1%), HLA-DRB1*04 (13.1%) and HLA-DRB1*07 (11.3%). The commonest allele group for each of HLA-C, HLA-DP and HLA-DR loci were HLA-C*07 (23.6%), HLA-DP4 (5.8%), HLA-DQ7 (31.2%) respectively. The five most frequently encountered haplotypes were HLA-A*02-B*13-DRB1*07 (2.1%), HLA-A*02-B*35-DRB1*04 (1.6%), HLA-A*02-B*18-DRB1*10 (1.3%), HLA-A*02-B*35-DRB1*11 (1.3%), HLA-A*24-B*35-DRB1*11 (1.3%).

**Conclusion:** This study provides the first data on the Major HLA allele and haplotype frequencies in Maltese kidney transplant candidates. Such data may be crucial in setting up international kidney exchange programmes.

#3961
A COMPARATIVE ANALYSIS OF EMOTIONAL RECOGNITION AND DIFFERENTIATION TWO YEARS FOLLOWING KIDNEY TRANSPLANTATION VERSUS HEMODIALYSIS.
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**Background and Aims:** Cognitive impairment is common in patients with End Stage Kidney Disease. There are conflicting reports regarding the degree and interval of improvement of cognitive functions with the different modalities of renal replacement therapy. Most of the published reports relied on screening tests not covering the emotional aspects of cognition. Also, the timings of assessment are different being at most during the first year of establishing the modality.

**Method:** Ninety age, gender, and educational level-matched participants were enrolled in the study. The participants were divided into three equal groups, thirty kidney transplant (KT) patients, thirty hemodialysis patients (HD) for more than two years, and thirty control non-diseased participants. The participants included were below 60 years of age and with no previous history of a neurological defect. All patients were subjected to three Computerized Neurocognitive Battery tests (Age differentiation test, emotional recognition, and differentiation). All the tests were judged for accuracy and the time consumed to answer.

**Results:** The median value of transplant duration was 59 months (24-168), and 66 months (27-180) of HD duration. Both groups were comparable in age, gender, educational level, socioeconomic, and marital status. KT patients were comparable to controls at all parameters of testing. KT patients’ answers were significant of higher accuracy than HD patients (P = 0.04 for age differentiation and emotion recognition, and 0.005 for emotion differentiation). KT and HD had comparable response times. Total correct responses of emotional differentiation tests were negatively correlated with KT duration (rho = −0.348, P = 0.02), and (rho = −0.345, P = 0.01) for HD duration. The cumulative steroid dose was not correlated with any of the tested parameters in the KT group.

**Conclusion:** KT offers a much better emotional and social cognitive improvement, an effect that is expected to positively impact the quality of life and involvement in society.
#6880
PREDICTION OF GRAFT SURVIVAL PRIOR TO ACCEPTING AN OFFER FOR LIVING DONOR KIDNEY TRANSPLANT: AN ARTIFICIAL INTELLIGENCE APPROACH
Hatem Kaies Ibrahim Elsayed Ali1,2, Bernard Burke1, Mahmoud Mohamed1, David Briggs3 and Nithya Krishnan1,2
1University Hospitals of Coventry and Warwickshire, renal department, UHCW, Coventry, United Kingdom, 2Coventry University, Research Centre for Sport, Exercise and Life Sciences, United Kingdom, 3University of Mississippi, United States of America and 4NHSBT, United Kingdom

Background and Aims: The current available models for evaluation of outcomes of living donor kidney transplant before accepting an offer are poorly developed, reported, validated and have small sample sizes. We aim to use Artificial Intelligence to build a model that can accurately predict death censored graft survival for living donor kidney transplant prior to accepting an offer.

Method: All living kidney transplant patients who were registered in the UNOS database between 1/1/2007 and 1/6/2021, maintained on TAC/MMF immunotherapy were included in our analysis. We excluded patients with age<18 years old and ABO incompatible transplant. We divided the data randomly into training and testing dataset with ratio 80:20. We performed recursive feature elimination to select the important ones for prediction. Features were selected based on their Gini impurity scores. We performed Artificial Neural Network analysis (ANN). We evaluated the model using Harrell Concordance-time-dependent score (for discrimination), and Integrated Brier score (for calibration). We also assessed dynamic AUC for model performance.

Results: 154,110 living donor kidney transplant patients were included in our study. Harrell C-Statistic scores were 0.50 at 5 years post-transplant, 0.68 at 10 years post-transplant and 0.68 at 10 years post-transplant, indicating very high discrimination power. Integrated Brier Score was 0.08, indicating very high calibration score for our model. Dynamic AUC scores were 0.71 at 5 years post-transplant and 0.68 at 10- and 13-years post-transplant, indicating adequate performance for our model. The key players in our model were recipient age (variable importance = 0.26), donor age (variable importance = 0.17), donor ethnicity (variable importance = 0.90), followed by dialysis vintage pre-transplantation.

Conclusion: The ANN model had high discrimination, calibration, and performance indices for predicting death censored graft survival prior to transplant. It can aid the clinical decision for management of the transplant patients. We are currently developing a user-friendly web application that can be used to apply the ANN model for prediction. Our model can help ranking potential living kidney donors based on graft outcomes. Therefore, our model can help improve current outcomes of kidney paired exchange schemes.

Method: We used data from stable KTRs ≥1 year after transplantation who participated in the TransplantLines Food and Nutrition Cohort study. Plasma cadmium and iron status parameters, i.e., ferritin, iron, and transferrin saturation (TSAT), were measured at baseline. ID was defined as TSAT<20% and ferritin <300 μg/L. Linear regression analyses were applied to study the association between iron status parameters and cadmium levels. Multivariable Cox regression analyses were used to investigate the association of plasma cadmium levels with all-cause mortality, adjusted for age, sex, BMI, smoking status, history of cardiovascular disease, glucose, HbA1c, systolic blood pressure, eGFR, cholesterol, and ID at baseline. In sensitivity analyses, we repeated these analyses using an alternative definition of ID, TSAT<20% and ferritin<100 μg/L (IDalt).

Results: We included 670 KTRs (age 53±13 years, 58% males, median 5.4 (IQR, 1.9-11.7) years after transplantation). KTRs with ID (30% of all KTRs, median plasma cadmium level 63 (IQR. 48-76) ng/L) had higher cadmium levels than KTRs without ID (median 56 (IQR. 42-75) ng/L, P = 0.01, Figure 1). ID was not associated with plasma cadmium after adjustment for age, sex, and smoking status. However, within the ID group, TSAT (β = -0.016, P = 0.01) and serum iron (β = -0.023, P = 0.01) were inversely associated with log-transformed cadmium levels, independently of age, sex, and smoking status. Sensitivity analysis yielded similar results: KTRs with ID (23% of all KTRs) had higher cadmium levels than KTRs without ID (median 61 (IQR. 49-76) ng/L vs median 57 (IQR. 42-75) ng/L, P = 0.03). Furthermore, in Cox regression analysis, KTRs in the highest tertile of plasma cadmium levels (70 ng/L to 330 ng/L) had an increased risk of mortality (hazard ratio 2.80, 95%CI 1.47-5.36, P = 0.01) compared to KTRs in the lowest cadmium tertile (19 ng/L to 48 ng/L) during a median follow-up of 4.9 (IQR. 3.5-5.5) years. No significant interaction by iron status was observed for the association between plasma cadmium and mortality.

Conclusion: KTRs with ID had higher cadmium levels than KTRs without ID, and higher plasma cadmium levels were independently associated with a higher mortality risk. The association of cadmium with mortality was not different between individuals with and without ID at baseline. Further investigations should determine whether ID correction prevents cadmium accumulation in KTRs.

#2981
IRON DEFICIENCY AND CADMIUM LEVELS IN KIDNEY TRANSPLANT RECIPIENTS
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Background and Aims: A higher plasma level of cadmium, a nephrotoxic divalent heavy metal, has been associated with an increased risk of graft failure in kidney transplant recipients (KTRs). The drivers of cadmium toxicity in KTRs are incompletely understood. We hypothesize that iron deficiency (ID) increases cadmium absorption and accumulation by upregulation of divalent metal transporters. Here, we first investigated whether ID is associated with higher plasma cadmium levels. As increased cadmium levels have previously been associated with cancer, cardiovascular disease, and diabetes in other populations, we also examined whether plasma cadmium levels are associated with all-cause mortality in KTRs.

Method: We used data from stable KTRs ≥1 year after transplantation who participated in the TransplantLines Food and Nutrition Cohort study. Plasma cadmium and iron status parameters, i.e., ferritin, iron, and transferrin saturation (TSAT), were measured at baseline. ID was defined as TSAT<20% and ferritin <300 μg/L. Linear regression analyses were applied to study the association between iron status parameters and cadmium levels. Multivariable Cox regression analyses were used to investigate the association of plasma cadmium levels with all-cause mortality, adjusted for age, sex, BMI, smoking status, history of cardiovascular disease, glucose, HbA1c, systolic blood pressure, eGFR, cholesterol, and ID at baseline. In sensitivity analyses, we repeated these analyses using an alternative definition of ID, TSAT<20% and ferritin<100 μg/L (IDalt).

Results: We included 670 KTRs (age 53±13 years, 58% males, median 5.4 (IQR, 1.9-11.7) years after transplantation). KTRs with ID (30% of all KTRs, median plasma cadmium level 63 (IQR. 48-76) ng/L) had higher cadmium levels than KTRs without ID (median 56 (IQR. 42-75) ng/L, P = 0.01, Figure 1). ID was not associated with plasma cadmium after adjustment for age, sex, and smoking status. However, within the ID group, TSAT (β = -0.016, P = 0.01) and serum iron (β = -0.023, P = 0.01) were inversely associated with log-transformed cadmium levels, independently of age, sex, and smoking status. Sensitivity analysis yielded similar results: KTRs with ID (23% of all KTRs) had higher cadmium levels than KTRs without ID (median 61 (IQR. 49-76) ng/L vs median 57 (IQR. 42-75) ng/L, P = 0.03). Furthermore, in Cox regression analysis, KTRs in the highest tertile of plasma cadmium levels (70 ng/L to 330 ng/L) had an increased risk of mortality (hazard ratio 2.80, 95%CI 1.47-5.36, P = 0.01) compared to KTRs in the lowest cadmium tertile (19 ng/L to 48 ng/L) during a median follow-up of 4.9 (IQR. 3.5-5.5) years. No significant interaction by iron status was observed for the association between plasma cadmium and mortality.

Conclusion: KTRs with ID had higher cadmium levels than KTRs without ID, and higher plasma cadmium levels were independently associated with a higher mortality risk. The association of cadmium with mortality was not different between individuals with and without ID at baseline. Further investigations should determine whether ID correction prevents cadmium accumulation in KTRs.
#4680

PATIENT OUTCOMES AND DYNAMICS OF THE AUSTRALIAN KIDNEY TRANSPLANT WAITLIST: SUSPENSIONS, RETURNING TO WAITLIST, TRANSPLANTATION AND DEATHS

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Background and Aims: People on the kidney waitlist are less informed about potential temporary or permanent suspensions. Disparities may exist among those who are suspended and who return to the waitlist. In Australia, average wait times vary by state/territory and blood group, but overall is X years. We aimed to describe and evaluate factors associated with waitlist transitions and subsequent outcomes after entering the waitlist for deceased donor kidney transplant.

Method: We included all incident patients waitlisted for their first transplant from deceased donors in Australia during 2006-2019. We described all clinical transitions after entering the kidney waitlist including: active on waitlist; suspended; kidney transplant; graft failure; and death. We predicted the restricted mean survival time from waitlist entry until first transplant with 5 year time horizon and summarized the annual percentages in each clinical state until 5 years. We used flexible parametric multi-state survival models to evaluate factors associated with transitions after entering the waitlist until first transplant, reporting the hazard ratio (HR) for each transition. We used Cox proportional hazards models to evaluate factors associated with death while waiting and first transplant, reporting HR for these outcomes.

Results: Of 8,466 people who entered the kidney waitlist, 6,741 people received their first transplant (6,163 deceased donor; 506 living donor; 99 paired kidney exchange donors), 381 people died while waiting (31 active on waitlist; 350 suspended) and 1,344 were still waiting for a transplant (844 active on waitlist; 500 suspended). Nearly two-thirds (63%) were not suspended while waiting, but 2,111 (25%) were suspended once and 1,016 (12%) were suspended ≥2 times. Of those suspended, 47% spent a total of <6 months off-waitlist. Predicted mean time from waitlist entry to transplant increased with number of suspensions, from 1.9 years (95% CI:1.8-1.9 years) in patients not suspended to 3.0 years (95% CI:2.8-3.2 years) in patients suspended once or more. For the entire cohort, the 1-year probability of transplant was 41%(95%CI:40-42%),

Figure 1: Annual percentages after entering kidney waitlist in Australia, 2006-2019.
Factors associated with transitions and clinical endpoints after entering kidney waitlist.

At 5 years, the active on waitlist was 42% (95% CI: 41-43%), suspended was 11% (95% CI: 10-12%) and death was 1.4% (95% CI: 1.2-1.7%) (Fig. 1). At 5 years, this increased to 63% (95% CI: 62-64%) transplanted, 5% (95% CI:4-5%) active on waitlist, 10% (95% CI:9-11%) suspended and 13% (95% CI:12-14%) died. Several patient factors were associated being suspended and returning to the waitlist, as well as with receiving transplant and death while waiting (Fig. 2). Having been suspended from the waitlist, increased the likelihood of further suspensions by 4.2 times (95% CI: 3.8-4.6; p < 0.001) and returning to the waitlist by 50% (95% CI: 36-65%; p < 0.001) but decreased the likelihood of receiving a transplant by 29% (95% CI: 62-82%; p < 0.001). Being previously suspended once reduced the risk of death while waiting by 31% (HR: 0.69, 95% CI: 0.52-0.91; p < 0.01), likely a paradox of being well enough to return to the waitlist at least once. Socio-demographic factors were modifiers of returning to the waitlist after suspension. Males of Australian or New Zealand ethnicity (non-Indigenous) were 13% (95% CI: 4-23%) more likely to return to the waitlist compared to females of the same ethnicity (p = 0.01). However, males of Aboriginal, Torres Strait Islander, Māori or Pacific Islander ethnicity had the same likelihood of returning to the waitlist as their female counterparts (p = 0.08).

Conclusion: The dynamics of the transplant waiting list were not straightforward. About one-third of patients were suspended at least once and wait 1 year longer for a transplant compared with those not suspended. Our findings will provide evidence to support more informed discussions about the patient journey from waitlist to transplantation, and aid in shared decision making.

MAGNETIC RESONANCE RADIOMIC ANALYSIS FOR THE PREDICTION OF GRAFT FAILURE IN PATIENTS WITH KIDNEY TRANSPLANTATION
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Background and Aims: Prediction of future graft failure with non-invasive investigations is a relevant objective for transplant clinicians. We previously demonstrated a promising discrimination capacity for interstitial fibrosis / tubular atrophy (IFTA) >50% in kidney biopsy of a machine learning (ML) based magnetic resonance imaging (MRI) radiomic algorithm. Aim of the present study is to evaluate accuracy of MRI radiomic-based ML algorithms in predicting future graft failure.

Method: Single-center retrospective observational cohort study on a previously characterized cohort of kidney transplant recipients who underwent graft biopsy and graft MRI imaging within 6 months from biopsy, both on clinical indication, at the “Azienda Ospedaliero-Universitaria di Modena”, Italy, from 1/1/2012 to 1/3/2021. The primary outcome was to identify the best combination of MRI radiomic features for the prediction of graft failure during follow-up. Segmentation of renal parenchyma, cortex and medulla on MRI sequences was performed using the 3DSlicer software. Radiomic features were then extracted using an in-house software based on pyradiomics applying Wavelet and Gaussian filters. LASSO algorithm was employed to select correlated features with outcome and summarize them in a radiomic signature. Using radiomic signature alone and then merged with meaningful clinical data we trained ML-algorithms using 70% of cases for training/validation, with a 10-fold internal cross-validation, and 30% for model testing. Model performance was assessed using AUC with a 95% confidence interval (CI).

Results: Seventy coupled tests (63 patients) were included and randomly subdivided into a training/validation cohort (n = 50) and a test cohort (n = 20). Median follow-up was 24.73 months (interquartile range 13.64-46.57). Radiomic model had an AUC of 0.88 (95% CI 0.70-0.97) in training and 0.57 (95% CI 0.23-0.86) in test cohort. Radiomic-clinical mixed model had an AUC of 0.90 (95% CI 0.73-0.98) in training and 0.66 (95% CI 0.33-0.88) in test cohort.

Conclusion: We produced an MRI radiomic-based ML algorithm with good prediction ability for future graft failure in patients with kidney transplant. Given the limited number of enrolled patients, validation in larger (and ideally prospective) cohorts is required to confirm our findings. Comparison of radiomic-based ML with histological parameters (i.e., IFTA) for the prediction of graft failure in our cohort is currently under assessment.
MEASURING CLINICAL JUDGEMENT IN PROSPECTIVE KIDNEY TRANSPLANT RECIPIENTS: A FEASIBILITY STUDY
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Background and Aims: Exercising clinical judgement is becoming more challenging in the context of ageing populations, increasing prevalence of multimorbidity and frailty, and insufficient evidence regarding how best to manage increasing complexity in clinical practice. Measures of clinical judgement are surprisingly absent from health information systems despite their clear importance and the potential costs of poor decisions. Suitability for kidney transplantation is a high-stake clinical judgement, requiring consideration of complex biopsychosocial patient and organ-utilisation factors. This study aimed to test if it is feasible to assess clinical judgement quantitatively from routine clinical documentation in kidney transplant recipients.

Method: Participants were identified from a regional register of patients on haemodialysis, who underwent deceased donor kidney transplantation (KTR) and had at least 1 year of follow-up. We identified 15 KTR who had poor outcomes, defined as more than 6 hospital admissions or death within one-year of transplantation. Fifteen KTR controls were matched using the United Kingdom Renal Recipient Index (UKRRI: a composite score of age, dialysis requirement at listing, wait time on dialysis and diabetes status). Six blinded raters (two nephrologists, two transplant surgeons and two kidney transplant coordinators) scored clinical letters written at the time of transplant assessment across four domains (Clinician Belief of Appropriateness [CBA] for perceived suitability, perceived benefit, predicted short-term harm, predicted long-term harm: from 1 = worst, to 5 = best). The total CBA score was calculated as the mean score across the 4 domains. CBA scores were compared between raters using the intra-class correlation coefficient (ICC: for two-way agreement). Logistic regression models tested odds of poor outcome by CBA scores across 4 domains.

Results: Practicing clinicians were eager to participate, suggesting this type of research will be worthwhile and feasible. Among 30 KTR, the median total CBA transplant suitability score was 3 (IQR 3-4, range 1-5). Overall agreement was moderate (ICC for the total CBA score: 0.63, 95% CI 0.51-0.74; p < 0.001), but with substantial variation in CBA scores across the domains and between raters (Figure 1). In 3 of the 4 domains (perceived suitability: OR 0.91, 95% CI 0.48-1.73; predicted short-term: OR 0.70, 95% CI 0.33-1.51; and predicted long-term harms: OR 0.82, 95% CI 0.35-1.91), CBA scores adjusted for UKRRI were associated with poor outcome after transplantation in the expected direction. For predicted benefit, the point estimate was not in the expected direction; individuals with greater predicted benefits were more likely to have poor outcomes (OR 1.46, 95% CI 0.28-7.47). Unsurprisingly, given the small numbers in this pilot and the substantial influence of the donor organ on outcomes in kidney transplantation, all the confidence intervals were wide and crossed the null, indicating considerable uncertainty.

Conclusion: In patients undergoing assessment for kidney transplantation, measuring clinical judgement retrospectively is feasible, though subject to variability across domains and between raters. We did not identify any clear associations between retrospective assessment of CBA and outcome after kidney transplantation in this small pilot. In future work, we will develop and validate measures of clinical judgement, collect these measures prospectively, and examine the relationship of measured clinical judgement with health outcomes.

E3 - TREATMENT & CLINICAL TRIALS

USE OF GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONISTS IN KIDNEY TRANSPLANT PATIENTS: A MULTI-CENTER STUDY
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Background and Aims: Diabetes mellitus (DM) is a frequent complication in kidney transplant (KT) patients, leading to a higher cardiovascular mortality and graft loss. The use of therapies such as Glucagon-like peptide-1 receptor agonist (GLP-1RA) could have benefits in KT, although the experience reported so far is limited. The aim of our study is to describe the effectiveness and safety of GLP-1RA in KT patients.

Method: Retrospective cohort study of KT with DM who started GLP-1RA in three Spanish hospitals (Puerta del Mar University Hospital, Jerez de la Frontera University Hospital and Puerto Real University Hospital) from February 2016 to July 2022. All patients had a minimum follow-up of 6 months after starting the treatment. Clinical and demographic variables were analyzed. We collected GLP-1RA type and dose. Glomerular filtration rate (eGFR), proteinuria, and weight were collected at the start of treatment and after 6 and 12 months. We analyze glycemic control, blood pressure and lipid profile. Acute rejections (AR), de novo donor-specific antibodies (DSA) and adverse effects were documented. Parametric and non-parametric tests were performed according to the normality of the sample.

Figure 1: Alluvial plot of differences in transplant suitability (CBA) scores across 4 domains, stratified by rater type.
Results: In this period, 102 KT with DM were treated with GLP-IRA from 19/02/2016 to 22/07/2022. At the time of the prescription mean body mass index was 35.8 kg/m² and the mean weight was 95 kg. Forty-two (44%) had developed post-transplant diabetes mellitus (PTDM). The mean age was 62 years and 56% were men. Mean baseline estimated glomerular filtration rate (eGFR) was 47.2 ml min/1.73 m² and the time post-KT was 47 months. The GLP-IRA mostly prescribed was semaglutide (66.7%). Fifty-five (55%) patients reached the maximum recommended dose of the drug. The maintenance immunosuppressive therapy used was steroids (94.7%), tacrolimus (97.4%), mycophenolate (94.7%) and everolimus (2.6%). Eighty-four KT recipients had a minimum follow-up of 6 months and sixty-four were followed for 12 months. We observed stability in eGFR and a reduction in proteinuria (−19.1 mg/g at 6 months, p = .000 and −3.6 Kg at 12 months, p = .000). Furthermore, Hba1c decreased (−1.2 mmol/L at 6 months, p = .000 and −1.5 mmol/L at 12 months, p = .000). Notably, insulin dose was also reduced (−2.2 UI/day at 6 months, p = .048) but the number of patients with sodium-glucose cotransporter 2 inhibitors increased at 12 months (p = 0.031). Finally, we observed a reduction in total cholesterol (−11.5 mg/dL at 6 months, p = .001 and −15.6 mg/dL at 12 months p = .000) and LDL-c (−9.2 mg/dL at 6 months, p = .002 and −16.8 mg/dL at 12 months, p = .000) during the follow-up. However, patients receiving statins and steroids and the dose remained unchanged. Fifteen patients (14.7%) suffered from side effects, mainly nausea and vomiting, and ten patients (9.8%) discontinued the treatment for this reason. No changes in the mycophenolate formulation were made. One patient discontinued the treatment due to the diagnosis of pancreatic cancer 8 months after starting the drug. We did not find differences in the levels in the dose of tacrolimus. Neither AR episodes nor de novo DSAs development were notified.

Conclusion: This is the first multicenter study that reports the effectiveness and safety of GLP-IRA in KT patients. Our results support that it can be an option for the management of DM in these patients. Its use is safe and it does not seem to alter tacrolimus trough levels, to induce AR episodes or de novo DSAs development.

#4233

FIXED LOW DOSE VERSUS CONCENTRATION-CONTROLLED INITIAL TACROLIMUS DOISING: RESULTS FROM A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL (SLOW&LOW STUDY)

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Background and Aims: Optimal initial tacrolimus dosing and early exposure of tacrolimus after renal transplantation is not well studied. Based on the assumption that current treatment protocols using frequent trough level determinations in the first week after transplantation may cause overexposure related nephrotoxic side effects and frequent monitoring is costly and not supported by basic pharmacokinetic principles, we had the hypothesis that early low and fixed tacrolimus dosing may be a safe and practical alternative.

Method: In this open-label, multicenter, randomized controlled, non-inferiority study, we randomly assigned 432 renal allograft recipients to receive basiliximab induction, mycophenolate and steroids and either standard prolonged-release tacrolimus (trough levels: 7-9 ng/ml; arm A), or an initial 7-day fixed 5 mg/day dose of prolonged-release tacrolimus followed by lower tacrolimus predose levels (trough levels: 5-7 ng/ml; arm B, see Figure 1). The primary end point was the combined incidence rate of biopsy-proven acute rejections (BPAR; including borderline), graft failure or death at 6 months with a non-inferiority margin of 12.5 %.

Results: The combined primary endpoint in arm B was non-inferior compared to the control arm A (22.1 % versus 20.2 %; difference 95 % CI: 1.9- 8.8 %). While overall rate of BPAR including borderlines were similar (B: 17.4 % vs. A: 16.1 % (see Figure 2), a statistically significant difference of higher than borderline graded BPAR was noted (B: 11.6 % vs. A: 5.2 %; p = 0.027). Safety parameters such as delayed graft function, kidney function, infections or post-transplantation diabetes mellitus did not differ.

Conclusion: An initial fixed low prolonged release tacrolimus dose of 5 mg/day followed by lower tacrolimus exposure is non-inferior compared to standard tacrolimus therapy and equally efficient and safe within 6 months after renal transplantation. (EudraCT-Nr: 2013-001770-19).

Figure 1: Study design.

Depicted is the study design over time. Treatment arm A allograft recipients received basiliximab induction, standard prolonged-release low dose tacrolimus (Low dose Tac), mycophenolate (MMF) and steroids. Treatment arm B allograft recipients received basiliximab induction, initial 7-day fixed 5 mg/day dose of prolonged-release tacrolimus followed by lower tacrolimus predose levels (S&L dose Tac), mycophenolate (MMF) and steroids.
Figure 2: Kaplan Meier Plot of Primary Endpoint & Graft Survival. Shown are a Kaplan-Meier plots for the primary endpoint in panel a) and for graft survival in panel b). Recipients of allografts in treatment arm A received basiliximab induction, standard prolonged-release low dose tacrolimus (low-dose Tac with target trough levels of 7–9 ng/ml), mycophenolate (MMF), and steroids. Allograft recipients in treatment arm B received basiliximab, an initial 7-day fixed dose of 5 mg/day of prolonged-release tacrolimus followed by lower tacrolimus predose levels (S&D dose Tac, with target trough levels of 5–7 ng/ml), mycophenolate (MMF), and steroids. BPAR = biopsy-proven acute rejection.

### #5264
CELLULAR IMMUNITY ACTIVATION IN RENAL TRANSPLANT RECIPIENTS AFTER VACCINATION WITH TOZINAMERAN: DIFFERENCES BETWEEN RESPONDERS AND NON-RESPONDERS

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**Background and Aims:** Response to vaccination is a complex procedure, resulting from the activation of various immune cell subpopulations and comprising stimulation of several interactive pathways. The aim of our study was to assess the differences in cellular subpopulations between Renal Transplant Recipients (RTRs) classified as “responders” and “non-responders” to vaccination with Tozinamern, against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**Method:** Our research was a prospective observational study. Our sample consisted of 39 RTRs on stable immunosuppression, who had a negative history of coronavirus disease 2019 (COVID-19) infection and had not achieved to develop protective humoral immunity (i.e., had a negative test for neutralizing antibodies - Nab-) three weeks after the 2nd vaccine dose (T0). We attempted to evaluate immune response 48 hours before (T1) and 3 weeks after (T2) the 3rd Tozinamern dose. Patients with serum Nab levels > 0.3AU/ml (calculated with chemiluminescence immunoassay -CLIA-) and/or enzyme-linked immunosorbent spot (ELISpot) values > 30SFC/5 × 10^5 PBMCs were regarded as responders. Results were subsequently correlated with variations in cellular subpopulation compositions. Concentrations of CD4+, activated CD4+, CD8+, activated CD8+ T-cells, CD3+CD16+CD56+ (Natural Killer T -NKT-), activated NKT cells, CD3-CD16+CD56+ (Natural Killer -NK-) cells, CD19+, CD19+CD27- (Naïve), CD19+IgD+CD27- (Marginal), CD19+CD24+CD38high (Transitional), CD19+CD27+CD38high (Plasmablasts) and CD19+CD27+ (Memory) B cells were measured with flow cytometry at T1 and T2. We compared the results in the “responders” and the “non-responders” group.

**Results:** The number of responders significantly increased from T1 [17/39, responders: Nab(-) - ELISpot(-)] to T2 [34/39, responders: Nab and/or ELISpot (+)] (x^2 = 16.2, p < 0.0001). No difference was observed between responders and non-responders regarding age, renal function, calcineurin inhibitor levels, dialysis and transplantation vintage. Compared to non-responders, responders presented increased concentrations of: activated CD8+ [23.6(29) vs 9.49(10)/μL, p: 0.044], activated NKT [4.77(8) vs 1.73(2)/μL, p: 0.001] and NK cells [198.91(161) vs 104.45(103)/μL, p: 0.024] at T1 and elevated levels of: total B cells [87.63(101) vs 26.86(42)/μL, p: 0.01], marginal [10.03(13) vs 1.12(5.9)/μL, p: 0.045] and memory B-cells [28.31(42) vs 10.57(19)/μL, p: 0.048] at T2 (see table). A significant increase of activated NKT and naïve B-cells from T1 to T2 [310(174) vs 241(200)/μL, p = 0.02 and 56.2(67) vs 1082(834)/μL, p<0.0001, respectively] was evident only in the responders’ group.

**Conclusion:** As anticipated, responders to vaccination against SARS-CoV-2 exhibited a quite different immune cell activation profile compared to non-responders. Besides, the 3rd Tozinamern vaccine dose substantially improved RTRs’ immune response and induced a prominent stimulation of the B lymphocyte compartment.

### Table 1: Differences in cellular subpopulation concentrations between responders and non-responders at T1 and T2.

<table>
<thead>
<tr>
<th>Cellular Subpopulation</th>
<th>Time Spot</th>
<th>Responders</th>
<th>Non-Responders</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activated CD8+</td>
<td>T1</td>
<td>23.6(29)</td>
<td>9.49(10)</td>
<td>0.04</td>
</tr>
<tr>
<td>Activated NKT cells</td>
<td>T1</td>
<td>4.77(8)</td>
<td>1.73(2)</td>
<td>0.001</td>
</tr>
<tr>
<td>NK cells</td>
<td>T1</td>
<td>198.91(161)</td>
<td>104.45(103)</td>
<td>0.02</td>
</tr>
<tr>
<td>B-cells</td>
<td>T2</td>
<td>87.63(101)</td>
<td>26.86(42)</td>
<td>0.01</td>
</tr>
<tr>
<td>Marginal B-cells</td>
<td>T2</td>
<td>10.03(13)</td>
<td>1.12(5.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>Memory B-cells</td>
<td>T2</td>
<td>28.31(42)</td>
<td>10.57(19)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

#3075
EFFECT OF KIDNEY TRANSPLANTATION ON CARDIORESPIRATORY FUNCTION ASSESSED WITH CARDIOPULMONARY EXERCISE TESTING: A SYSTEMATIC REVIEW AND META-ANALYSIS

Eva Pella1, Maria Eleni Alexandrou1, Afroditou Boutou2, Marieta Theodorakopoulou1, Erasmia Sampanis1, Konstantina Dipla1, Andreas Zafeiridis3 and Pantelis Sarafidis3

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**Background and Aims:** Patients with kidney failure often present with reduced functional cardiovascular reserve and exercise intolerance. Kidney transplantation is the optimal treatment for patients with end-stage kidney
disease as it is associated with longer survival and improved quality of life compared to hemodialysis or peritoneal dialysis.

Method: This is a systematic review and meta-analysis of studies using cardiopulmonary-exercise-testing (CPET) to examine the cardiorespiratory fitness of patients with kidney failure before and after kidney transplantation. The primary outcome was differences in pre- and post-transplantation values of peak oxygen uptake (VO2peak). Literature search involved PubMed, Web of Science and Scopus databases, manual search of article references and grey literature. Quality assessment was undertaken with Newcastle-Ottawa-Scale.

Results: From 379 literature records initially retrieved, 6 studies (207 participants) were included in final meta-analysis. A marginal, but not significant, improvement was observed in oxygen consumption during peak exercise compared to pre-transplantation values (standardised mean difference [SMD]: 0.32, 95%CI −0.02; 0.67). Oxygen consumption at anaerobic threshold (VO2AT) was significantly improved after kidney transplantation (weighted MD [WMD]: 3.97; 24.86). In subgroup analysis, consistent results were shown between changes were observed in maximum heart rate (WMD: 10.45 bpm, 95%CI −3.97; 24.86). In subgroup analysis, consistent results were shown between changes in VO2peak was observed when pooling data reported from follow-up assessments undertaken at least 3 months post-transplantation surgery (SMD: 0.17, 95%CI −0.03; 0.38), but not earlier (WMD: −0.03 ml/kg/min, 95%CI −4.28; 4.23).

Conclusion: Several major indices of cardiorespiratory fitness tend to improve after kidney transplantation compared to pre-transplantation values. This finding may represent another modifiable factor contributing to better survival rates of kidney transplant recipients compared to patients undergoing dialysis.

Method: Potential KTRs were screened for eligibility and approached by their consultant nephrologist, and if interested, further study details were explained by a researcher. Those who consented to take part were randomised (1:1) to either a 12-week structured home-based exercise programme (INT, n = 22) or 12-week usual care control (CTR, n = 23). Figure 1 outlines the home-based exercise programme. The a priori thresholds for specific feasibility and acceptability criteria are as follows: recruitment success of 20% of eligible participants (≥2 participants per month), adherence (an average of three exercise sessions per week) and attrition (<30%).

Results: Ninety patients were approached and 45 (50%) recruited across 22 months of recruitment (currently ongoing). Participant characteristics were: 50±14 years (INT 48±13; CTR 52±13), 21 male (INT 8; CTR 13), eGFR 59±19 ml/min/1.73 m2 (INT 62±19; CTR 58±19), 31 White British (WB) and 14 Asian ethnicity (INT 14 WB, 8 Asian; CTR 17 WB, 6 Asian). Two participants withdrew from the intervention group (1 due to COVID-19 infection, 1 due to recurrent urine infections unrelated to the trial) and one from the control group (lost to follow-up; 7.3% attrition). There were no adverse events reported related to the exercise intervention or trial procedures. Intervention participants (n = 16 completed) recorded an average of 4.5±1.4 exercise sessions per week (aerobic 2.9±1.2; strength 1.6±0.4).

Conclusion: Results suggest engagement with the home-based exercise programme in KTRs is excellent. The study is comfortably exceeding a priori thresholds relating to recruitment, retention and completion suggesting patients are interested in the study and the programme of exercise despite the current evidence showing physical activity levels are low. The groups are well matched and there is encouraging representation of female participants and participants from a non-white background. These initial results support study continuation and further assessment and development of home-based programmes of exercise and activity for KTR.

Figure 1: Change in VO2peak values before and after kidney transplantation.

#3030
FEASIBILITY OF HOME-BASED EXERCISE IN KIDNEY TRANSPLANT RECIPIENTS: PARTICIPANT CHARACTERISTICS AND INITIAL RESULTS FROM THE ECSERT TRIAL
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Background and Aims: Kidney transplant recipients (KTR) are prone to high rates of infection, malignancy and cardiovascular disease. Poor physical fitness and physical inactivity remain pertinent targets to improve post-transplant clinical outcomes. Only 27% of KTR are classified as physically active for health. The ECSERT pilot randomised controlled trial aims to assess the feasibility of delivering a structured, home-based exercise intervention in 50 KTR at increased cardiometabolic risk and evaluate the putative effects on cardiovascular structure and function, cardiorespiratory fitness, physical function, quality of life, metabolic and inflammatory markers. We present interim feasibility data describing engagement with the home-based programme of exercise for all patients who have completed the programme to date.
EXERCISE AND PREDIABETES AFTER RENAL TRANSPLANTATION: THE EXPRED I STUDY

Raul Morales Febles1, Domingo Marrero Miranda2, Alejandro Jiménez Sosa1, Coriolano Cruz Perera1, Laura Diaz Martin1, Natalia Negráñ Mena1, Ana González Rinne2, Alejandra Maxorata Álvarez González2, Aurelio Rodríguez Hernández2, Lourdes Pérez Tamajón3, Armando Torres4 and Esteban Porrini4

Natalia Negrán Mena3, Ana González Rinne2, Alejandra Maxorata Álvarez González2, Aurelio Rodríguez Hernández2, Lourdes Pérez Tamajón3, Armando Torres4 and Esteban Porrini4

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Background and Aims: Post-Transplant Diabetes Mellitus (PTDM) is a severe disease that may affect about 30% of renal transplant patients. PTDM beyond 12 months (late PTDM) mostly develops in subjects with prediabetes. Although exercise may have a potential role in preventing late PTDM, there is scarce evidence on the effect of exercise in renal transplantation. We designed a 12-month exploratory study to test the capacity of therapeutic exercise in reverting prediabetes to prevent the development of late-PTDM.

Method: This is a pilot study in which renal transplant patients with prediabetes were treated with exercise for 12 months. To detect prediabetes and to evaluate the reversibility, relapse, or persistence of prediabetes, the oral glucosetolerancetest(OGTT)wasperformedatbaselineandevery3months to the end of the study; Prediabetes was defined by the presence of Impaired Fasting Glucose (IFG) in 100-125 mg/dl and/or Impaired Glucose Tolerance (IGT) between 140-199 mg/dL after the OGTT. The protocol included a stepped incremental plan of aerobic and/or strength training. The frequency, intensity, and duration of aerobic exercise, as well as the addition of strength training depended on the recovery, persistence, or recurrence of prediabetes.

All patients started with moderate aerobic exercise (brisk walking), 30 min/day and 5 times per week and, based on that, changes in prescription were considered every 3 months. Additionally, we evaluated: (a) an active plan for promoting adherence to exercise (telephone calls, digital technology, and visits) and (b) improvements in metabolic risk factors: obesity, dyslipidaemia, and blood pressure. Since prediabetes may spontaneously revert to normal glucose metabolism in 25-30% [1], we assume that in 60 cases, the spontaneous reversibility could be of 30% (n = 18) and the reversibility induced by exercise may account for another 30% (n = 18), so the total reversibility will be 60%. Considering an expected drop out of 20%, the number of cases necessary to include was 72 patients.

Results: The study was early interrupted due to efficacy after the evaluation of 27 patients that reach 12 months of follow-up. Mean age was 54.2 ± 9.6 and 67% were men. Half of the patients were obese and most had overweight. At baseline IGT or IFG alone were found, respectively, in 13 (48%) and 5 (19%) patients, and the combination of both in 9 (33%). All patients were on prednisone and tacrolimus with the addition of mycophenolate on 20 subjects and 7 on everolimus. Of the group, 16 (60%) reverted to normal glucose levels (fasting and 120 min after an OGTT): this was two time higher than the 30% reversibility rate shown in a previous publication [1], p <0.05, assuming a potency of 85%. In parallel, 11 (40%) subjects had prediabetes (9) or developed PTDM (2). No significant changes were found in weight during follow-up in all groups whereas triglycerides diminished in patients on whom prediabetes reverted (154 mg/dL ± 61 to 96 ± 27; p = 0.016). At the end of follow up, adherence to exercise was good (≥70%) in 13 patients (~50%), moderate (40-70%) in 9 (~30%) and bad (<40%) in 5 (~20%). Finally, all patients with good adherence reverted to normoglycaemia, 3 out of 9 (33%) cases with moderate adhered to normal glucose metabolism and no cases with bad adherence improved on follow-up. No relevant injuries attributed to exercise were observed during the study.

Conclusion: Therapeutic exercise is safe and effective to improve glucose metabolism in renal transplant patients with prediabetes. Adherence is a crucial aspect to consider in the planification of exercise treatment.

REFERENCE


SAFETY AND EFFICACY OF EVOLOCUMAB AMONG KIDNEY TRANSPLANT PATIENTS AT HIGH CARDIOVASCULAR RISK

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1OTC Kuwait, Nephrology, Ff, Kuwait and 2Mansoura university, Nephrology, Mansoura, Egypt

Background and Aims: Proprotein convertase subtilisin/Kexin type A (PCSK-9) inhibitors have not been evaluated among kidney transplant recipients (KTR) despite its favorable cardiovascular profile. We aimed to evaluate the safety and efficacy of evolocumab in reducing lipids and cardiovascular events among risky KTR.

Method: One hundred ninety-five KTR - who were followed up in Hamed Al-Essa organ transplant center with high cardiovascular risk score (>20)- were enrolled in this prospective randomized controlled study between June 2017 and June 2018. Patients who received statin and evolocumab (140 mg/ 2 weeks, group1, n = 97) while those maintained on statin alone comprised group 2(n = 98). After 24 months, they were followed up clinically and by laboratory investigations.

Results: The two groups had comparable demographics. Before enrollment in the study, we observed a higher prevalence of NODAT in group 2 and...
Relativereceptor binding domain (RBD) fading over time in different patient groups and dependent on vaccine type. Each thin line corresponds the anti-Spike S1 protein RBD antibody values (Euroimmun) of a study participant from T2 (eight weeks after vaccination start) via T3 (six months after vaccination start) to T4 (nine months after vaccination). The thicker lines represent median responses by vaccine type (green-BNT162b2mRNA and red 1273-mRNA) in each group. Only patients with successful de novo seroconversion at T2 (IgA or IgG antibody positivity against the SARS-CoV-2 S1 protein) after 2x mRNA vaccination and without SARS-CoV-2 nucleocapsid (NCP) antibodies were considered. Reference range of the test used, < 20 = negative, ≥ 20 - < 35 = grey range (the latter two categories synonymous with below positivity level), ≥ 35 = positive test result. The vertical axis is depicted on log_{10} scale with corresponding unit % inhibition. MP = Medical Personnel, DP = Dialysis Patients, KTR = Kidney Transplant Recipients, AP = Lipidapheresis Patient.
Table 1: Receptor binding domain (RBD) antibody decrease rate over time for all patients (n = 762).

<table>
<thead>
<tr>
<th>Overall decrease rate over time (per month)</th>
<th>95% confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical personnel</strong></td>
<td></td>
</tr>
<tr>
<td>10.089%</td>
<td>[6.928 - 13.143]</td>
</tr>
<tr>
<td>22.662%</td>
<td>[20.593 - 23.904]</td>
</tr>
<tr>
<td>16.630%</td>
<td>[13.341 - 19.794]</td>
</tr>
<tr>
<td>16.197%</td>
<td>[11.463 - 20.678]</td>
</tr>
<tr>
<td><strong>Dialysis patients</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Kidney transplant recipients</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Apheresis patients</strong></td>
<td></td>
</tr>
</tbody>
</table>

The table summarizes the average group rates of antibody decline that were estimated using a hierarchical linear mixed-effects model with the natural logarithm of raw RBD-antibody values as response, fixed effects for group, time, and their interaction, random intercept (per subject) and random slope (over time). The 95% confidence intervals were obtained from posthoc pairwise analysis.

participants including healthy MP (125), DP (595), KTR (111), and apheresis patients (49-AP) with positive seroconversion (de novo IgA or IgG antibody positivity by ELISA) after eight weeks.

**Results:** Nine months after first vaccination, receptor binding domain (RBD) antibodies were still positive in 90 % of MP, 86 % of AP, but only 55 %/48 % of DP/KTR, respectively. Seroconversion remained positive in 100 % of AP and 99·2 % of MP, but 86 %/81 % of DP/KTR, respectively. Compared to MP, DP but not KTR or AP were at risk for a strong RBD decline, while KTR kept lowest RBD values over time (see Fig. 1 and Table 1). By multivariate analysis, BNT162b2mRNA versus 1273-mRNA vaccine type was an independent risk factor for a strong decline of RBD antibodies. Within the DP group, only time on dialysis was another (inverse) risk factor for the DP group. Compared to humoral immunity, T-cell immunity decline was less prominent.

**Conclusion:** While seroconverted KTR reach lowest RBD values over time, DP are at specific risk for a strong decline of RBD antibodies after successful SARS-CoV-2mRNA vaccination, which also depends on the vaccine type being used. Therefore, booster vaccinations for DP should be considered earlier compared to normal population.

**REFERENCE**


**#5687**

SARS-COV-2 PREEXPOSURE PROTECTS FROM IMMUNITY-FADING AFTER MRNA VACCINATION IN KIDNEY TRANSPLANT RECIPIENTS, DIALYSIS PATIENTS, AND MEDICAL PERSONNEL.

Julian Stumpf1, Leona Anders2, Torsten Siepmann3, Jörg Schrödel2, Claudia Karger2, Tom H. Lindner2, Robert Faulhaber-Walter2, Annett Pietzonka4, Torsten Langer5, Katja Escher6, Kirsten Anding-Rost12, Harald Seidel13, Jan Hüther14, Frank Pistrosch15, Heike Martin16, Jens Scheve17, Thomas Stehr18, Frank Meistring19, Alexander Paliege1, Daniel Schneider2, Ingolf Bast3, Anne Steglich4, Florian Gembardt1, Friederike Kessel1, Hannah Krüger1, Patrick Arndt1, Jan Sradnick1, Kerstin Frank20, Sarah Skrzypczyk21, Moritz Anft22, Anna Klimova23, René Mauser24, Ingo Röder20, Torsten Tom24,25, Nina Babel21,26 and Christian Hugo1,2

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**Result:** Risk of strong antibody decline in dialysis or renal transplant patients compared to general population. We hypothesized that COVID-19 preexposure influences not only vaccination dependent development of immunity but also protects from immunity fading depending on vaccine type and patient group.

**Method:** We evaluated two and nine months follow up data in our observational DIA-Vacc study exploring specific cellular (interferon-γ release assay = IGRA) or/and humoral immune responses after 2x SARS-CoV-2mRNA vaccination in 2615 participants including medical personnel (300 MP), dialysis patients (1831 DP), kidney transplant recipients (484 KTR). Study participants were separated into COVID-19 preexposure positive (n = 405) versus negative (n = 2210) groups, where symptomatic or asymptomatic COVID-19 disease before start of vaccination was confirmed by clinical symptoms, PCR positivity and/or Spike S1/core antiSARS-CoV-2 antibodies.

**Results:** Two months (T2) after first vaccination, seroconversion and T-cell immunity success rates for MP and DP were excellent (86-100%) and independent on COVID-preexposure. In KTR, vaccination-related seroconversion rate on T2 almost doubled with COVID-preexposure (84% versus 45% without), a result consistent with all different antibody measurements (IgA, IgG, or receptor binding domain-RBD). Nine months after first vaccination in COVID-19 negative study patients, the percentage of patients with RBD-antibody fading results >50% remained low in MP (18%), high in DP (53%) and intermediate in KTR (39%). In contrast, in all patient groups with COVID-19 preexposure RBD-antibody fading reactions >50% within nine months after vaccination were almost vanished (4% in MP, 8% in DP and 0% in KTR). COVID-19 preexposure in DP also reduced T-cell immunity fading as measured by IGRA, where only 9% of patients showed a >50% titer decrease compared to 34% of DP without any COVID-19 preexposure. Similar results were also seen regarding vaccination dependent regulation of antiSARS-CoV-2 IgG antibodies dependent on COVID-19 preexposure. These results are also reflected by increased mean antibody titers for IgG- and RBD-antibodies nine months after vaccination in all COVID-19 preexposed compared to non-exposed groups. In addition, the degree of antibody fading after vaccination was not just dependent on COVID-19 preexposure status but also on mRNA vaccine type being used. In MP with COVID-preexposure, 22% of BNT162b2mRNA but 0% of 1273-mRNA vaccinated study participants experienced RBD-antibody fading >50% within nine months after vaccination start. This significant difference was even greater in COVID-19 preexposed DP, in whom vaccination with BNT162b2mRNA caused RBD-antibody fading >50% in 3% compared to 6% of 1273-mRNA treated DP. The patient number in the KTR group was not high enough for a vaccine type comparison. This vaccine dependent influence of antibody fading is consistent with our results in patient groups without COVID-19 preexposure.

**Conclusion:** Long term immunity time course is markedly modified via COVID-preexposure in a mRNA vaccine dependent manner. Hybrid immunity after COVID-19 preexposure almost completely lacks immunity fading between two and nine months especially in 1273-mRNA vaccinated MP, DP, or KTR. Immune monitoring shows great individual variability dependent on personal patient history and should be especially used for pandemic patient management in vulnerable groups such as DP and KTR.
#5841
UTILITY AND ACCEPTANCE OF TELENEPHROLOGY AMONG KIDNEY TRANSPLANT RECIPIENTS IN A PUBLIC SECTOR HOSPITAL IN A DEVELOPING COUNTRY
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All India Institute of Medical Sciences (AIIMS), Nephrology, New Delhi, India

Background and Aims: The importance of telemedicine in delivering renal health care has come to light during the COVID-19 pandemic. Moreover, specialist care to transplant recipients is often limited to urban areas especially in developing countries. Telenephrology offsets this discrepancy enabling quality care to patients in rural areas. But, apart from availability, the true success and future of telenephrology depends primarily on patients’ acceptance. This study was performed to assess the feasibility, patient attitude and acceptance of telenephrology services among renal transplant recipients at our institute, a public sector hospital in a developing country.

Methods: This single-centre cross-sectional study included renal transplant recipients who availed our telenephrology services for at least 3 months. A total of 100 transplant recipients were selected by stratified random sampling from the list of attendees of telenephrology consultation and included in this study.

The study questionnaire was administered in local language by the telephone interview method.

Results: The mean age of our study cohort was 32.83 ± 9.96 years (16–55yrs) and 92% were males. The median number of teleconsultations availed by the patients was 3 (1–20). The questionnaire was answered by the patient himself/herself in 89% cases, spouse in 7% and children in 3% cases.

Only thirty-nine (39%) patients were graduates or post graduates. Over one-half (51%) of the patients belonged to the lower-middle socioeconomic class as per the modified Kuppuswamy classification. Prior to initiation of the telenephrology service, the median distance travelled to attend our outpatient department (OPD) was 304.5 Km (6 – 1673 km). Most (87%) of our patients used public transport to attend OPD. Three-fourths (79%) of the patients were accompanied by family members for their OPD visit. Attendees incurred productivity loss due to missed work days in 57% of the cases. The median cost of each OPD visit was 3000 (40-15000) INR. Almost all the transplant recipients felt that Telenephrology service was a right approach during the COVID-19 pandemic. 98% of the patients said that they were confident discussing their complaints over phone while 99% of our patients were comfortable sharing reports over phone. Majority (>90%) of the patients gave a satisfaction score of 4 (out of 5) for their telenephrology experience.

The most important benefit (79%) of telenephrology as perceived by the transplant recipients was financial benefit of avoiding travel and workdays saved. Regarding the problems faced during teleconsultation, 22% patients responded that they wish to see the doctor in person to feel satisfied; 5% had problems with availability of investigations locally. Only a small fraction (2%) of patients had difficulty in explaining symptoms over a tele-consult. A significant (97%) patients felt that Telenephrology services should continue in combination with physical OPD services.

Conclusion: Telenephrology is feasible and acceptable to kidney transplant recipients irrespective of literacy status across all socio-economic classes. In developing countries like India, telenephrology has immense potential to provide quality nephrology care.

#3185
INFLUENCE OF COMBINED CYP 3A4/5 AND POR*28 GENETIC POLYMORPHISMS ON TACROLIMUS AND CYCLOSPORINE DOSE REQUIREMENTS IN INCIDENT RENAL TRANSPLANT PATIENTS
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Background and Aims: Calcineurin inhibitors, cyclosporine and tacrolimus have a narrow therapeutic index and have wide intra- and inter individual pharmacokinetic variability. They are metabolized mainly by CYP3A4 and CYP3A5. The P450 oxidoreductase POR*28 variant allele has been associated with changes in cytochrome P450 enzymatic activity that can affect the therapeutic level of both medications. The aim of this study is to investigate the allelic frequency of the POR*28 in Egyptian renal transplant patients and to evaluate the effect of the presence of CYP3A4*3/CYP3A5*1 genotypes on calcineurin inhibitos dose requirements and adjustments.

Method: A prospective clinical trial that included 130 renal transplant patients placed on either tacrolimus or cyclosporine. Patients were genotyped for either of the following POR*28 genotypes CYP3A4*22, CYP3A4*22 and CYP3A4*22, CYP3A5*1.

Figure: POR*28, CYP3A4*22, and CYP3A5*1. The relation between the present genetic polymorphisms and tacrolimus and cyclosporine doses and dose adjustments were studied at days 14, 30, and 90 post-transplantation.

Results: The POR*28 allele frequency in the studied population was 29.61%. The tacrolimus dose-adjusted trough concentration ratio (C0/D) was highly statistically significant in the fast metabolizers group (CYP3A4*1/POR*28 carriers) than in the slow metabolizers group (CYP3A4*3/*3/CYP3A5*22 carriers) throughout the study (14, 30, and 90 days) (p value 0.001, <0.001, and 0.003, respectively). There was no significant effect for this gene combination on cyclosporine (C0/D).

Conclusion: Combining the CYP3A4*1, POR*28, and CYP3A4*22 genotypes can be of significant value in early tacrolimus dose requirements and adjustments. However, it does not have any influence on cyclosporine dose requirements.

#3805
A FEASIBILITY STUDY EXPLORING THE IMPACT OF A LOW ADVANCED GLYCAZATION END-PRODUCT DIET ON SKIN AUTOFLUORESCENCE IN KIDNEY TRANSPLANT RECIPIENTS
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Background and Aims: Advanced glycation end-products (AGEs) are uremic toxins that result from hyperglycaemia and oxidative stress. AGEs are also formed in food, especially during cooking using dry-heat methods. AGE accumulation can be measured by skin autofluorescence (SAF) and increased SAF is a strong predictor of death and graft loss in kidney transplant recipients (KTR). Previous studies have reported that reduction of dietary AGE intake is associated with a decrease in circulating AGE levels, suggesting that a low-AGE diet may slow the progression of atherosclerotic disease in KTR.

Methods: Ten KTR were included in this feasibility study and were randomly assigned to a low-AGE diet (LAE) or a usual-care diet (UC). A high-AGE diet was used as a comparator. Dietary AGE intake was assessed using dietary AGE questionnaires and food frequency questionnaires. A validated AGE food database was used to estimate AGE intake. AFP, NGAL, SAF, and urinary AGEs were assessed at baseline and at 3 months.

Results: Participants in the LAE group had a decrease in AGE intake of 91% compared to the UC group. A decrease in circulating AGE levels was reported in both groups, with a significantly greater decrease in the LAE group. SAF was significantly reduced in the LAE group compared to the UC group. No significant changes in urinary AGE levels were observed.

Conclusion: A low-AGE diet is feasible in KTR and leads to reduced AGE intake and improved skin autofluorescence.
Table 1: Changes in skin autofluorescence, dietary AGE intake and nutritional markers from baseline to 6 months in intervention and control groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention group (n = 13)</th>
<th>Control group (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Month 6</td>
</tr>
<tr>
<td>Skin autofluorescence (AU)</td>
<td>3.1 ± 0.8</td>
<td>2.8 ± 0.5</td>
</tr>
<tr>
<td>Dietary AGE intake (kU/day)</td>
<td>18047 (IQR 13103 to 25941)</td>
<td>5515 (4206 to 8631)</td>
</tr>
<tr>
<td>Energy intake (kcal/kg/day)</td>
<td>25.8 ± 5.5</td>
<td>21.5 ± 6.3</td>
</tr>
<tr>
<td>Fat intake (g/day)</td>
<td>70.5 ± 20.8</td>
<td>55.2 ± 20.0</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>37.4 ± 4.0</td>
<td>36.5 ± 3.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>88.7 ± 17.8</td>
<td>87.4 ± 18.5</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.6 ± 3.7</td>
<td>28.2 ± 4.1</td>
</tr>
<tr>
<td>Handgrip strength (kg)</td>
<td>33.8 ± 11.6</td>
<td>34.3 ± 10.1</td>
</tr>
</tbody>
</table>

P-values in columns are for comparison of baseline and 6-month data within each group.

diet may also be associated with a decrease in SAF. The aim of this feasibility study was to investigate whether a low-AGE diet leads to a reduction in SAF levels in KTR.

Methods: Thirty-eight KTR were randomly allocated to a usual diet (control group, n = 19) or a low-AGE diet (intervention group, n = 19) and then followed-up for 6 months. The intervention group was provided with detailed written advice and counselling on how to choose foods low in AGES, and to use high-water content cooking methods (stewing, steaming, boiling, poaching), instead of dry-heat methods (frying, grilling, roasting). The goal was to reduce dietary AGE intake to < 8000 kilounits/day (kU/day). SAF was measured at baseline, 3 and 6 months. Rate of change in SAF (i.e., SAF trend) was calculated using the SLOPE function in Microsoft Excel. Dietary AGE intake, biochemistry and nutritional assessments were performed at baseline and 6 months.

Results: Mean age of the whole cohort was 56±11 years. Mean SAF was high at 2.9±0.7 arbitrary units (AU) compared to the reference value of 2.1±0.4 AU. Transplant vintage ranged from 42 to 126 (median 88) months. The majority of the participants were male (71%) and of white ethnicity (84%). Prevalence of diabetes, hypertension and heart disease was 16%, 53%, and 10%, respectively. Median dietary AGE intake was high at 18558 (15164 to 25341) kU/day. SAF was measured at baseline, 3 and 6 months. Rate of change in SAF (i.e., SAF trend) was calculated using the SLOPE function in Microsoft Excel. Dietary AGE intake, biochemistry and nutritional assessments were performed at baseline and 6 months.

P-values in columns are for comparison of baseline and 6-month data within each group.

significant in the intervention group but remained high in the control group. Body weight, energy, and fat intake decreased in the intervention group but there was no significant change in SAF (Table 1). The mean SAF trend observed was a decrease of 0.45±1.19 and 0.22±0.75 AU/year in the intervention and control groups, respectively (p = 0.7 for comparison between groups).

Conclusion: In this feasibility study, we observed a high drop-out rate in the intervention group, which may explain our finding that reduction in dietary AGE intake did not seem to have any significant effect in decreasing SAF levels. This highlights the need for a larger trial to determine the effect of dietary AGE restriction on SAF levels in KTR.

#3895 COMPARABLE RENO-CARDIAC PROTECTIVE EFFECTS OF SGLT2 INHIBITION VERSUS DPP-4 INHIBITION IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS: KUWAIT EXPERIENCE

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Abstracts i941
Background and Aims: Diabetes is the most common cause of chronic kidney disease (CKD) globally. The renal and cardiovascular benefits of the new anti-diabetic agents are not assessed comprehensively. We aimed to evaluate the short term renal and cardio-protective effects of Sodium-Glucose Cotransporter-2 Inhibition (SGLT2i) Vs. Dipeptidyl peptidase-4 Inhibition (DPP4i) among diabetic kidney transplant recipients.

Method: In this observational trial, 222 diabetic kidney transplant recipients (NODAT or type 2 diabetes) were enrolled and were categorized into two groups. Group 1 (n = 99) received SGLT2i while group 2 (n = 123) received DPP4i as an add on anti-diabetic medications. All patients in the two groups were followed up for 12 months.

Results: Most patients in the two groups (182) were men (59.6 vs. 61.7%, p = 0.73) in their middle age (58.3±11.9 vs. 54.4±12.9, p = 0.016) years respectively. The two groups were matched regarding their demographics especially the type of donor, type of immunosuppression (induction or maintenance), number of cardiovascular events before enrollment in the study and the number of patients who were maintained on ACEi or ARB(p>0.05). The minority of patients were smokers (12.9 vs.8.7%), and chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% in the two groups, respectively. Most of the enrolled patients (72.8 vs. 76.8%) underwent hemodialysis pre-transplant. During follow up period, patients in both groups were comparable regarding mean blood pressure, body weight, HbA1C, 24-hour urine protein, and graft function (represented by the mean serum creatinine at different time intervals and compared to base line values(p>0.05). However, the mean HbA1C was significantly higher in group 1 during the whole follow up period of the study (p<0.05) but it did not drop significantly compared to baseline values (p>0.05). We did not report any macroangiopathic events (cerebral stroke, acute myocardial infection, or peripheral arterial disease) in the two groups during the study.

Conclusion: Both GLT2i and DPP-4 I are comparable regarding renal and cardio-vascular protection among diabetic kidney transplant recipients.

#5045

CARDIORESPIRATORY FITNESS IN KIDNEY TRANSPLANT RECIPIENTS: A CASE-CONTROL STUDY AND INITIAL REVIEW OF THE EFFECTS OF A HOME-BASED EXERCISE PROGRAMME

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Background and Aims: Kidney transplant recipients (KTRs) have an increased burden of cardiovascular disease (CVD) due to clustering of traditional and non-traditional risk factors. Poor cardiorespiratory fitness (CRF) is linked to higher levels of morbidity and mortality. Cardiorespiratory fitness is a significant predictor of 7-year risk of mortality, with each 1 ml/kg/min increase in VO2 associated with a 1% decrease in risk of mortality.[1] Although KTRs have higher CRF than patients with kidney failure, performance compared to the general population has not been quantified. Neither has the link between CRF and physical function. We assessed differences in CRF between KTRs and healthy volunteers in a case-control study. We then explored relationships between CRF and physical function and possible effects of a 12-week structured home-based exercise programme in KTRs.

Method: Case-control: 20 KTRs (10 male; age 61.2 ±8.1 years; body mass 84.1 ±19.9 kg) and 20 healthy volunteers (10 male; age 61.9 ±7.7 years; body mass 76.7 ±18.1 kg) completed a continuous ramp cardiopulmonary exercise test (CPET) to volitional exhaustion on a cycle ergometer. CPET variables were compared between groups using independent samples t-tests. Thirteen KTRs (6 male; age 47.8 ±15.9 years; eGFR 64.6 ±19.1/ml/min/1.73 m2), to date, have completed a 12-week structured, combined aerobic and resistance, home-based exercise programme as part of a pilot randomised controlled trial.[2] Bivariate correlations were used to explore the association between cardiorespiratory fitness and physical function measures (sit-to-stand 60 [STS60], timed up and go [TUG], gait speed [GS] and handgrip strength [HGS]). Paired samples t-tests were used to compare pre- and post-intervention variables.

Results: Case-control: Cardiorespiratory fitness (VO2 peak) was lower in KTRs (18.4±5.2 ml/kg/min) than in healthy volunteers (24.3 ±5.9 ml/kg/min), a difference of 5.9 ml/kg/min (95% CI, 2.4-9.5), t(38) = 3.35, p <.001. Peak heart rate achieved was higher in healthy volunteers than in KTRs (154 v 136 bpm; p = .009). Maximum power achieved was higher in healthy volunteers but did not reach significance (147 v 116 W; p = .052). There was a positive correlation between STS60 and VO2 peak (r = .652, p = .016) and between GS and VO2 peak (r = .583, p = .037). There was a negative correlation between TUG and VO2 peak (r = -.664, p = .013) and no association between HGS and VO2 peak. There was an increase in VO2 peak after the 12-week exercise programme (19.4±4.5 ml/kg/min to 20.4±4.5 ml/kg/min, p = .018). Maximum power achieved did not change post-intervention (118 v 121 W; p = .423). STS60 was the only physical function test to improve post-intervention (24 v 27; p = .010).

Conclusion: Cardiorespiratory fitness in KTRs is significantly impaired compared to healthy control subjects. In KTRs, aerobic fitness assessed with VO2 peak correlated with field tests assessing physical function. Initial findings suggest that CRF may improve following a structured, home-based programme of exercise, but these data need confirming in larger studies and will be assessed in the final analysis of this pilot randomised trial.

REFERENCES
LOW DOSE THYMoglobulin-BASILIXIMAB INDUCTION PROTOCOL ON INCIDENCE OF ACUTE REJECTION AND POSTTRANSPLANT NEOPLASIA: AN OBSERVATIONAL RETROSPECTIVE STUDY

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Background and Aims: Induction therapy plays a key role in the prevention of 1-year acute rejection in kidney transplantation. Several studies suggest that depleting drugs, including thymoglobulin (ATG), are superior to anti-CD25 antibodies in reducing the incidence of acute rejection. However, large retrospective investigations demonstrate a close and significant association between the use of depleting agents and the development of post-transplant neoplasia, in particular post-transplant lymphoproliferative disease. Thus, in the attempt to improve the risk/benefit profile of antibody therapy, we implemented an induction protocol based on low-dose ATG and anti-CD25 blocker basiliximab (Bas). The aim of the present study was to evaluate the efficacy and safety of this approach compared to standard dose ATG alone and basiliximab alone.

Method: This is an observational, retrospective, single center study including 957 patients receiving a single kidney transplant the Gemelli kidney transplant center from January 2000 to February 2022. The primary efficacy outcome was biopsy proven acute rejection and the primary safety outcome was the development of post-transplant neoplasia. Patients in the ATG group received a cumulative dose of 7mg/kg in the first week after transplantation; patients in the Bas group were administered the anti-CD25 antibody at a dose of 20 mg before surgery and 20 mg 4 days after transplantation. Finally, patients in the ATG-Bas group received ATG at a cumulative concentration of 3mg/kg over the first 6 days after transplantation and Bas at a dose of 20 mg before surgery and 20 mg 4 days after transplantation.

Results: In our study population we evaluated 154 patients in the standard ATG group, 492 patients in the low ATG-Bas group and 311 patients in the Bas group. No statistical difference for age, mismatches, donor type and donor age, pre-transplant PRA was observed among groups. Use of mTOR inhibitors was more frequent in the standard ATG and low ATG-Bas groups compared to Bas group (80/154, 155/492, 76/311, respectively; p<0.001). We did not observe any significant difference in the use of other maintenance immunosuppressive drugs. Multivariate analysis (Cox model, including number of mismatches, presence of DSA at transplantation and use of mTOR inhibitors) demonstrated that only low ATG-Bas treatment (HR 0.509 95%CI 0.344-0.754, p<0.001), but not standard ATG (HR 0.819 95%CI 0.472-1.423, p=0.5, was able to reduce the risk for acute rejection compared to Bas alone. On the other hand, multivariate analysis (Cox model including acute rejection, age, use of mTOR inhibitors) demonstrated that standard ATG induction (HR 1.677 95%CI 1.035-2.717, p=0.03), but not low ATG-Bas (HR 1.324 95%CI 0.930-1.884, p=0.1), significantly increased the risk for the development of post-transplant neoplasia compared to Bas alone.

Conclusion: In this retrospective analysis we demonstrated that low ATG-Bas protocol was the most effective treatment in preventing biopsy-proven acute rejection. In addition, on the contrary of standard ATG dose protocol it did not increase the risk of post-transplant neoplasia compared to Bas alone induction therapy.

#5876

ISLET TRANSPLANTATION VERSUS INSULIN ALONE IN TYPE 1 DIABETIC KIDNEY TRANSPLANT Recipients: A FRENCH NATIONWIDE STUDY ON BEHALF OF THE TREPID GROUP

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Background and Aims: Islet transplantation is associated with a benefit on glycemic control compared to optimized insulin therapy in recent clinical trials. However, there is a lack of evidence concerning the long-term impact of islet transplantation on type 1 diabetic kidney transplant recipients’ prognosis.

Method: Every type 1 diabetic recipient transplanted with a kidney in France between 2000 and 2017 was included. Patients transplanted with pancreatic islets were compared to controls treated with insulin alone according to a matching method based on time-dependent propensity scores (using the following variables: yera of transplantation, donor age, and recipient age, serum creatinine, HBA1c, BMI, cardiovascular background) which allow to ensure patients comparability at the time of islet transplantation. The primary outcome was graft failure, defined by death or return to dialysis.

Results: Among 2393 type 1 diabetic patients transplanted with a kidney during the study period, 381 were eligible to islet transplantation, including 47 that were actually transplanted with islets. Median time for islet transplantation was 34.8 months [21.8–48.4]. Probabilities of insulino-independence and islet graft survival at 1, 5 and 10 years were respectively 63.8% [51.5-79.2], 46.3% [33.9-63.2], 38.7% [25.9-57.8] and 89.4% [81.0-98.6], 87.2% [78.2-97.3], 78.2% [66.2-92.4]. After matching, we observed a significant benefit of islet transplantation compared to insulin alone on graft failure, with a HR of 0.48 [0.20-0.94], mainly explained by a protective effect on the risk of death (HR = 0.38 [0.11-0.95]). We finally estimated the life-expectancy for a 10-year follow-up and found 9.61 years [9.02-10.00] in the islet transplantation group versus 8.85 years [7.97-9.56], with a difference of 8.88 months [-2.16-20.44]

Conclusion: We observe a significant benefit of islet transplantation on the risk of graft failure and death in type 1 diabetic kidney transplant recipients. These results provide incentives to promote islet transplantation in this population.
#3754
GLUCAGON-LIKE PEPTIDE TYPE 1 (aGLP1) AGONISTS AND THEIR INITIATION IN KIDNEY TRANSPLANTATION
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Background and Aims: Glucagon-like peptide type 1 agonists (aGLP1) is an important therapy to consider for patients with type 2 diabetes (DM2), especially those with chronic disease with glomerular filtration rates (GFR) up to 15ml/min. They stimulate the production and secretion of insulin from pancreatic β cells, delay gastric emptying, promote weight loss, reduce appetite by acting on the central nervous system, and decrease glucagon secretion from pancreatic α cells.

OUTCOMES: To assess the serum, urinary and clinical effects of treatment with aGLP1 in kidney transplant (KT) patients.

Method: This is a retrospective observational study of 32 KT patients from our center who met criteria for treatment with aGLP1. In the sample, serum and urinary data are compared, six months before, after and at the time of intervention. The management of DM was evaluated with glycosylated hemoglobin (HbA1C) and basal glycemia levels, before and after the start of treatment. Changes in cardiovascular risk are studied with the number of heart failure episodes, hospital admissions, and changes in the left ventricular ejection fraction. In addition, other parameters such as: hemoglobin (Hb), iron, ferritin, calcium, phosphorus, magnesium, potassium, uric acid, proteinuria and clinical data such as body weight were assessed.

Results: The sample presented a mean GFR by CKD EPI of 43.2ml/min. A significant drop in body weight was observed, from 93.3kg to 89.2kg (p = 0.001). Regarding the control of DM, no statistically significant results were obtained, a decrease in glycemia figures from 136 to 133 g/dl and HbA1C was obtained, with a reduction of 2.7%, p = 0.404 and p = 0.105, respectively. Regarding the progression of kidney disease, a decrease in proteinuria from 0.33g/day to 0.25 g/day was obtained, as well as a 9.5% protein/creatinine ratio, p = 0.480 and p = 0.721, respectively. Serum creatinine levels unchanged, with a mean of 1.6 mg/dl.

Conclusion: The aGLP-1 are a valuable treatment option for initiation in KT patients with DM2, having significant efficacy in weight loss. More studies with large samples are required to assess its safety in this population highly affected by DM2 and with borderline GFR.

#6674
SAFETY AND EFFICACY OF SODIUM-Glucose coT RANSPORTER 2 INHIBITORS IN KIDNEY TRANSPLANT PATIENTS WITH TYPE 2 OR POST-TRANSPLANT DIABETES
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Background and Aims: Diabetes mellitus (DM) is a complication in kidney transplant (KT) patients, leading to a higher cardiovascular mortality and graft loss. Therapies such as sodium-glucose cotransporter 2 inhibitors (SGLT2i) have been a cardio-protective and nephroprotective effect and may offer benefits in KT. The aim of our study is to describe the effectiveness and safety of SGLT2i in KT patients.

Method: Retrospective cohort study of KT with DM who started SGLT2i in three Spanish hospitals (Puerta del Mar University Hospital, Jerez de la Frontera University Hospital and Puerto Real University Hospital) between May 2018 and December 2020. Clinical and demographic variables were compared patient and kidney allograft outcomes between 31 KTRs who were temporarily switched from MPA to mTOR-I and 67 KTRs who underwent a reduction of MPA dose.

Results: A switch to mTOR-I was performed more often in case of a CMV high-risk status (50% vs. 21%, p = 0.009), CMV primary infection (68.2% vs. 22%, p < 0.001), and more severe leucopenia (median nadir of neutropenia: 0.52 G/L vs. 0.86 G/L, p = 0.023). The median duration of leucopenia was comparable between the two groups (69 vs. 80 days), 9 of 67 KTRs (13%) developed de novo donor-specific antibodies (dnDSA) under reduced MPA compared to 1 of 31 KTRs (3%) under mTOR-I (p = 0.17). Biopsy-proven rejections were comparable between the two groups (1 in each). There was a slight but insignificant improvement of eGFR under mTOR-I compared to MPA (ΔeGFR +17 vs. +7 ml/min/1.73m2, p = 0.13) and no difference in proteinuria.

Conclusion: A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leucopenia, especially in cases of CMV high-risk status and CMV primary infection. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy may have the potential to reduce the risk of allosensitization.

#4364
LEUCOPENIA AFTER KIDNEY TRANSPLANTATION: SWITCHING MYCOPHENOLEATE TO MTOR INHIBITOR APPEARS SAFE AND FEASIBLE TO REDUCE THE RISK OF ALLOSENSITIZATION
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Background and Aims: Mycophenolate acid (MPA) is a standard component of maintenance immunosuppression after kidney transplantation. MPA, however, increases the risk of leucopenia. In the past, mTOR inhibitors (mTOR-I) in combination with calcineurin inhibitors (CNI), were considered immunologically safe but showed higher mortality in the long term.

Method: We conducted a retrospective single-center study analyzing 98 kidney transplant recipients (KTRs) under standard triple maintenance immunosuppression between 2020 and 2022 who developed leucopenia. We compared patient and kidney allograft outcomes between 31 KTRs who were temporarily switched from MPA to mTOR-I and 67 KTRs who underwent a reduction of MPA dose.

Results: A switch to mTOR-I was performed more often in case of a CMV high-risk status (50% vs. 21%, p = 0.009), CMV primary infection (68.2% vs. 22%, p < 0.001), and more severe leucopenia (median nadir of neutropenia: 0.52 G/L vs. 0.86 G/L, p = 0.023). The median duration of leucopenia was comparable between the two groups (69 vs. 80 days), 9 of 67 KTRs (13%) developed de novo donor-specific antibodies (dnDSA) under reduced MPA compared to 1 of 31 KTRs (3%) under mTOR-I (p = 0.17). Biopsy-proven rejections were comparable between the two groups (1 in each). There was a slight but insignificant improvement of eGFR under mTOR-I compared to MPA (ΔeGFR +17 vs. +7 ml/min/1.73m2, p = 0.13) and no difference in proteinuria.

Conclusion: A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leucopenia, especially in cases of CMV high-risk status and CMV primary infection. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy may have the potential to reduce the risk of allosensitization.
in renal transplant recipients diagnosed with antibody-mediated rejection (AMR).

**Method:** This was a multicenter, open-label, prospective, randomized analysis. The patients were randomized by therapy type (eg, eculizumab infusions or standard of care [SOC]: plasmapheresis/intravenous immunoglobulin). The patients (ie, eculizumab arm: 7 patients, SOC arm: 4 patients) were evaluated for the continued presence of donor-specific antibodies (DSAs) and C4d (staining on biopsy), as well as histologic evidence, using repeat renal biopsy after treatment.

**Results:** The allograft biopsies revealed that eculizumab did not prevent the progression to transplant glomerulopathy. Cases of AMR were diagnosed in the early post-transplantation period in 2 patients (eculizumab arm: 1 patient, SOC arm: 1 patient) and in the late period in 9 patients. Most of the reports show that eculizumab, in combination with other therapeutic measures such as PP and/or IVIG, effectively reversed rejection. However, eculizumab alone could not treat AMR effectively. Only 2 patients in the SOC arm experienced rejection reversal, and no graft losses occurred in either group. After AMR treatment, the DSA titers generally decreased compared to titers taken at the time of AMR diagnosis. There were no serious adverse effects in the eculizumab arm.

**Conclusion:** Eculizumab alone cannot treat AMR effectively and does not prevent acute AMR from progressing to chronic AMR or transplant glomerulopathy. However, it should be considered as a potential alternative therapy because it may be associated with decreased DSA levels.

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**#4809**

**EFFECT OF RITUXIMAB DOSE ON INDUCTION THERAPY IN ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION: A NETWORK META-ANALYSIS USING RECENT DATA**

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**Background and Aims:** Rituximab is an essential inducible immunosuppressive agent for ABO-incompatible kidney transplantation (ABOi KT). However, studies on the dosage by country and transplant center are lacking. Therefore, we retrospectively investigated the effects of rituximab induction doses on patient mortality, transplant failure and adverse events.

**Method:** We included studies mentioning at least two of the eligible induction doses (200 mg, 200–500 mg, or 500 mg) of rituximab during ABOi KT and associated outcomes such as patient survival, graft failure, and bacterial and viral infections. We performed direct and indirect network meta-analyses using a Bayesian model and ranked different rituximab doses using generational mixed treatment comparisons. Publications from 1970 to 2020 were searched and analyzed using the CENTRAL, MEDLINE, EMBASE, and Science Citation Index Expanded databases. GRADE of network meta-analysis approaches specified four levels of certainty for a given outcome: high, moderate, low, and very low.

**Results:** Among 5378 patients in 25 trials, glomerular filtration rate, graft loss, antibody-mediated rejection, T-cell-mediated rejection, fungal infection, bacterial infection, and CMV infection did not differ between ABOi groups treated with different doses of rituximab. The effect on mortality was significantly higher in the rituximab 200-500 mg and rituximab 500 mg groups (odds ratio [OR] 2.4, 95% Crl: 1.5-7.4 and OR 1.8, 95% Crl 1.2-11.2). The incidence of BK virus was significantly lower in the rituximab 200 mg group than in the other groups.

**Conclusion:** In ABO-incompatible kidney transplantation, low-dose rituximab is more effective than high-dose rituximab and reduces the risk of serious infection. Due to the small sample size, further randomized controlled trials may be needed to confirm these findings.

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**#5774**

**REAL-WORLD EXPERIENCE WITH COVID-19 THERAPY IN KIDNEY TRANSPLANT PATIENTS DURING THEOMICRONVARIANT PERIOD**

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**Background and Aims:** The development of new drugs against SARS-CoV-2 has improved the prognosis of COVID-19. Large studies often exclude transplant recipients or patients with chronic kidney disease, so the experience in kidney transplant (KT) patients is very limited.

**Method:** Retrospective cohort study of KT patients with mild-moderate COVID-19 in our area who were treated from 01/01/2022 to 12/31/2022. The indication to treat was made according to age, post-KT time and comorbidities. The type of drug depended on anti-spike serology and glomerular filtration rate. We did not use nirmatrelvir/ritonavir due to the risk of interactions.

**Results:** During the period of the study, 106 KT (55 women, 51 men) with mild-moderate COVID-19 were treated, with a mean age of 61 years and a KT vintage at the time of infection of 59 [29-186] months. Of them, 37.7% were diabetics and 83% were fully vaccinated prior to the infection. The anti-spike antibody titer prior to the treatment was significantly lower in those patients who received sotrovimab compared to those who did not receive any treatment (p = 0.000).

**Conclusion:** Our results suggest that treatment of mild-moderate COVID-19 in high-risk KT patients may be effective in preventing progression to severe disease requiring admission. The highest rate of progression was observed in those treated with molnupiravir.

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**#6888**

**COMPARISON OF COMBINATION OF RITUXIMAB WITH LOW DOSE THYMoglobulin VERSUS LOW DOSE THYMoglobulin ALONE AS INDUCTION AGENT IN RENAL TRANSPLANTATION**

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**Background and Aims:** Current immunosuppressive therapies and protocols have led to significant improvements in early patient and graft survival rates following kidney transplantation. However full dose rATG induction therapy (7-10 mg/kg) has been associated with increased morbidity. There is not much...
data available on the use of single dose low dose rATG and rituximab, a
Anti CD 20 chimeric antibody in low sensitized Indian transplant recipients.
To compare the efficacy of low dose single dose rATG(1–1.2mg/kg) versus
combination of rituximab with low dose single dose rATG in ABO compatible
low sensitization renal transplant recipients.
Method: Retrospective analysis of all renal transplant recipients between
2010 and 2022 in our center who received low dose rATG(1-1.2mg/kg) or a
combination of single dose rituximab(375mg/m²) and low dose thymoglobulin
were studied. Demographic data, donor characteristics, HLA matches,
infected rejections were collected. Grant function at 3.6 and 12 months post
transplant if available was collected. Data was analysed using SPSS 16.
Results: Of 86 patients studied, 58(67.4%) received single dose of low dose
rATG(1–1.2 mg/kg/day) (Grp 1) and 28 received a combination of single low
dose rATG & Rituximab(375mg/m²)(Grp 2)(32.5%). There was no significant
difference between the Grp 1 and Grp 2 in terms of age, gender, vintage
of diaylsis, PRA status prior to transplant, no of HLA Matches, donor age and
Donor GFR. There were 9(15%) of Acute cellular rejections (ACR) in Group
1 when compared to 8 (28%) in-group 2 (p = 0.263). The number of steroid
resistant ACR were 2 (3%) in Grp 1 when compared to 3 (10%) in Grp 2 (p =
0.365). The number of ABMR were 5(8.6%) in group 1 when compared to
1(3.5%) in grp 2(p = 0.658). 15.5% had graft loss by 1 year in group 1 compared
to none in grp 2 (p = 0.322).CMV and BKV infections were seen in 1 and no pts
and 1 patient in each group respectively.Overall infection rate was 24% when
compared to 46.4% in grp 2 (p = 0.03). The mean eGFR(ml/min/1.73m²)
at the end of 3 months, 6 months and 1 year was 89.5, 69.3, 94 respectively in grp 1
when compared to 92, 69.4 & 84.3 in grp 2. Conclusion: The % of steroid resistant ACR and the number of infections were
higher in the 1 year in the Single low dose rATG+Rituximab induction when
compared to low single dose rATG alone. However ABMR was lower in the
combination grp. Further prospective RCT’s are required to establish the role
of Rituximab in ABO Compatible transplants.

#3722
CARBAPENEM-RESISTENT ENTEROBACTERIACEAE URINARY TRACT INFECTION IN RENAL TRANSPLANT RECIPIENTS: ROLE OF A NOVEL ANTIBIOTIC REGIMEN
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Lucknow, India
Background and Aims: Urinary tract infection (UTI), the most common bacterial infection among renal transplant recipients (RTRs), remains a challenge, particularly given the increased incidence of MDR organisms, including Carbapenem-resistant Enterobacteriaceae (CRE). CRE infections were associated with inferior patient and graft outcomes compared to other bacterial infections. Paradoxically, there have been no guidelines on managing CRE in RTRs besides multiple challenges, including the bacteriostatic nature, poor urinary concentration, and dose-limiting adverse effects of various antibiotics. The current study designed and assessed the outcomes of protocol-based therapy consisting of high-dose Meropenem in combination with other antibiotics followed by prolonged oral administration.
Method: This is a single-centre retrospective study conducted in the department of Nephrology and Renal transplantation, Sanjay Gandhi Post

Graduate Institute of Medical Sciences, India, between 1st August 2016 till 31st July 2022. All the RTRs aged ≥ 18 years admitted between 1st August 2016 and
31st July 2018 with symptomatic UTI and a urine culture positive for CRE were included in the study. Patients who received various antibiotics conventionally based on the treating physician’s decision from August 2016 to July 2017 were considered under the Best available treatment (BAT) group, while the Standardized Therapeutic Antibiotic Regimen (STAR) group included patients treated from August 2017 to July 2018. The treatment of the STAR group consisted of a therapeutic phase for at least six weeks (IV therapeutic phase for two weeks total or one week after the clinical recovery, whichever is later + Oral Therapeutic phase for four weeks) followed by an oral chemoprophylaxis phase for three months. Following the treatment of index UTI episodes due to CRE, follow-up both groups’ follow-up data until a minimum of four years were collected. Appropriate statistical tools were applied, and analyses were performed by SPSS software, version 25.
Results: A total of 37 patients fulfilling the inclusion criteria were included in the study, of which 13 patients were under the BAT group, and 24 were treated by the STAR-based protocol. The mean age of the study population was 37.6 ± 12.3 years, and all were males. Most patients (70.2%) had the UTI due to CRE within one-month post-transplant, and the median duration of UTI post-transplant was 6.1 days (IQR: 4.5 – 33). The primary outcome, recurrence rates of UTI at 48-month follow-up among the patients in the STAR group, was significantly lower than those in the BAT group (30.4% vs 77.8%, p = 0.011). The death-censored graft survival was also significantly better among the STAR group than the BAT group (100% vs 75%, p = 0.03) after 48 months. Graft function at 48 months was also better in the STAR group (Serum creatinine-1.4 ± 0.8 mg/dl vs 2.9 ± 2.2 mg/dl, p = 0.007). The patient survival, however, was similar among the two groups (95.8% vs 88.9%, p = 0.47).
Conclusion: Prolonged and combination antibiotic therapy followed by long-term antibiotic prophylaxis significantly reduced the recurrence of UTI due to CRE among the RTRs. Graft function and death-censored graft survival were also considerably better. Hence, the current study may pave the path for future RCTs based on combination antibiotic therapy as a solution to combat the challenge of CRE in RTRs.

#3911
DIETARY OXALIC ACID INTAKE AND PLASMA OXALIC ACID CONCENTRATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE
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Background and Aims: High oxalic acid concentration may be caused by genetic disorders, enteric diseases, but also by kidney insufficiency per se. It may result in kidney oxalic acid stones, kidney function decline, and failure. This study aimed to investigate whether dietary oxalic acid intake influences plasma oxalic acid concentration in a population undergoing kidney transplantation.
Method: Dietary oxalic acid intake was assessed using a Food Frequency Questionnaire. Based on frequency and portion size, average daily oxalic acid intake in the past year and in the last 24 hours was calculated. A blood sample for determination of plasma oxalic acid concentration was drawn on the operation ward before transplantation. For multivariable analysis seventeen recipient related variables were gathered.
Results: 418 patients were included. The median age of the participants was 62
year, 60% were male, all had an eGFR <20 ml/min/1.73 m², and 66% were on dialysis with a median dialysis vintage of 13 months. The median plasma oxalic acid concentration was 32.2 μmol/L (range 4.6-243.2). In 98.3% of patients oxalic acid concentration was above the upper limit of normal. The average oxalic acid intake was 199 mg/day (range 4-1599), while it was 138 mg/day in the last 24 hours before transplantation (range 0-3900). Multivariable linear regression analysis showed that plasma oxalic acid concentrations were significantly higher in recipients with higher average (p<0.001) and last 24 hours oxalic acid intake (p = 0.002), lower age (p<0.001), lower residual diuresis (p<0.001), higher body mass index (p<0.001), longer dialysis vintage (p = 0.032), hemodialysis (p<0.001), and peritoneal dialysis (p<0.001) versus preemptive status.
Conclusion: In pre-kidney transplant patients, plasma oxalic acid concentration is above upper normal limit in 98.3% of patients and is multifactorially determined. As all other factors are not modifiable, the only way to decrease plasma oxalic acid concentration is dietary restriction.

#4776
RENA L RESER V E ASSESSMEN T IN PATIENTS WHO UN D ERWENT DONOR N P HRECTOMY O V ER A 15-YEAR FOLLOW-UP PERIOD AND COMPARISON WITH 2 OTHER PATIENTS

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Background and Aims: Since the beginning of living related/non-related transplantation programs, the long-term risks for kidney donors after donor nephrectomy have not been given enough significance. Initially, the emphasis was only on the good health of the living donor at the time of donation, but there was no monitoring of the donor’s health and life quality post-op. In recent years, special attention has been given to kidney donors after living transplantation, as a result of a long-term follow-up and the fact that they are more susceptible to develop certain diseases, e.g. an increased risk of chronic kidney disease (CKD) and terminal renal failure (ESRD).

Method: The study was conducted as a retrospective case-control study. In our study, 243 patients, who were divided into three groups, were analysed. The case group consisted of patients who underwent donor nephrectomy (108 patients), the first control group consisted of patients who were being monitored because of simplex or parapelvic cysts with preserved renal function parameters (40 renal cyst patients with Bosniak classification ≤2) of similar age and sex, while the second control group consisted of patients who underwent a unilateral radical nephrectomy due to kidney cancer in T1bNoMo clinical stage (95 patients).

Results: The kidney donors from the case group were mainly females (60.2%) with the average age of 55.87 years at the time of transplantation. In comparison to the control groups, we observed a statistically significant difference in the radical nephrectomy group of patients, who were, on average, younger Caucasian males, with the average age of 46.84 years. The renal reserve recovery (GFR) was faster in the donor nephrectomy group (85%) than in the radical nephrectomy group, whose recovery was 76.67% of the initial values. Also, the values of serum creatinine (sCr) in the donor nephrectomy group after only one month were very similar to the values of sCr after ten years of follow-up (median was approximately 83 μmol/l). GFR according to the CKD EPI formula was initially the best in the group of patients with cysts, and this trend continued over the 15-year follow-up. After one year, eGFR CKD EPI corresponded to the second degree of renal impairment in both the donor and radical nephrectomy groups, bearing in mind the fact that in the group with radical nephrectomy it was lower than sCr by median of 1.73μmol/l after one year, and that the trend of declining kidney function was maintained even after 15 years of follow-up. On the other hand, in the donor nephrectomy group, after 10 years of follow-up, eGFR CKD EPI was above 65 ml/min/1.73m², i.e. above 60 ml/min/1.73m² after 15 years of follow-up. In contrast, in the group of patients with renal cysts, a reduced kidney function was verified only after 10 years of follow-up - less than 90 ml/min/1.73m², while it was maintained above 80 ml/min/1.73m² even after 15 years of follow-up.

Conclusion: Comparing these three groups, only in the donor nephrectomy group, one patient ended up on chronic hemodialysis treatment (0.92%), while in the other two groups there were no patients with terminal kidney failure. The values of serum creatinine - the median, were the same after 6 months and after 5 years post-op in the donor nephrectomy group (79 μmol/l). The aforementioned findings can help us predict the expected values of serum creatinine after donor nephrectomy in the future. In donors as well as in patients with renal cysts, the reason for higher mortality was not ESRD, but more often it was a sudden cardiac death or a cardiovascular disease. The well-being of the giver must be ensured both in the short and long term, but the potential harmful consequences for the recipient must be determined as well.

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Background and Aims: The lower humoral immunity response after COVID-19 vaccine in kidney transplant recipients (KTRs) has been reported in several studies. However, the study regarding efficacy of ChAdOx1 nCoV-19 (AstraZeneca) vaccine among various immunosuppressive treatments in Asian population is scarce.

Method: We conducted a cross-sectional study in Siriraj Hospital, Bangkok, Thailand. Adult KTRs who received two doses of the ChAdOx1 nCoV-19 vaccine at intervals of 6 months were enrolled. Anti-SARS-COV-2 S-RBD-IgG antibody (anti-RBD) was assessed at the one month after the second vaccine dose and considered positive if the level ≥ 50 AU/mL. Primary outcome was seropositivity of anti-RBD. Association between type, dose and level of immunosuppressive regimen, and seropositivity of anti-RBD were analyzed. The statistical analysis was performed using SPSS version 23.0.

Results: Between October 2021 and January 2022, 153 KTRs with median follow-up time of 59 (30 – 125) months, were enrolled. Mean age was 49.3 ± 11 years and 61.4% were male. Regimen of tacrolimus (TAC)/mycophenolate mofetil (MPA)/prednisolone (CS), everolimus (ER)/MPA/CS and TAC/ER/CS were prescribed for 92 (60.1%), 23 (15%) and 24 (15.7%) patients, respectively. The anti-RBD ≥ 50 AU/mL after vaccination was observed in 82 patients (53.6%) with median level of 476.7 (129 – 1253.2) AU/mL. Patients received TAC/ER/CS had significantly higher proportion of seropositivity than ER/MPA/CS (95.8% vs 65.2%; p = 0.008) and TAC/MPA/CS regimen (95.8% vs 37%; p < 0.001). Among the seropositive KTRs, the median level of anti-S is significantly highest in TAC/ER/CS treatment when compared to ER/MPA/CS and TAC/MPA/CS group, respectively (1,204 vs 260.7 vs 315.4; p < 0.001). Among KTRs who received tacrolimus, the seropositivity was significantly higher in patients who had tacrolimus trough level < 3 ng/mL (83.3% vs 45.7%; p = 0.014).

Conclusion: The seropositivity of anti-S after vaccination with ChAdOx1 nCoV-19 in KTRs was 53.6% which was lower than general population. KTRs who received TAC/ER/CS regimen had highest immune response after vaccination, which is relatively comparable to healthy control in Thailand. Immunosuppressive regimen should be considered for vaccine dose and schedule in the future.

#5729
HIGHER DAILY PROTEIN INTAKE CAN IMPROVE THE GRAFT FUNCTION OF KIDNEY TRANSPLANT RECIPIENTS IN THE EARLY POSTTRANSPLANT PERIOD

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Background and Aims: Protein-energy wasting (PEW) is commonly seen among uremic patients, which may still exist after they received kidney transplantation,[1,2] and it is a determining factor in the progression of chronic kidney disease (CKD).[3] The use of immunosuppressants and glucocorticoids after transplantation will also affect the patients’ metabolism and aggravate their malnutrition.[4,5] Adequate daily protein intake (DPI) in the early posttransplant period facilitates the rapid recovery of surgical wounds.[6] However, few studies focused on the impact of DPI on the early recovery of graft function. This study aimed to explore the relationship between DPI and graft function at month 3 posttransplant, which may provide a basis for clinical nutritional regimen of kidney transplant recipients.

Method: This is a retrospective observational study, 176 kidney transplant recipients (KTRs) who underwent kidney transplant in West China Hospital from December 2021 to June 2022 were included and followed up regularly. 24-hour urine urea data were collected at month 3 posttransplant to calculate their DPI. These KTRs were further divided into two groups according to the recommended DPI for KTRs by the 2021 Practice Guidelines for the Nutritional Management of Chronic Kidney Disease,[7] namely high intake group (Group 1, with DPI ≥ 1.4 g/kg·d, n = 66) and low intake group (Group 2, with DPI < 1.4 g/kg·d, n = 110). Laboratory data and posttransplant adverse events within 3 months were recorded. Multiple logistic regression was used to analyze the relationship between DPI and early posttransplant graft function.
Results: Mean DPI levels at month 3 posttransplant were 1.75±0.56 g/kg·d in Group 1 and 0.98±0.24 g/kg·d in Group 2, respectively. There was no significant difference in age, gender, pretransplant body mass index (BMI), dialysis type and time, donor type, or the ratio of delayed graft function (DGF) between the two groups. The levels of estimated glomerular filtration rate (eGFR), body mass index (BMI), hemoglobin (Hb), high-density lipoprotein cholesterol (HDL), and urinary protein at month 3 posttransplant in Group 1 were significantly higher than those in Group 2 (P < 0.005, Fig. 1). No statistical difference was found in the incidence of adverse events between the two groups at month 3 posttransplant. The results of multiple logistic regression analysis showed that higher DPI in the early posttransplant period was a protective factor for graft function after kidney transplantation.

Conclusion: In the early posttransplant period, higher dietary protein intake (DPI ≥ 1.4 g/kg·d) may improve graft kidney function, lipid metabolism, and renal anemia.

REFERENCES

#6797
EFFICACY OF DESENSITIZATION TREATMENT IN HYPERIMMUNIZED PATIENTS AWAITING A CADAVERIC KIDNEY TRANSPLANTATION
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Background and Aims: On all kidney waiting lists, patients who have antibodies against more than 80% of a panel reactive antibody (PRA) are difficult to transplant, even with national or regional programs. Desensitization treatment with high-dose intravenous immunoglobulin and rituximab could be offered to patients with a long waiting time for a cadaveric donor to improve their odds of finding a kidney.

Method: Retrospective, single-center study including all hyperimmunized patients on the waiting list for a cadaveric kidney donor who received a desensitization treatment between 2010-2020. To be considered to the desensitization protocol, all the patients must have a PRA above 75% and have been on the waiting list more than 3 years, without any offer. Our treatment was based on the modified Cedars-Sinai Medical Center protocol. Eight hyperimmunized patients on the waiting list for a cadaveric donor kidney transplant (50% male with a mean age of 41.5±16.4 years) received desensitization treatment with intravenous immunoglobulin and Rituximab. Six of the 8 patients (75%) were on renal replacement therapy with hemodialysis and two on peritoneal dialysis (mean time on dialysis 48±14 months). 75% had received a previous transplant. The median PRA calculated was 98%. The time between desensitization and kidney transplantation, the percentage of reactivity against panel cells (PRA) before and after therapy, graft and donor survival, as well as episodes of acute rejection and viral infections were analyzed. The mean follow-up time after transplantation was 67 months.

Results: No patient presented significant side effects to desensitization treatment. Seven of the 8 patients (87.5%) could be transplanted from a cadaveric donor (negative crossmatch test), in a median 8 months after desensitization. No significant changes were observed in the PRA levels. In the immediate post-transplant period, there were 2 graft losses (28.6%) due to non-immunological causes (1 venous thrombosis in a patient with a coagulation disorder and 1 primary graft failure). Creatinine at discharge was 1.6±0.4 mg/dl and 1.4±0.2 a year after the transplant. Five-year censored death graft survival was 100%. Three patients presented viral replication (1 due to cytomegalovirus (CMV), 1 due to polymavirus (BK) and another CMV+BK), which became negative after switching to m-Tor therapy. There were no episodes of acute rejection. No patient developed cancer during the follow-up.

Conclusion: Desensitization treatment with immunoglobulin and rituximab on hyperimmunized patients on the cadaveric waiting list is a safe and effective treatment that increases the chances of achieving a kidney transplant in highly sensitized patients.

#3641
DOES IBANDRONATE OR CALCIUM AND VITAMIN D MAINTAIN OR IMPROVE BONE MICROARCHITECTURE IN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION?
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¹Oslo University Hospital, Rikshospitalet, Department of Surgery, Inflammation Medicine and Transplantation, Section of Nephrology, Oslo, Norway, ²Smerud Medical Research International AS, Oslo, Norway and

<image>
Conclusion: BMD in any of the groups, and change in TBS was not significantly correlated with change in lumbar spine. These patients could benefit from anti-resorptive therapy.

Method: We analyzed TBS changes and potential treatment effects in 179 de novo KTR. 118 of whom had participated in a randomized controlled trial[1] evaluating the effect of ibandronate (active/placebo) on top of calcium and vitamin D in the first year after kidney transplantation. Trial participants were compared to 61 patients transplanted in the same time-period, meeting the same study inclusion criteria, but receiving no specific bone-directed treatment. Correlations between changes in TBS and lumbar spine BMD were investigated. We used ANOVA and ANCOVA with adjustment for baseline TBS values to evaluate the potential effects of calcium and vitamin D with/without concomitant ibandronate on TBS 12 months after transplantation, as compared to no treatment.

Results: Mean TBS increased in all groups from baseline to 12 months after transplantation (2.1% for ibandronate/calcium/vitamin D, 2.7% for calcium/vitamin D, and 3.4% for no treatment). Adjusting for baseline TBS, there were no significant differences in TBS at 12 months, neither with overall comparison (p = 0.377) nor when comparing the groups pairwise. The correlation between TBS and BMD was weak (r = 0.170, p = 0.02) at baseline, and change in TBS was not significantly correlated with change in lumbar spine BMD in any of the groups.

Conclusion: In a group of de novo KTR with reasonably well-preserved bone mass, it does not appear that one year of treatment with ibandronate or calcium and vitamin D significantly affects bone quality as measured by TBS. We found surprisingly weak correlation between changes in TBS and BMD over the study period, indicating that these measurements reflect different aspects of bone integrity and metabolism. This study strengthens the view that focus should be on identifying KTR at high risk of fracture at time of transplantation, as these patients could benefit from anti-resorptive therapy.

REFERENCE

Increased serum levels of tacrolimus (\(n = 3.82^{±0.94}\)) were observed in patients on DOACs as compared to patients on AVK, who had similar clinical presentation. There was no difference in terms of eGFR decline from start to long-term follow-up. There were no thromboembolic events among patients treated with DOACs or AVK.

Cyclosporin levels were stable at serial evaluation during 18-month follow-up. There were no differences observed in terms of renal function and serum levels of immune modulating agents between patients treated with DOACs and AVK.

Conclusion: DOACs are a potential therapeutic option among kidney transplant recipients treated with immune modulating drugs. Careful evaluation of immunomodulating agent levels during the first two weeks of therapy should be recommended. No difference in terms of bleeding, thromboembolic events and renal function decline was found when comparing with avk therapy.

#5184

THE RELATIONSHIP OF BONE MINERAL DENSITY AND VITAMIN K IN RENAL TRANSPLANT PATIENTS

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Background and Aims: Kidney transplantation is the best treatment for end-stage renal disease (ESRD). Osteoporosis is a common health problem in kidney transplant recipients. It is known that the risk of bone fracture increases by 30% in the first 3 years after transplantation in kidney transplant recipients. Vitamin K is a cofactor involved in the activation of osteocalcin. This protein plays a role in bone mineralization. Currently, vitamin K cannot be measured directly from blood samples, and markers such as proteins induced in the activation of osteocalcin (PIVKA-II) and undecarboxylated osteocalcin (ucOC) are used for indirect measurement of vitamin K. In our study, we aimed to investigate the relationship between vitamin K and osteoporosis by measuring serum PIVKA-II, ucOC and BMD in kidney transplant recipients.

Method: It was a cross-sectional observational study. Patients were selected from kidney transplant patients over 18 years old. A control group was formed from dialysis patients over the age of 18. For vitamin K levels, PIVKA-II and ucOC levels were measured in serum samples taken from patients. The relationship between vitamin K markers, bone mineral densitometry and the risk of major osteoporotic fracture calculated by FRAX in kidney transplant patients. It is known that the risk of bone fracture increases by 30% in the first 3 years after transplantation in kidney transplant recipients. Vitamin K is a cofactor involved in the activation of osteocalcin.

Results: 68 kidney transplant patients and 20 dialysis patients followed in our clinic were included in this study. As results, it was observed the increased risk of osteoporosis in postmenopausal women followed in our clinic were included in this study. As results, it was observed the increased risk of osteoporosis in postmenopausal women followed in our clinic were included in this study. As results, it was observed the increased risk of osteoporosis in postmenopausal women followed in our clinic were included in this study. As results, it was observed the increased risk of osteoporosis in postmenopausal women followed. It was a cross-sectional observational study. Patients were selected from kidney transplant patients over 18 years old. A control group was formed from dialysis patients over the age of 18. For vitamin K levels, PIVKA-II and ucOC levels were measured in serum samples taken from patients. The relationship between vitamin K markers, bone mineral densitometry and the risk of major osteoporotic fracture calculated by FRAX in kidney transplant patients. It is known that the risk of bone fracture increases by 30% in the first 3 years after transplantation in kidney transplant recipients. Vitamin K is a cofactor involved in the activation of osteocalcin.

Conclusion: In our study, it has been proven that as the vitamin K level decreases in kidney transplant patients, the vertebral bone mineral density decreases while the risk of osteoporosis increases. This result shows that vitamin K replacement may have positive effects on bone metabolism.

Table 1: Results according to the different treatment combinations.

<table>
<thead>
<tr>
<th></th>
<th>Tacrolimus + Mycophenolate (n = 19)</th>
<th>Tacrolimus + mTOR inhibitor (n = 49)</th>
<th>Mycophenolate + mTOR inhibitor (n = 13)</th>
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<tr>
<td>Healing time: Median months</td>
<td>17 (2.5-28.4)</td>
<td>4.8 (3.0-10.3)</td>
<td>3.5 (2.2-6.4)</td>
</tr>
<tr>
<td>Recurrences: n (%)</td>
<td>6 (31.6)</td>
<td>11 (23.4)</td>
<td>6 (46.2)</td>
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<td>No healing: n (%)</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Last viremia (copies/ml): n (%)</td>
<td>&lt;500 – 19 (100)</td>
<td>&gt;10.000 – 2 (4.1)</td>
<td>&lt;500 - 13 (100)</td>
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<tr>
<td>Last viruria (copies/ml): n (%)</td>
<td>10⁶ – 3 (15,8)</td>
<td>&gt;10⁶ – 4 (8,2)</td>
<td>&gt;10⁶ – 3 (23,1)</td>
</tr>
<tr>
<td>Follow-up time: Median years</td>
<td>6,2 (4,9-7)</td>
<td>5,7 (3,8-8,3)</td>
<td>6,9 (3,7-8,2)</td>
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<td>Death: n (%)</td>
<td>3 (15.8)</td>
<td>6 (12.2)</td>
<td>3 (23,1)</td>
</tr>
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<td>Graft loss: n (%)</td>
<td>1 (5,3)</td>
<td>3 (6,1)</td>
<td>3 (23,1)</td>
</tr>
<tr>
<td>Mean glomerular filtration rate at 1 year of follow-up (ml/min)</td>
<td>48,7 (17,9)</td>
<td>50,7 (22,7)</td>
<td>47 (16)</td>
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<tr>
<td>Median protein/creatinine ratio at 1 year of follow-up (mg/g)</td>
<td>157 (86-390)</td>
<td>208 (23-375)</td>
<td>271 (187-408)</td>
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<tr>
<td>Median glomerular filtration rate at 5 years of follow-up (ml/min)</td>
<td>45.7 (31,9-69,8)</td>
<td>45.6 (28,4-64,0)</td>
<td>36.0 (14,9 – 51,1)</td>
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</table>
E4 - COMPLICATIONS IN TRANSPLANTATION

#2846 DEVELOPMENT OF THE JAPANESE VERSION OF THE BASEL ASSESSMENT OF ADHERENCE TO IMMUNOSUPPRESSIVE MEDICATIONS SCALE
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Background and Aims: One of the major barriers for long-term transplant outcomes in kidney transplant recipients is medication non-adherence, which is a risk factor for de novo donor-specific antibody development leading to antibody-mediated rejection and graft loss. Identifying non-adherent patients is the first step in minimizing the risk of complications of medication non-adherence. However, to date, there is no validated Japanese self-report instrument to evaluate the MA for transplant patients. This study aimed to determine the reliability and validity of the Japanese version of the Basel Assessment of Adherence to Immunosuppressive Medications Scale (J-BAASIS).

Method: We conducted a single-center cross-sectional study for kidney transplant recipients who visited our hospital. The eligible and willing participants were randomly assigned to two groups, the J-BAASIS group and the J-BAASIS+MEMS group, with random numbers generated by computer. All participants filled out a questionnaire including the J-BAASIS (the first survey). They filled out a questionnaire again including the J-BAASIS in similar conditions during their following outpatient visit 4-6 weeks later (the second survey). The participants in the J-BAASIS+MEMS group took the methylprednisolone tablets daily using the MEMS until the second survey. We analyzed the reliability (test-retest reliability and measurement error) and validity of the J-BAASIS (concurrent validity with the medication event monitoring system (MEMS) and the 12-item Medication Adherence Scale) referring to the COSMIN Risk of Bias tool.

Results: A total of 106 kidney transplant recipients (the J-BAASIS group, 56; the J-BAASIS+MEMS group, 50) were included in this study. In the analysis of test-retest reliability, Cohen’s kappa coefficient was 0.62. In the analysis of measurement error, the positive and negative agreement were 0.78 and 0.84, respectively. In the analysis of concurrent validity with the MEMS, sensitivity and specificity were 0.84 and 0.90, respectively. In the analysis of concurrent validity with the 12-item Medication Adherence Scale, the point-biserial correlation coefficient for the “medication compliance” subscale was 0.38 (p<0.001).

Conclusion: The J-BAASIS was determined to have good reliability and validity. Using the J-BAASIS to evaluate medication adherence may help clinicians to identify non-adherent transplant patients and institute appropriate corrective measures to improve transplant outcomes. Moreover, this study, which demonstrated the concurrent validity with the MEMS, the gold standard for measuring medication adherence, further strengthens the evidence for the psychometric properties of the original BAASIS.

#3571 GROWTH PATTERNS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE SINGLE CENTER STUDY
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Background and Aims: Attainment of a normal adult height remains a great challenge in the care of children with end stage kidney disease. Moreover, the incidence of overweight and obesity increases post kidney transplantation (KT). We aimed to describe growth parameters and predictive factors in children post KT.

Method: We retrospectively reviewed the records of 28 children who underwent KT in our center between 2002-2022. Height (hSDS) and body mass index (BMIzSDS) z-scores at various time points and possible predictors were assessed.

Results: Median age at KT was 11.2 years (5.3-14), 20 were male, mean time on dialysis was 5.95 years. KT from a living donor (LRD) was performed in 18 patients. Mean follow-up time was 4.88 (1-10) years. rhGH was administered pre-KT in 15/28 patients and in 3 post KT. Following the first year post KT, steroid-free, alternate day and daily steroid regimes were adopted for 9, 11 and 8 patients, respectively. Mean hSDS at the time of KT, one year after and at last visit were -1.76, -1.87, and -1.77 (p<0.005). Mean BMIzSDS at the respective time points were 0.13, 0.65 and 0.05 respectively (p<0.05). At last visit, 29% and 17% of children showed moderate and severe height deficit. hSDS at last visit was associated with preoperative hSDS, whereas difference between hSDS pre and last visit post KT (ΔhSDS) was associated with the type of KT (mean ΔhSDS for LRD and DDT -1.45 (95%CI -1.87, -1.03) and -2.66 (95%CI -3.4, -1.93) respectively, p = 0.002) and steroid regime (mean ΔhSDS for daily and alternate day steroid treatment -0.39 (95%CI -0.77, -0.003) and 0.55 (95%CI -0.07, 1.17) respectively, p = 0.037). There was no association between ΔhSDS and rejection episodes or rhGH administration pre-KT. At the time of KT and at last visit 25% and 10.7% were overweight, respectively, whereas only 1 patient was obese preoperatively but none at last visit. The overall incidence of overweight and obesity had reduced at last visit compared to pre-KT (p = 0.01).

Conclusion: Linear growth post KT remained limited, resulting in short stature in nearly half of children. Strategies to improve height post pediatric KT could include height optimization pre-KT, steroid withdrawal/avoidance protocols, and LRD KT.

#3654 ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION LOWERS INCIDENCES OF DE NOVO DONOR-SPECIFIC ANTIBODIES AND CHRONIC ANTIBODY-MEDIATED REJECTION
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Background and Aims: ABO-incompatible kidney transplantation has been associated with an increased risk for antibody-mediated rejection (ABMR) and early graft loss attributable to isoagglutinins. Its impact on the development of de novo donor-specific HLA antibodies (DSA) and DSA-induced chronic ABMR, however, remains less well studied.

Method: We analyzed 297 kidney transplant recipients (KTRs) who underwent living donor transplantation at the University Hospital Zurich from 2009 to 2021. 58 ABO-incompatible (iABO) KTRs were compared to 239 ABO-compatible (cABO) KTRs concerning the development of de novo donor-specific antibodies (DSA) and antibody-mediated rejection (ABMR). ABO desensitization was performed using rituximab and antigen-specific immunoadsorption. The HLA-derived epitope-mismatches were calculated per HLA-locus and in total using the Predicted Indirectly Recognizable HLA-Epitope (PIRCH-E-II) algorithm. High-resolution re-typing was performed from protocol kidney allograft biopsies if necessary.

Results: The incidence of TCMR/ABMR in the first post-transplant year was comparable between iABO KTRs (19%) and cABO KTRs (13%; p = 0.207). De novo DSA were detected in only 1 of 58 iABO KTRs but 12 of 239 cABO KTRs in the first post-transplant year and 2 of 58 iABO KTRs but 50 of 239 cABO KTRs in the long-term follow-up (p = 0.001). ABMR was diagnosed in only 1 of 58 iABO KTRs but 28 of 239 cABO KTRs after the first post-transplant year (p = 0.021). iABO kidney transplantation decreased the risk of de novo DSA development (HR 7.222, CI 1.755-29.722, p = 0.006) and ABMR (HR 7.362, CI 1.000-54.239; p = 0.050) after the first-post-transplant year independent from the presence of preformed DSA. Total PIRCH-E-II scores and PIRCH-E-II scores per locus were not associated with the development of de novo DSA in all 297 living-donor KTRs (p<0.05).

Conclusion: Our findings suggest that iABO kidney transplantation is associated with a lower incidence of de novo DSA and ABMR in the long term, independent from the HLA-derived epitope mismatch load. Whether this protective effect offers new therapeutic options against kidney allograft injury needs to be investigated in future studies.

Abstracts
Post-transplant diabetes mellitus (PTDM) is a frequent complication after kidney transplantation (KT), with an incidence between 20-30%. PTDM increases the risk of cardiovascular disease, which is one of the main causes of death with functioning grafts. The pathophysiology of PTDM involves beta-cell dysfunction, with impaired insulin secretion and insulin resistance overlaid immunosuppression accelerating preexisting damage. The major risk factor in the post-transplant period is immunosuppression therapy, such as steroids, calcineurin inhibitors (CNI), and mTOR inhibitors (mTORi). It is also a major modifiable risk but must be balanced with rejection risk. This systematic review aims to investigate the effect of different immunosuppressive regimens on the risk of PTDM incidence.

Methods: Relevant studies were obtained from a systematic literature search. We searched MEDLINE and CENTRAL (Cochrane Central Register of Controlled Trials) until 15 May 2022. We searched randomized controlled trials (RCT) including KT recipients receiving any immunosuppression and reporting PTDM outcomes. The definition of PTDM was whatever was used by the authors. Meta-analysis was done by pooling data for calculating the relative risks (RR) of the outcome by comparing different immunosuppression strategies.

Results: We identified 1,848 reports. After removing duplicates and screening titles and abstracts 156 full-text reports were assessed. We finally included 52 studies. Eight RCTs reported the outcome of PTDM using different induction therapies at ≤ 5 years post KT, with a total inclusion of a population of 1,495 recipients. The meta-analysis of all studies did not show differences by comparing different doses or formulations of the same drug (Table 1). The cumulative incidence of PTDM was 14% (95% CI [11.4-16.9]). The estimated incidence of PTDM after 2 years post KT showed an increased risk of PTDM (15 studies, 3,200 participants, RR 1.60, 95% CI [1.4-2.23], p < 0.01). We found 39 RCTs that reported PTDM outcomes in KT receiving CNI. In de novo KT, there was an increased risk of developing PTDM with tacrolimus rather than with ciclosporin (26 studies, 5,635 patients, RR 1.71, 95% CI [1.38-2.11], p < 0.01) after ≤ 5 years post KT. There were no differences comparing different doses or tacrolimus formulations. When belatacept was compared to CNI we found a 38% reduction at 1-year post KT in the risk of developing PTDM (6 studies, 2,100 participants, RR 0.62, 95% CI [0.42-0.91], p = 0.02).

Conclusion: A higher risk of PTDM was observed in patients receiving TAC vs GA, and mTORI inhibitors. Belatacept showed a 38% reduction in PTDM compared to CNI. However, the risk of PTDM should be balanced with the risk of rejection.

REFERENCES
#6130

COMMON VARIABLE IMMUNODEFICIENCY WITH A TNFRSF13B GENE MUTATION IN A KIDNEY AND PANCREAS TRANSPLANT RECIPIENT: WHAT SHOULD WE AIM FOR?

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1Hospital Espírito Santo de Évora, E.P.E., Nefrologia, Évora, Portugal and 2 Centro Hospitalar Universitário de Santo António, Nefrologia e Transplante, Porto, Portugal

Background and Aims: Common Variable Immune Deficiency (CVID) is a primary immunodeficiency disorder, where genetic defects are commonly present, with hypogammaglobulinemia (typically IgG) and increased susceptibility to recurrent infections, autoimmune disorders, granulomatous diseases and malignancy. It can also potentially lead to nephropathy, with increased risk of proteinuria and metabolic acidosis, higher risk of acute tubular injury caused by Immunoglobulin replacement therapy, and the data available in current literature shows a higher incidence of tubulointerstitial nephritis and membranous glomerulopathy, with IgG deposits on immunofluorescence in most cases. Our aim is to report the challenges of a kidney and pancreas transplant in a recipient with chronic kidney disease and a primary immunodeficiency disorder, to outline an immunosuppression strategy with potential alternatives, and to report on the short-term outcomes.

Case Report: Here-in, we report the case of a 27-year-old patient, with type 1 diabetes mellitus, diagnosed with end-stage chronic kidney disease, who has a history of chronic inflammatory response dysregulation, with chronic monoarthritis, persistent elevation of inflammation markers, recurrent infections and low IgG levels. Genetic screening revealed a heterozygous pathological mutation in TNFRSF13B gene, and a Variant of Uncertain Significance (VOUS) in BACH2 gene. At 24 years-old, she experienced a high-risk pregnancy with HELLP syndrome, and serum creatinine and non-nephrotic proteinuria progressively worsened after postpartum. A native kidney biopsy revealed diabetic nephropathy, with C3 and IgG pseudolinar deposits on immunofluorescence. Eventually, disease progression led to hemodialysis induction. 10 months later, she received a kidney and pancreas cadaveric transplant from a standard criteria donor (SCD). Serum baseline donor creatinine was 0.9 mg/dl, and cause of death was a hemorrhagic stroke. Both donor and recipient had blood group type A (ABO system) and positive cytomegalovirus (CMV) IgG levels. Compatibility analysis showed donor Histocompatibility Leukocyte Antigens (HLA) class I: A 01,32; B08,64; C07,08; and class II: DR 17,07; DQ 02,02; DP 03,45; and recipient HLA class I: A 02,02; B 35,44; C 04,05; and class II: DR 03,04. Flow cytometry showed no receptor class I or class II anti-HLA antibodies. Panel Reactive Antibodies (PRA) test score was 0%, and flow cytometry cross-match (FCCM) was negative. Immunosuppression induction regimen included thymoglobulin, mycophenolate mofetil and prednisolone, with optimal pancreatic graft function. Creatinine at discharge was 2.1 mg/dL. After discharge, maintenance immunosuppression protocol included tacrolimus, mycophenolate mofetil and prednisolone, and pancreas and renal graft function remained successfully stable, with no serious infections until current date.

Discussion: Common variable immunodeficiency with a heterozygous TNFRSF13B gene mutation is associated with increased risk of hypogammaglobulinemia, lymphoma, gastrointestinal cancer and autoimmunity. The VOUS BACH2 gene is also likely pathological, since there have been BACH2 polymorphisms associated with autoimmune endocrine diseases, including Addison's disease, Graves' disease and type 1 diabetes mellitus. A hyper-regulated inflammatory state can accelerate kidney function deterioration, but chronic treatment with corticosteroids should be cautious due to the underlying diabetic nephropathy. After transplantation, recipients with CVID are at higher risk of atypical infections, autoimmune complications and disease recurrence with suboptimal long term graft survival. The evidence of current immunosuppression maintenance regimens is weak due to the paucity of CVID cases described in current literature. In the future, we believe that belatacept could offer benefits in terms of reducing the risk of graft loss or the incidence of serious infectious in a transplant recipient with a primary immunodeficiency disorder. Nevertheless, therapy management should be accomplished in a patient-to-patient basis.

Table 1: Follow-up and outcome.

<table>
<thead>
<tr>
<th>No after TX (mo)</th>
<th>Follow-up</th>
<th>Serum Creatinine mg/dl</th>
<th>Proteinuria g/L</th>
<th>Serum Proteinuria</th>
<th>No of AA V patients</th>
<th>Anti-rejection therapy Cys (%)/Tcr (%)</th>
<th>N° patients with infection needed hospitalization (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>142</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.09</td>
<td>0.66</td>
<td>0.16</td>
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<td>0.8</td>
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<td>0.2</td>
<td>0.12</td>
</tr>
<tr>
<td>3</td>
<td>127</td>
<td>1.2</td>
<td>1.5</td>
<td>1.4</td>
<td>0.08</td>
<td>0.06</td>
<td>0.08</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>2.4</td>
<td>2</td>
<td>1.7</td>
<td>0.16</td>
<td>0.12</td>
<td>0.06</td>
</tr>
<tr>
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<td>1.7</td>
<td>1.3</td>
<td>0.2</td>
<td>0.18</td>
<td>0.01</td>
</tr>
<tr>
<td>6</td>
<td>93</td>
<td>1.3</td>
<td>1.3</td>
<td>1</td>
<td>0.2</td>
<td>0.14</td>
<td>0.26</td>
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<tr>
<td>7</td>
<td>197</td>
<td>0.8</td>
<td>1.1</td>
<td>1.1</td>
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<tr>
<td>8</td>
<td>198</td>
<td>1</td>
<td>1.1</td>
<td>0.9</td>
<td>0.18</td>
<td>0.14</td>
<td>0.26</td>
</tr>
<tr>
<td>9</td>
<td>12</td>
<td>1.6</td>
<td>1.9</td>
<td>2.4</td>
<td>0.2</td>
<td>0.2</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Abbreviations: KTx Kidney Transplant, CYS Cyclosporine, TCR Tacrolimus, NA Not Available
URINARY CXCL9 AND CXCL10 CONCENTRATIONS AND KIDNEY TRANSPLANT INJURY

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Background and Aims: Kidney transplant rejection is diagnosed by the kidney biopsy which is an invasive diagnostic method, however, non-invasive biomarkers, distinguishing normal kidney transplant from transplant rejection would be preferred but are lacking. CXC chemokine ligand 9 (CXCL9) and CXC chemokine ligand 10 (CXCL10) are gamma interferon inducible small cytokines. The aim of this study was to evaluate urinary CXCL9 and CXCL10 as potential biomarkers of allograft rejection.

Method: 117 kidney transplant recipients undergoing kidney transplant biopsy (surveillance or indication) were included into this study. Spot urine samples were collected before kidney biopsy for urinary creatinine, CXCL9 and CXCL10 measurement. The ratios of CXCL9 over urinary creatinine and CXCL10 over urinary creatinine were calculated. Kidney biopsies were analyzed according to Banff criteria by an experienced pathologist.

Results: 26 (22.2%) of kidney biopsies were defined as normal histology, 24 (20.5%) – antibody mediated rejection, 9 (7.7%) – T cell mediated rejection, 10 (8.6%) mixed rejection, 5 (4.3%) BK virus nephropathy and 43 (36.8%) were defined as other histological lesions. Average CXCL9/creatinine was 0.408, p = 0.01 and CXCL10/creatinine was 2.47, p < 0.01. ROC curve for CXCL9/creatinine detecting antibody mediated rejection was 0.79, CI 0.67 to 0.90, p < 0.01. ROC curve for CXCL10/creatinine detecting antibody mediated rejection was 0.79, CI 0.64 to 0.94, p < 0.01.

Conclusion: Urinary biomarkers CXCL9/creatinine and CXCL10/creatinine has a potential to distinguish normal renal histology from allograft rejection and correlates to proteinuria at the time of the biopsy.

INDIRECT INSULIN RESISTANCE INDICES AND THEIR CUT-OFF VALUES FOR POST-TRANSPLANTATION DIABETES MELLITUS IN KIDNEY TRANSPLANT RECIPIENTS

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1 University Medical Center Groningen, Nephrology, Groningen, Netherlands, 2 University Medical Center Groningen, Nephrology, Groningen, Netherlands, 3 University Medical Center Groningen, Clinical pharmacology, Groningen, Netherlands and 4 University Medical Center Groningen, Endocrinology, Groningen, Netherlands

Background and Aims: Insulin resistance determination in kidney transplant recipients (KTRs) plays an important role to identify KTRs at risk of post-transplantation diabetes mellitus (PTDM) development. Current methods to measure insulin resistance include the hyperinsulinemic-euglycemic (HIEG) clamp technique, and minimal model approximation of the metabolism of glucose (MMAMG). These methods, however, require considerable time and are expense, complex, and invasive. As a result, indirect insulin resistance indices such as homeostasis model assessment-insulin resistance (HOMA-IR), visceral adiposity index (VAI), lipid accumulation product (LAP), or triglycerides-glucose (TyG) index, are used in epidemiological and clinical studies in the general population due to their simplicity and ease of use. However, it is unknown to what extent those indices may contribute to determine insulin resistance and PTDM development in KTRs. Therefore, this study aimed to investigate the role of indirect insulin resistance indices to determine insulin resistance and PTDM development in KTRs.

Method: We included 472 stable outpatient KTRs (with a functioning graft ≥ 1 year) without diabetes from a prospective cohort study. Crude and multivariable Cox proportional hazards regression analysis were performed to determine whether indirect insulin resistance indices (HOMA-IR, VAI, LAP, and TyG index) were prospectively associated with incident PTDM. We analyzed each measure using receiver operating characteristic (ROC) curve for the development of PTDM. The cut-off value was determined as the value with the highest Youden index score in the specificity dominant area.

Results: During a median 9.6 years [interquartile range (IQR) 6.6–10.2] of follow up, 68 (14%) KTRs developed PTDM. In Cox regression analyses, all indirect insulin resistance indices associated with incident PTDM, independent of potential confounders. ROC curve was 0.764 (95% CI 0.703-0.826) for HOMA-IR, 0.685 (95% CI 0.615-0.757) for VAI, 0.743 (95% CI 0.678-0.808) for LAP, and 0.698 (95% CI 0.629-0.766) for TyG index, with no significant difference between them (p = 0.05). The cut-off values with their corresponding sensitivity and specificity for each indices are presented in Table 1. To test this cut-off value, the association between the indices and incident PTDM was examined by using each index as a categorical variable (HOMA-IR < 2.47 vs ≥ 2.47; VAI < 4.01 vs ≥ 4.01; LAP < 87.04 vs ≥ 87.04; TyG index < 4.94 vs ≥ 4.94). Indirect insulin resistance indices as a categorical variable predicted incident PTDM independent of age, sex, smoking, time to transplantation, systolic blood pressure, eGFR, and medication.

Conclusion: Indirect insulin resistance indices could be used to predict incident PTDM in KTRs. In addition to HOMA-IR, insulin-free surrogates of insulin resistance might serve as useful methods to identify KTRs at risk for PTDM development.
Table 1: Mean bias, precision and accuracy of eGFR formulas.

<table>
<thead>
<tr>
<th>Insulin resistance index</th>
<th>AUC(95% CI)</th>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>HR (95% CI) per SD-increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA-IR</td>
<td>0.764 (0.703-0.826)</td>
<td>2.47</td>
<td>75.0</td>
<td>71.3</td>
<td>6.42 (3.67-11.25)</td>
</tr>
<tr>
<td>VAI</td>
<td>0.685 (0.615-0.757)</td>
<td>4.01</td>
<td>61.8</td>
<td>72.8</td>
<td>4.10 (2.48-6.77)</td>
</tr>
<tr>
<td>LAP</td>
<td>0.743 (0.678-0.808)</td>
<td>87.04</td>
<td>64.7</td>
<td>75.2</td>
<td>5.82 (3.46-9.80)</td>
</tr>
<tr>
<td>TyG index</td>
<td>0.698 (0.629-0.766)</td>
<td>4.94</td>
<td>51.5</td>
<td>83.9</td>
<td>5.73 (3.45-9.52)</td>
</tr>
</tbody>
</table>

HRs (95% CIs) were derived from Cox proportional hazard model adjusted for age, sex, smoking, time since transplantation, SBP, eGFR, medication use (prednisolone dosage, calcineurin inhibitors, proliferation inhibitor).

AUC: area under the curve; HOMA-IR: homeostasis model assessment-insulin resistance; VAI: visceral adiposity index; LAP: lipid accumulation product; TyG index: triglycerides-glucose index; HR: hazard ratio; SBP: systolic blood pressure

#2948

β-2-MICROGLOBULIN AND β-TRACE-PROTEIN DO NOT IMPROVE ESTIMATION OF GFR IN KIDNEY TRANSPLANT RECIPIENTS COMPARING TO CREATINEIN AND CYSTATIN C

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1 Aarhus University Hospital, Department of Renal Medicine, Aarhus N, Denmark, 2 Copenhagen University Hospital, Rigshospitalet, Department of Nephrology, København, Denmark, 3 Sahlgrenska University Hospital, The Transplant Institute, Gothenburg, Sweden, 4 Aarhus University Hospital, Department of Clinical Medicine, Aarhus, Denmark and 3 Aarhus University Hospital, Department of Renal Medicine, Aarhus N, Denmark

Background and Aims: Precise estimates of glomerular filtration rate (eGFR) are important in kidney transplant recipients (KTRs). Current eGFR formulas based on plasma creatinine and/or cystatin C are associated with significant bias. We investigated whether race free formulas based on plasma β-2-microglobulin and/or eGFR-β-2-microglobulin performed better than formulas based on creatinine and cystatin C in a Scandinavian cohort of KTRs.

Method: We included samples and data from the randomised, controlled trial CONTEXT. eGFR was measured by plasma clearance of [51Cr]-EDTA or iodothalamate. eGFR was calculated using the new race-free CKD-EPI eGFR-creatinine and/or cystatin C (2021) formulas as well as the CKD-EPI eGFR-β-2-microglobulin and/or eGFR-β-trace-protein formulas. GFR estimates were evaluated at 3 (n = 82) and 12 (n = 64) months post-transplant using mean bias, precision, and accuracy. Also, formulas were analysed for their ability to correctly classify changes in measured GFR from 3 to 12 months.

Results: At 12 months eGFR-creatinine-cystatin C performed best according to mean bias (−4.54 ml/min/1.73 m²), precision (SD = 8.18 ml/min/1.73 m²) and accuracy (P10 = 47%) among creatinine and cystatin C based formulas (Table 1). Among the β-trace-protein and β-2-microglobulin based formulas, eGFR-β-trace-protein-β-2-microglobulin performed best according to precision (SD = 7.64 ml/min/1.73 m²) and accuracy (P10 = 36%) (Table 1). eGFR-β-trace-protein-β-2-microglobulin and eGFR-creatinine-cystatin C performed similar when comparing residuals (p = 0.481). eGFR-β-trace-protein, eGFR-β-trace-protein-β-2-microglobulin and eGFR-creatinine-cystatin C performed best in correctly classifying changes in mGFR from 3 to 12 months.

Conclusion: β-trace-protein and β-2-microglobulin do not improve the measurement of GFR compared to creatinine and cystatin C based formulas in KTRs.

#6456

DSA-NEGATIVE MICROVASCULAR INFLAMMATION IN KIDNEY TRANSPLANT BIOPSIES: GENE EXPRESSION COMPARISON WITH NATIVE AND TRANSPLANT KIDNEY CONTROLS

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1 University of Alberta Hospital, Laboratory Medicine and Pathology, Canada, 2 Hospital del Mar, Nephrology, Barcelona, Spain, 3 University of Manitoba, Pathology, Canada, 4 University of Manitoba, Internal Medicine, Canada and 5 Hospital 12 de Octubre, Nephrology, Madrid, Spain

Background and Aims: Microvascular inflammation (MVI) in kidney transplant (KT) biopsies from patients without detectable anti-HLA donor-specific antibodies (DSA) presents a diagnostic and therapeutic dilemma. This study aimed to further understand the significance of these changes by characterizing their molecular phenotype compared to other native and transplant kidney biopsies.

Method: The NanoString B-HOT panel (770 genes) was used to measure the expression of six literature-derived gene sets in 195 archival FFPE kidney biopsies from four centers, including transplant biopsies with MVI (g + p ≥1c) but no detectable DSA (MV1, n = 47), antibody-mediated rejection with DSA (ABMR, n = 42), pure T-cell mediated rejection without DSA (TCMR, n = 25), mixed MVI and TCMR without DSA (MV1+TCMR, n = 47), normal implant biopsies (Normal, n = 11), and native kidney biopsies with either endocapillary proliferative glomerulonephritis (GN, n = 12) or minimal change disease (MCD, n = 11). The evaluated gene sets included transcripts previously associated with ABMR, DSA (DSAST), endothelial injury (ENDAT), TCMR, early injury, and late injury. Gene expression was compared between groups using principal component and class comparison analyses.

Results: Principal component analysis demonstrated significant molecular overlap between sample groups (Fig. 1A). However, gene set analysis showed lower expression of ABMR-related, DSAST (Fig. 1B), and ENDAT gene sets in DSA-negative MVI compared to ABMR. DSAST and ENDAT gene set expression was similar between MV1, MV1+TCMR, and TCMR groups; but higher than native biopsies (p ≤0.002). TCMR and early injury gene set expression was higher in TCMR than all other groups (p ≤0.002), except MV1+TCMR. Late injury gene set expression was lower in MV1 compared to ABMR, MV1+TCMR, and TCMR groups (p ≤0.031); but higher than the Normal and MCD groups (p ≥0.016).

Table 1: AUC and cut-off values indirect insulin resistance indices with their corresponding sensitivity, specificity, and hazard ratio (HR).

<table>
<thead>
<tr>
<th>Insulin resistance index</th>
<th>AUC(95% CI)</th>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>HR (95% CI) per SD-increase</th>
</tr>
</thead>
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<td>HOMA-IR</td>
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<td>75.0</td>
<td>71.3</td>
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<td>VAI</td>
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<td>61.8</td>
<td>72.8</td>
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<td>LAP</td>
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<td>64.7</td>
<td>75.2</td>
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<td>TyG index</td>
<td>0.698 (0.629-0.766)</td>
<td>4.94</td>
<td>51.5</td>
<td>83.9</td>
<td>5.73 (3.45-9.52)</td>
</tr>
</tbody>
</table>

Abstracts
Figure 1:

Conclusion: These results suggest that DSA-negative MVI displays a lower expression of ABMR-related genes than ABMR, but similar to MVI, TCMR and higher than native kidney biopsies with or without glomerulonephritis. Further work is underway to evaluate the potential role of non-HLA DSA and recognition of missing self in these cases.

#2794

ISOLATED GLOMERULITIS IS STRONGLY ASSOCIATED WITH THE ABSENCE OF ANTIBODY-MEDIATED REJECTION BY MOLECULAR DIAGNOSTICS

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Background and Aims: According to the 2018 Banff classification, the Molecular Microscope Diagnostic System (MMDx) is indicated in cases when histology is insufficient to diagnose antibody-mediated rejection (ABMR) due to an absence of diagnostic criteria groups 2 and/or 3. The impact of isolated glomerulitis (g > 0, ptc0) on the likelihood of ABMR diagnosis by the MMDx appears critical to the implementation of this new biomarker.

Method: We analyzed 251 kidney allograft biopsies by histology and molecular diagnostics at the University Hospital Zurich from October 2018 to November 2022. Histologic findings were classified concerning the absence of (1) diagnostic criteria groups 2 and 3 (n = 18), (2) diagnostic criteria group 2 only (n = 18), and (3) diagnostic criteria group 3 only (n = 28). In addition, cases with histologically proven ABMR were used for comparison (n = 65). High-resolution re-typing was performed from the kidney allograft biopsies if necessary.

Results: The MMDx diagnosed ABMR in 1 of 18 cases (6%) with absent diagnostic criteria groups 2 and 3, 4 of 18 cases (22%) with absent diagnostic criteria groups 2, and 19 of 28 cases (68%) with absent diagnostic criteria groups 3. On the contrary, MMDx confirmed the diagnosis of ABMR in 42 of 65 cases (65%) with histologically proven ABMR but did not in 23 of 65 cases (35%). Among 28 cases with absent diagnostic criteria group 3, only 2 of 19 cases (11%) with ABMR by MMDx but 6 of 9 cases (67%) with no ABMR by MMDx showed isolated glomerulitis (p = 0.0048). Among 65 cases with histologically proven ABMR, only 7 of 42 cases (17%) with ABMR by MMDx but 14 of 23 cases (61%) with no ABMR by MMDx showed isolated glomerulitis (p < 0.001). Overall, 14 of 65 cases (21%) with isolated glomerulitis showed ABMR diagnosis by MMDx.

Conclusion: Isolated glomerulitis is strongly associated with the absence of ABMR by MMDx not only when diagnostic criteria group 2 is missing but also when diagnostic criteria 3 is missing or ABMR is proven by histology. Our results may help to guide the indication for MMDx in clinical practice. However, the clinical significance of these results needs further investigation.

#6026

EVOLUTION OF MONOCLONAL GAMMOPATHY OF UNCERTAIN SIGNIFICANCE IN KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: Monoclonal gammopathy of uncertain significance (MGUS) is a frequent condition with an estimated prevalence of 3% in people over 50 years of age in the general population. Nowadays, more kidney transplants (KT) are performed in a population susceptible to present MGUS, and the evolution of this entity in KT recipients is currently unknown.

Method: We carried out a retrospective study of a cohort of KT recipients diagnosed with MGUS between 1996 and 2020, including patients with MGUS identified prior to kidney transplantation or during follow-up. We describe baseline, kidney transplantation, and hematological characteristics, analyzing the evolution of the hematological parameters according to the moment of appearance of MGUS.

Results: A total of 51 patients were included; in 28 (54.9%) MGUS appeared before transplantation, and in 23 (45.1%) after transplantation. Thirty-two (62.7%) were male, with glomerular pathology in 17 (33.3%) as the leading cause of chronic kidney disease. Hypertension (90.2%) and diabetes (27.5%) were the most common comorbidities. At renal transplantation, the median age is significantly higher in the pre-transplant MGUS group (62 years [IQR 54-66]) vs. 48 years [IQR 40-68]; p = 0.04). This group had a higher induction immunosuppression load than the post-transplant MGUS group (p = 0.01) due to a greater incidence of immunized KT recipients (p = 0.05). There were no differences in rejection, infections, or post-transplant neoplasia between both groups; however, higher renal graft loss was observed in the post-transplant MGUS group (10.7% vs. 43.5%; p = 0.02), probably explained by a longer follow-up time in this group. The most detected paraprotein was IgG (60.8%) and lambda light chain (51%), with a median blood concentration of 0.4 g/dl (IQR 0.2-1.4). In 45.1% of the cases, the paraprotein remained stable; it disappeared in 27.5%, and MGUS progressed to hematological neoplasia in 21.6%, including multiple myeloma, amyloidosis, and post-transplant proliferative syndrome. We did not detect significant differences in the evolution according to the moment of diagnosis of the MGUS (p = 0.7). Twelve renal biopsies were performed during post-transplant follow-up, detecting renal involvement by paraprotein in 5 (9.8%). Only 1 of them (1.96%) was defined as a monoclonal gammopathy of renal significance for not meeting the criteria for malignancy.

Conclusion: Close monitoring of MGUS in KT recipients is still necessary given the possibility of progression to hematological neoplasia, with a non-negligible percentage in our series of patients. Our cohort does not allow us to detect significant differences with an impact on the clinical course of MGUS or KT regarding the moment of the development of MGUS before or after transplantation.
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Cytokines IL-6, IFN-γ, TGF-β, and IL-10 were measured using the enzyme-linked immunosorbent assay, and SARS-CoV-2 spike protein-specific IgG titer by chemiluminescent microparticle immunoassay methods.

Results: We found a seroconversion rate of 115/132 (87.12%), with a median antibody titer of 706.40 au/ml (IQR, 215.45-1844.42) in the infection group and 63/78 (80.76%) with a median titer 145.20 (IQR, 80.52-3838.75) au/ml in the vaccinated group. The IL-6, IFN-γ, TGF-β, and IL-10 levels were significantly higher in both, the infection and vaccination groups as compared to the healthy control group. In the infection group, the pro-inflammatory cytokines IL-6 (55.41±24.30 vs. 31.64±16.98 pg/ml; p < 0.001), IFN-γ (91.21±33.09 vs. 61.69±33.28 pg/ml; p = 0.001), and IL-10 (91.31±40.59 vs. 61.69±25.67 pg/ml; p = 0.08) were significantly high in the seroconverter group as compared to non-seroconverter. Anti-inflammatory cytokines TGF-β (730.48±400.47 vs. 765.47±566.39 pg/ml; p = 0.92), and IL-10 (91.31±48.54 vs. 96.73±59.53 pg/ml; p = 0.88) were not significantly different between the seroconverter and non-seroconverter group respectively. Similarly, in the vaccination group, the pro-inflammatory cytokines IL-6 (50.31±25.67 vs. 30.00±11.19 pg/ml; p = 0.002), and IFN-γ (65.70±39.78 vs. 32.14±17.48 pg/ml; p = 0.001) were significantly high in seroconverter post-vaccination compared to non-seroconverter. In contrast, TGF-β (820.96±415.78 vs. 1045.57±204.66; p = 0.046) was elevated in non-seroconverter, and although IL-10 (93.18±35.45 vs. 112.90±59.61 pg/ml; p = 0.11) was not significantly high in non-seroconverter.

Conclusion: Inflammatory cytokines IL-6 and IFN-γ were significantly associated with seroconversion after SARS-CoV-2 infection and vaccination.
correlation between ECMO duration, age (p = 0.012), and LDH (p = 0.041); a significant positive correlation between D-dimer, CRP (p = 0.006) and PaO2 (p = 0.015). We found that post-discharge ventilatory support among survivors was needed in 48.1% and 11.4% (as O2 supplementation or CPAP, respectively).

**Conclusion:** ECMO should be considered for critically ill COVID-19 patients who develop refractory respiratory failure despite standard care.

**#4240** SUCCESSFUL PROPHYLAXIS WITH STROVAC VACCINE AGAINST URINARY TRACT INFECTION AFTER KIDNEY TRANSPLANTATION

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**Background and Aims:** Urinary tract infections (UTI) are the most common infections after renal transplantation with an estimated incidence between 10 and 98%. Recurrent urinary tract infections (rUTIs) increase mortality and reduce graft survival after renal transplantation. The present case describes an immunization strategy against bacterial strains after kidney transplantation.

**Method:** We administered urinary tract vaccine for prophylaxis for rUTIs after kidney transplantation. A kidney transplant recipient with 3 or more UTI episodes/year underwent immunization with 3 subcutaneous injections (once a week) of inactivated bacteria-StroVac (follow-up 12 months before to 12 months after immunization). StroVac contains 10 strains of inactivated bacteria (6 types of Escherichia coli, Proteus mirabilis, Morganella morganii, Enterococcus fecalis, Klebsiella pneumoniae). A year later the StroVac Booster was administered once. Urine culture analysis was given every 3 months for a year. Clinical and laboratory comparisons were made. The results were evaluated statistically.

**Results:** Before initiation of prophylaxis, patient had a UTI incidence of 5. The patient had symptoms such as fever, dysuria, or urgency and were positive in urine dipstick examination for pyuria or nitrutria. Vaccination with StroVac significantly reduced the incidence of UTI yielding a mean annual incidence of 1 (p<0.05).

**Conclusion:** StroVac is an effective and lasting non-antibiotic prophylaxis for rUTI, easy to administer with low rates of adverse events and should be offered to patients with rUTI after kidney transplantation.

**#5296** CYTOMEGALOVIRUS INFECTION AFTER COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

Gonçalo Pimenta, Sara Queiroz Conde and André Weigert

Centro Hospitalar Lisboa Ocidental, Nephrology, Lisbon, Portugal

**Background and Aims:** Kidney transplant recipients (KTR) have adverse COVID-19 outcomes due to the immunosuppressed status and multiple comorbidities. Cytomegalovirus (CMV) is one of the most frequent opportunistic infections after kidney transplantation. However, data concerning its reactivation after COVID-19 is scarce. Herein, we present a single-center cohort of KTR presenting with CMV infection after COVID-19 and its clinical outcomes.

**Method:** Single-center cross-sectional study including 22 KTR with CMV viraemia detected by quantitative polymerase chain reaction up to 6 months after COVID-19, between 2020 and 2022. Demographic and clinical data were collected from the electronic records.

**Results:** A total of 22 KTR (13 male) were included with a mean age of 55.5±15.5 years and a median Charlson score of 4 (IQR 3-6). Median time after transplantation was 65 months (IQR 12.5-174.5; 3 KTR with <6 months) and only one patient had been submitted to living-donor transplantation. Eight patients received induction therapy with antithymocyte globulin (ATG). At transplantation time, CMV serologic status had been: 50% D+/R+, 13.6% D+-/R- and 4.5% D-/R+. CMV infection prior to COVID-19 had been documented in 6 patients. Concerning COVID-19, severe or critical disease had been reported in 8 patients. Specific therapy had been used in 4 patients: 2 with remdesivir/baricitinib, one with remdesivir and one with molnupiravir. Moreover, immunosuppressive therapy had been adjusted in 11 patients, namely by withdrawing the antimetabolite and increasing steroids (7 patients). Median maximum steroid dose (expressed as equivalents of prednisone dose) had been 40 mg (IQR 20-40) and mean cumulative steroid dose had been 416±317 mg. CMV disease was documented in 8 patients (4 with gastrointestinal involvement) and the mean time of diagnosis after COVID-19 was 10±6 weeks. Maintenance immunosuppression included tacrolimus, antimetabolite and steroid in 12 patients; 6 patients had supratherapeutic levels of tacrolimus at CMV infection diagnosis. Median initial viraemia was 770 copies/mL (IQR 288-4106). Valganciclovir was used in 14 patients (one was already taking it as prophylaxis), ganciclovir in 4 patients and CMV enriched human intravenous immunoglobulin was used in one patient. Nine patients required hospitalization and 2 were transferred to an intensive care unit; one of these 2 patients died. Induction therapy with ATG. CMV serologic status at transplantation time, previous CMV infection, COVID-19 severity or supertherapeutic immunosuppressive drug levels were not associated with CMV infection severity or hospitalization. However, higher maximum steroid dose during COVID-19 was associated with CMV disease (p = 0.038), higher viraemia at diagnosis (p = 0.032) and hospitalization (p = 0.018).

**Conclusion:** CMV infection is a common and clinically relevant complication in KTR. Altered immunologic status after COVID-19 may predispose to this infection. In addition, immunosuppressive therapy adjustments, namely the increase in steroid dosing may be very relevant to favor reactivation of CMV. Larger studies are warranted, but careful monitoring could help identifying risk patients earlier and prophylaxis may be considered when increased corticosteroids are prescribed.

Figure 1: Annual incidence of urinary tract infection (UTI) before (baseline) and after initiation of StroVac vaccination (follow-up). Differences were tested for significance by Wilcoxon test, p < 0.05 was regarded as significant.
CLINICAL AND MOLECULAR SPECTRUM OF V-LESION
Anna Buxeda1,2, Maria José Pérez-Saéz2, Betty Odette Chamoun Huacón1,3, Javier Gimeno1,2, Irina Torres Rodriguez1, Julio Pascual1,2,3, Benjamin Adam2 and Marta Crespo1
1Hospital del Mar, Nephrology, Barcelona, Spain, 2University of Alberta, Laboratory Medicine and Pathology, Edmonton, Canada, 3Hospital Universitari Vall d’Hebron, Nephrology, Barcelona, Spain, 4Hospital del Mar, Pathology, Barcelona, Spain and 5Hospital Universitario 12 de Octubre, Nephrology, Madrid, Spain

Background and Aims: Isolated v-lesion is an increasingly recognized but clinically challenging entity. Some studies suggest that isolated v lesion may be caused by non-alloimmune etiologies such as ischemic injury. We aimed to characterize the allograft outcomes of isolated v-lesions according to post-transplant time (early: 0-1 month vs. late: >1 month) and further understand the significance of this lesion by characterizing its molecular phenotype in comparison with other forms of rejection v+.

Method: The NanoString B-HOT panel (770 genes) was used to measure the expression of six literature-derived gene sets in 92 archival FFPE kidney biopsies from two centers, including transplant biopsies with isolated v-lesion (n = 23), antibody-mediated rejection (ABMR) with v+ (n = 26), pure T-cell mediated rejection (TCMR) with v+ (n = 10), mixed rejection v+ (n = 23), and normal implant biopsies (Normal, n = 10). The evaluated gene sets included transcripts previously associated with ABMR, DSA (DSAST), endothelial injury (ENDAT), TCMR, early injury, and late injury. Gene expression was compared between groups using principal component and class comparison analyses. Death-censored graft survival according to diagnosis and time after KT was assessed.

Results: Isolated v+ early conferred the worst death-censored graft survival one year after the biopsy (40%) when compared to isolated v+ late (100%) or other forms of rejection (≥82%, p = 0.034). The principal component analysis demonstrated significant molecular overlap between sample groups (PC1: 29.4%, PC2: 8.1%). However, gene set analysis showed lower expression of TCMR-related genes in isolated v+ groups compared to TCMR and mixed rejection (p < 0.001). Both isolated v+ early and late had lower ABMR-related genes than ABMR, mixed rejection, and TCMR groups (p ≤ 0.022). Moreover, isolated v+ late showed lower DSAST and ENDAT gene set expression than ABMR (p ≤ 0.046); and lower early injury gene set expression than isolated v+ early, ABMR, TCMR, and mixed rejection (p ≤ 0.026). Late injury gene set expression was highest in TCMR and mixed rejection compared to the other groups (p ≥ 0.034).

Conclusion: These results suggest that early and late isolated v+ lesions display lower expression of TCMR-related genes than TCMR and mixed rejection and lower expression of ABMR-related genes than ABMR. Isolated v+ early confers a bad prognosis and is associated with higher expression of early injury genes compared to isolated v+ late, suggesting a different ethiology.

EBV-NEGATIVE KIDNEY TRANSPLANT RECIPIENTS AND PTLD: THE IMPACT OF INDUCTION THERAPY
Rose Mary Attieh1, Shenhen Mao1, Michael Mao1, Surakit Punghapong1, Wisit Cheungpasitporn2,3, Tambi Jarri1, Hani Wadel1, Burcin Tane1 and Napat Leepaphorn1
1Mayo Clinic Florida, Department of Transplantation, Jacksonville, United States of America and 2Mayo Clinic, Nephrology and Hypertension, Rochester, United States of America

Background and Aims: Individuals who are most susceptible to developing PTLD are those who are EBV-negative and receive organs from EBV-positive donors (EBV R-/D+). The evidence regarding the connection between ATG induction therapy and PTLD is inconsistent. No studies have specifically examined the relationship between ATG use and PTLD in subgroups of EBV-negative transplant recipients (EBV R-). Using the UNOS database, we studied the association between the use of induction agents and PTLD in EBV R-patients.

Method: We analyzed data from 2007 to 2022 of EBV R- patients who underwent their first kidney-only transplant and excluded those who received induction agents other than ATG, basiliximab, or alemtuzumab. We used logistic regression to evaluate the association between induction agents and PTLD.

Results: Of 20,531 recipients, 50.7% received ATG, 19.13% received basiliximab, 13.42% received alemtuzumab, and 16.75% received no induction. The overall PTLD incidence was 2.14%. ATG recipients had higher rates of deceased donor transplants, higher degree of HLA mismatch, longer dialysis vintage, and were less likely to be white, compared to non-ATG recipients. Multivariate analysis showed ATG recipients had a higher risk of PTLD compared to non-ATG (odds ratio = 1.47, p < 0.001). After excluding recipients who did not receive induction, ATG remained a significant independent risk factor for PTLD when compared to recipients who received either basiliximab or alemtuzumab (odds ratio = 1.35, p = 0.007). There was no statistically significant difference in PTLD risk among patients treated with basiliximab, alemtuzumab, or no induction (refer to Table 1).

Conclusion: The use of ATG induction in EBV-negative kidney transplant recipients is associated with a higher risk of PTLD compared to basiliximab, alemtuzumab, and no induction. The risk of PTLD should be considered when choosing induction therapy for this patient population.

Figure 1:
### Table 1:

<table>
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<tr>
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<th>P</th>
<th>Adjusted OR (95% CI)</th>
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<td><strong>PTLD</strong></td>
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<tr>
<td>ATG vs others</td>
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<tr>
<td>• ATG vs non-ATG</td>
<td>1.37 (1.13–1.66)</td>
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<td>1.47 (1.21–1.79)</td>
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<td>1.42 (1.05–1.94)</td>
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<td>1.26 (1.02–1.56)</td>
<td>0.03</td>
<td>1.35 (1.09–1.67)</td>
<td>0.007 &lt;0.001</td>
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<td>• ATG vs no induction</td>
<td>1.64 (1.22–2.22)</td>
<td>0.001</td>
<td>1.78 (1.31–2.42)</td>
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</table>

### No induction vs others

- **ATG vs no induction**
  
- **basiliximab vs no induction**
  
- **alemtuzumab vs no induction**
  
- **basiliximab + alemtuzumab vs no induction**
  
- **Alemtuzumab vs basiliximab**
  
- **alemtuzumab vs basiliximab**

*Adjusted for age, sex, race, transplant type, diabetes, dialysis duration, cPRA, HLA mismatch, acute rejection within a year, transplant era, and CMV serostatus.

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**#5146**

**KINETIC ESTIMATION OF GFR AND URINARY CREATININE EXCRETION RATE AS PREDICTORS OF DELAYED GRAFT FUNCTION IN RENAL TRANSPLANTS FROM DECEASED DONORS**

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**Background and Aims:** Delayed graft function (DGF) is a common complication after renal transplant. Definitions of DGF are based on analysis of estimated glomerular filtration rate (eGFR) underlying the plasma creatinine fluctuations after renal transplant. We tried to validate an early parameter of DGF in a renal transplant population based on the kinetic estimation of glomerular filtration rate, since this formula adds a quantitative dimension to the assessment of kidney function, and consequently predicting DGF could get a better post-transplant management.

**Method:** This is a longitudinal study of 886 renal transplant recipients from our center during the first post-transplant month. As we are searching for functional biochemical markers in renal transplant from deceased donors, we excluded patients with primary graft dysfunction. The final simple was composed of 574 adult kidney transplant recipients, 348 renal transplant from donors after circulatory death (DCD) and 226 from donors after brain death (DBD). The following are analyzed S-creatinine concentrations, serum Lactate dehydrogenase (LDH) and urinary creatinine excretion rate (CER).

**Results:** In DCD there was a significant correlation between DGF duration and all KeGFR and CER determinations during the first post-transplant week. The parameters that achieved the best correlation to predict DGF were KeGFR (r = 0.515; p < 0.001) and CER on the fourth day (r = 0.59; p < 0.001). We observed that serum LDH on the first day in the DBD group is associated with worse renal graft function at first, third month and one year after transplantation (p < 0.045, p < 0.05 and p < 0.067 respectively).

**Conclusion:** The determination of KeGFR and CER could predict the duration of DGE especially in DCD recipients. DCD recipients with DGF have significantly better graft survival at one year than DBD recipients with DGF (p < 0.001).

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**Figure 1:** a ROC curve of the KeGFR on day 4 to predict DGF greater than one and two weeks in recipients from renal transplant from donor after circulatory death.(AUC 0.80. P <.01). 1.b ROC curve of the urinary creatinine excretion rate on day 4 to predict DGF greater than one and two weeks in recipients from renal transplant from donor after circulatory death.(AUC 0.82 p <.01)
HLA COMPATIBILITY DOES NOT INFLUENCE KIDNEY GRAFT SURVIVAL AND DOES NOT IMPACT THE DEVELOPMENT OF POST-TRANSPLANT NEOPLASIA

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Background and Aims: HLA compatibility is a key issue in deceased and living kidney allocation, although the continuous improvement of immunosuppressive protocols might have reduced its relevance. However, an increased immunosuppression is associated with several adverse events, including the development of post-transplant neoplasia. Indeed, several reports demonstrated that the improvement in immunosuppressive drug efficiency corresponded to an increase incidence of malignancies after kidney transplantation. Thus, the aim of our study was to investigate the effect of HLA compatibility on kidney graft survival and incidence of post-transplant neoplasia.

Method: This is an observational, retrospective, multicenter center study including 1506 patients receiving a single kidney transplant at the Gemelli and Policlinico “Consorziale” kidney transplant centers from 1/1/2000 to 1/2/2022. The primary outcomes were death-censored graft survival and the development of post-transplant neoplasia. HLA compatibility was measured as the number of HLA mismatches (MM) at the three main class I (A and B) and class II (DR) loci. To this purpose, both donor and recipients were genotyped for HLA A, B and DR. We included in the analysis all deceased and living kidney donor transplants and excluded recipients from ABO incompatible living kidney donors and with pre-transplant donor specific antibodies.

Results: Based on HLA compatibility, we divided our patients’ population in three groups (0-2 MM, 369 patients 3-4 MM, 856 patients and 5-6 MM, 281 patients). At univariate analysis (Kaplan-Meyer) number of MM were not associated with death-censored graft survival and the development of post-transplant neoplasia. HLA compatibility was measured as the number of HLA mismatches (MM) at the three main class I (A and B) and class II (DR) loci. To this purpose, both donor and recipients were genotyped for HLA A, B and DR. We included in the analysis all deceased and living kidney donor transplants and excluded recipients from ABO incompatible living kidney donors and with pre-transplant donor specific antibodies.

Conclusion: In this observational retrospective multicenter analysis, we demonstrated that HLA incompatibility, as indicated by the number of HLA A, B and DR MM, does not predict death-censored graft survival and does not impact the development of post-transplant neoplasia. Our observation would suggest that the missing effect of HLA compatibility on graft outcome is not associated with an increased long-term over-immunosuppression.

CINACALCET IMPACT ON ESTIMATED GLOMERULAR FILTRATION RATE AMONG KIDNEY TRANSPLANT RECIPIENTS WITH SECONDARY HYPERPARATHYROIDISM: A CASE-CONTROL STUDY

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1 University Hospital of Nantes, Department of Nephrology and Clinical Immunology, Nantes, France, 2University Hospital of Nantes, Data Clinic, Nantes, France, 3University Hospital of Nantes, Center for Research in Transplantation and Translational Immunology, Nantes, France and 4University Hospital of Nantes, Institute for Digestive Tract Diseases, Nantes, France

Background and Aims: Secondary hyperparathyroidism (sHPT) is common in kidney transplant recipients. It remains unknown if Calcimimetic agents (as cinacalcet), oftenly used in this context, have an impact on mortality or morbidity. The objective of this work was to compare the renal and cardiovascular outcome of kidney transplanted patients with sHPT.

Method: Data from January 2008 to December 2019 were retrospectively extracted from the DIVAT database. 575 kidney transplant recipients with sHPT (PTH > 100 pg/ml) followed in Nantes University Hospital were separated into two groups: Treated (cinacalcet) and sHPT Controls (no cinacalcet). A propensity score was used to match the patients (age, sex, first transplant, transplantation before/after 2015, time on dialysis, history of cardiovascular disease, initial condition, anti-HLA class I and II immunization, corticosteroids, serum parathormone level). Biological data (including estimated glomerular filtration rate by CKD-Epi formula), cardiovascular events (coronaropathy, obliterating arteriopathy of the lower limbs, stroke), return in dialysis or related death were extracted from one year of transplantation to the last follow-up. Time-varying exposure Cox PH model was used.

Results: 292 patients were included after matching (146 Treated, 146 sHPT Controls). After one year of transplantation, serum parathormone was significantly higher in Treated patients compared to sHPT Controls (152 pg/mL vs 111 pg/mL respectively, p < 0.001), suggesting a more severe sHPT in Treated patients. 7% of Treated and 10% of sHPT Controls suffered from a cardiovascular event or related death during the follow up (HR = 1.28 [0.52; 3.14], p = 0.6). Return to dialysis or related death were more frequent in the Treated patients (HR: 1.90 [0.97 - 3.75], p = 0.06). At 48 months post-transplantation, estimated glomerular filtration rate was significantly decreased in Treated patients compared to sHPT controls (52.3 mL/min/1.73 m² vs 44.1, p = 0.006).

Conclusion: Our study highlights that kidney transplant recipients with sHPT treated with cinacalcet have a worse kidney graft outcome than non-treated sHPT patients. It remains to be assessed if this reflects an underlying more severe sHPT condition or a direct effect of cinacalcet on the graft function. This study needs to be completed by the assessment of bone mineralization. Parathyroidectomy for sHPT should be discussed in kidney transplant recipients with impaired glomerular filtration rate and/or cardiovascular events.

PROSPECTIVE ASSESSMENT OF THE NEED FOR AND ADDED VALUE OF MOLECULAR DIAGNOSTICS OF KIDNEY ALLOGRAFT BIOPSIES: AN EVALUATION IN CLINICAL PRACTICE

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1 University Hospital Zurich, Division of Nephrology, Zurich, Switzerland and 2University Hospital Zurich, Institute of Pathology, Zurich, Switzerland

Background and Aims: The Molecular Microscope Diagnostic System (MMDx) may resolve inconclusive histology findings, as preserved biopsy material can be examined after histology findings have been obtained. The extent to which this proposed approach can be implemented in clinical practice remains an open question.

Method: We prospectively analyzed 104 consecutive indication kidney allograft biopsies by histology and molecular diagnostics at the University Hospital Zurich from April 2022 to December 2022. Pathologists and clinicians with experience in molecular diagnostics assessed the need for MMDx by questionnaire when the histology report was available. Clinicians then assessed the added value of the molecular diagnostics by questionnaire when the MMDx report was available.

Results: 29 of 104 cases (28%) showed rejection by histology, 42 of 104 cases (40%) showed no rejection by histology, and 33 of 104 cases (32%) showed histologic findings insufficient to diagnose ABMR due to an absence of diagnostic criteria groups 2 and/or 3. Pathologists considered molecular diagnostics indicated in 42 of 104 cases (40%), 9 cases to give extra confidence, and 33 cases for diagnostic clarification concerning rejection. Clinicians considered molecular diagnostics indicated in 54 of 104 (52%) cases, 5 cases to give extra confidence, and 49 for diagnostic clarification concerning rejection. In 33 cases with histologic findings insufficient to diagnose ABMR, molecular diagnostics were considered indicated by pathologists and clinicians. Molecular diagnostics allowed the diagnosis of ABMR in 8 of 33 cases (24%). In addition, 11 of 104 cases (11%) showed a discrepancy between the histologic findings and the molecular diagnosis. Clinicians considered adjustment of treatment based on the MMDx report in 3 of 11 discrepant cases. Pathologists and clinicians considered molecular diagnostics indicated in 2 of 11 and 3 of 11 discrepant cases, respectively.

Conclusion: The need for molecular diagnostics goes beyond the recommendation of the 2018 Banff classification for histologic findings insufficient to diagnose ABMR. However, the added value of molecular diagnostics appears to be largely limited to these cases.
Results: A total of 1498 patients underwent renal transplant in this center. Only 33 patients had unusual/rare infections like nocardiosis, Rhodococcus, Melioidosis, Pneumocystis, Aspergillosis, Histoplasmosis, Parvovirus, and Parvovirus. The high index of suspicion should be present when patient is not responding to empirical antibiotics and culture didn’t grow routine organisms. The role of invasive investigations like bronchoscopy with BAL fluid would be considered whenever atypical infections like nocardiosis and aspergillosis were considered. Post-transplant cutaneous abscesses should not be treated with empirical antibiotics and always culture should be done to rule out infections like nocardiosis, pheohyphomycosis and histoplasmosis as treatment is different for each organism. Overall, the high index of suspicion, timely diagnosis, correct drug and duration of treatment will save the graft and patient.
a reduction in 77%, gastrointestinal side effects in 34%, EBV in 19% (two KTRs developed PTLD), CMV in 15%, and BK polyomavirus in 15%. The reduction was significantly more pronounced in KTRs under 11 years (87% vs. 61%, p=0.044). Tacrolimus seemed well tolerated and was sufficiently regulated according to a target through of five microg/L two months after transplantation (Figure 2).

**Conclusion:** Despite 74% of the KTRs receiving reduced immunosuppressive medication according to our protocol, the rejection rate was low, the graft survival was comparable to European reports, and only 11% developed dnDSA during follow-up. Scheduled reduction of MMF shortly after transplantation could decrease the adverse side effects and improve the treatment of paediatric KTRs.

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**Figure 1:** Mycophenolate mofetil dose (mg) per body surface area (m²) over time from transplantation. The mean and the alterations in each paediatric kidney transplant recipient.

**Figure 2:** Blood Tacrolimus through level over time from transplantation. The mean and the alterations in each paediatric kidney transplant recipient.

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**#5440**

**BONE TURNOVER MARKERS AND BONE MINERAL DENSITY 1 YEAR AFTER KIDNEY TRANSPLANTATION**

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**Background and Aims:** Alterations of bone metabolism are a hallmark of chronic kidney disease (CKD) patients and do not completely ameliorate after kidney transplantation. In the setting of a secondary analysis of a RCT, we evaluated changes of bone turnover biomarkers (BTM) and their associations with changes of bone mineral density (BMD) as assessed by DXA.

**Method:** Sixty-six Kidney Transplant (KTx) recipients were enrolled between 2014-2017. In these patients, at baseline (T0) and 12 months (T12) we measured BTM (Figure 1). The prevalence of vitamin K deficiency was assessed based on undercarboxylated-BGP (uc-BGP) cut-off: > = 4.5 ng/ml, whilst dephosphorylated-ucMGP (dp-ucMGP) we considered a cut-off > 500 pmol/L levels. DXA data were assessed at lumbar spine, femoral neck, total hip, one-third and ultradistal radius both baseline and after one year, evaluating the changes in areal BMD (aBMD). Results were expressed as mean ±SD or median and inter-quartile range, as appropriate. Correlations were investigated by Spearman’s analysis.

**Results:** The mean age of enrolled patients was 51 ± 13 years, 34% were female. BMI was on average 27.8 ± 5.5 kg/m². 24 patients (39.3%) were pre-emptive and 37 (60.7%) on dialysis and 19% of patients had a history of fracture. In Figure 1 the trend of BTM 1 year after KTx. We highlighted a significant reduction of PTH, CTX, P1NP, and VKDPs. This latter while improving but was not completely restored. Table 1 shows the correlations between the percentage variation of BTM and percentage variation of BMD at several sites evaluated.

**Conclusion:** In the first-year post-transplant, along with the improvement of renal function, PTH values were reduced as well those of CTX and P1NP. Moreover, we observed an inverse correlation between BTM and BMD, the reduction of bone turnover expressed by the trend of BTM translates into an improvement of BMD.
**Figure 1:** Significative changes of BTM (A) and VKDPs (B) in first-year post-transplant.

**Table 1: Spearman Correlation between BTM and percentage change of aBMD at 12 moths. Significative correlations are expressed in bold. P values are given when < 0.05.**

<table>
<thead>
<tr>
<th></th>
<th>LS BMD %</th>
<th>FN BMD %</th>
<th>One-third radius BMD %</th>
<th>Ultradistal radius BMD %</th>
<th>Total Hip BMD %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MGP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.4119 (0.0102)</td>
<td>0.2987</td>
<td>−0.2549</td>
<td>−0.0294</td>
<td>0.3423 (0.0354)</td>
</tr>
<tr>
<td>T12</td>
<td>−0.0140</td>
<td>−0.2405</td>
<td>−0.1296</td>
<td>0.0789</td>
<td>−0.1990</td>
</tr>
<tr>
<td>% change</td>
<td>−0.2816</td>
<td>−0.4674 (0.0053)</td>
<td>0.0778</td>
<td>0.1704</td>
<td>−0.5374 (0.0010)</td>
</tr>
<tr>
<td><strong>Dp-ucMGP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.2262</td>
<td>0.1062</td>
<td>0.1003</td>
<td>−0.1069</td>
<td>0.0844</td>
</tr>
<tr>
<td>T12</td>
<td>−0.2112</td>
<td>−0.3465 (0.0265)</td>
<td>−0.0293</td>
<td>0.1239</td>
<td>−0.2495</td>
</tr>
<tr>
<td>% change</td>
<td>−0.3806 (0.0264)</td>
<td>−0.2639</td>
<td>−0.2388</td>
<td>0.0827</td>
<td>−0.3137</td>
</tr>
<tr>
<td><strong>ucBGP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.4478 (0.0048)</td>
<td>0.4900 (0.0018)</td>
<td>−0.0197</td>
<td>0.0167</td>
<td>0.4534 (0.0041)</td>
</tr>
<tr>
<td>T12</td>
<td>−0.1396</td>
<td>−0.1085</td>
<td>−0.0204</td>
<td>0.0786</td>
<td>−0.2136</td>
</tr>
<tr>
<td>% change</td>
<td>−0.3381</td>
<td>−0.3702 (0.0312)</td>
<td>−0.1453</td>
<td>0.0301</td>
<td>−0.5141 (0.0019)</td>
</tr>
<tr>
<td><strong>BGP</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.6226 (&lt; 0.001)</td>
<td>0.3771 (0.0196)</td>
<td>−0.1196</td>
<td>−0.0286</td>
<td>0.5060 (0.0012)</td>
</tr>
<tr>
<td>T12</td>
<td>0.2017</td>
<td>0.0326</td>
<td>−0.3117 (0.0473)</td>
<td>−0.0071</td>
<td>−0.1596</td>
</tr>
<tr>
<td>% change</td>
<td>−0.4735 (0.0047)</td>
<td>−0.3678 (0.0324)</td>
<td>−0.2358</td>
<td>−0.1413</td>
<td>−0.6306 (0.0001)</td>
</tr>
<tr>
<td><strong>P1NP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.5015 (0.0002)</td>
<td>0.4602 (0.0009)</td>
<td>0.1517</td>
<td>0.0156</td>
<td>0.5757 (&lt; 0.001)</td>
</tr>
<tr>
<td>T12</td>
<td>−0.0570</td>
<td>−0.1400</td>
<td>−0.2670</td>
<td>−0.1862</td>
<td>−0.1548</td>
</tr>
<tr>
<td>% change</td>
<td>−0.4616 (0.0011)</td>
<td>−0.4593 (0.0013)</td>
<td>−0.3602 (0.0139)</td>
<td>−0.1255</td>
<td>−0.5373 (0.0001)</td>
</tr>
<tr>
<td><strong>CTX</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.4160 (0.0027)</td>
<td>0.4162 (0.0029)</td>
<td>−0.0126</td>
<td>0.0630</td>
<td>0.5430 (0.0001)</td>
</tr>
<tr>
<td>T12</td>
<td>0.0308</td>
<td>−0.2228</td>
<td>−0.3988 (0.0045)</td>
<td>−0.1295</td>
<td>−0.2585</td>
</tr>
<tr>
<td>% change</td>
<td>−0.2254</td>
<td>−0.4343 (0.0029)</td>
<td>−0.4107 (0.0051)</td>
<td>−0.1730</td>
<td>−0.5514 (0.0001)</td>
</tr>
<tr>
<td><strong>Bone ALP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0.4270 (0.0028)</td>
<td>0.2900</td>
<td>−0.0363</td>
<td>−0.1596</td>
<td>0.3967 (0.0063)</td>
</tr>
<tr>
<td>T12</td>
<td>0.1072</td>
<td>−0.1982</td>
<td>−0.3133 (0.0267)</td>
<td>−0.3100 (0.0284)</td>
<td>−0.2231</td>
</tr>
<tr>
<td>% change</td>
<td>−0.2282</td>
<td>−0.3917 (0.0094)</td>
<td>−0.2289</td>
<td>−0.1007</td>
<td>−0.5405 (0.0002)</td>
</tr>
<tr>
<td><strong>PTH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>−0.2866</td>
<td>−0.4607 (0.0021)</td>
<td>−0.4274 (0.0048)</td>
<td>−0.1002</td>
<td>−0.5666 (0.0001)</td>
</tr>
<tr>
<td>T12</td>
<td>0.1918</td>
<td>−0.2071</td>
<td>−0.3390 (0.0160)</td>
<td>−0.0570</td>
<td>−0.2911 (0.0402)</td>
</tr>
</tbody>
</table>
| % change       | 0.4891 (0.0006)    | 0.4098 (0.0052)    | 0.1555                 | 0.1044                   | 0.4504 (0.0019)       

**#6011**

**VIRAL INFECTION AND DE NOVO PRODUCTION OF DONOR SPECIFIC ANTIBODIES IN KIDNEY TRANSPLANTATION: DCD VS DBD**

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AOU Careggi, Nephrology Dialysis and Transplantation, Florence, Italy

**Background and Aims:** Viruses are among the most common causes of opportunistic infection after transplantation and an accurate screening and follow-up is needed in order to prevent related complication as systemic damages and worsening of kidney function. On the other hand, in the first years after transplantation, antibody-mediated rejection (ABMR) is one of the first cause of graft lost and de novo production of donor specific antibody (dnDSAs) is the main source. In this monocentric study we analysed data of 255 patient transplanted from January 2016 to February 2022. We studied the incidence of viral infection and dnDSAs in the first one year after transplantation in different sub-groups of patients.

**Method:** Data was obtained from our monocentric registry, from January 2016 to February 2022. Starting from 299 kidney transplantation we obtained 255 patients with a complete annual follow-up for viral infection and DSA monitoring. We compared the incidence of viral infection and dnDSAs in
Abstracts

IMMUNOLOGIC EFFECTS OF THE DECREASE OF IMMUNOSUPPRESSION AFTER SARS-COV-2 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

Marina Urrutia, Javier Paúl, Maria Molina Gomez, Josep Riera, Carles Cañameras Fugasot, Ines Perezpaya, Omar Taco, Rosana Gelpi, Angela Casas, Laura Cañas, Rosely Rodriguez, Jordi Bover and Ana Vila

Hospital Universitari Germans Trias i Pujol, Badalona, Spain

Background and Aims: The decrease of immunosuppression (IS) in kidney transplant (KT) recipients with SARS-CoV-2 infection was proposed during the first years of the pandemic due to the lack of knowledge of the course of the infection and the absence of vaccines and specific treatment. The effects of this decrease are being assessed in a medium-long term.

Method: Unicentric retrospective study that included 19 patients with a kidney biopsy after a SARS-CoV-2 infection (120 days). We measured acute kidney injury (AKI) after de infection, decrease in the IS during the infection, rejection episodes and renal function evolution during 24 months after the infection.

Results: The studied group was constituted by 19 patients from which 57.9% (11/19) men, age 56 (51, 70), being the first KT in 78.9% (15/19) of them. The IS induction was in a 57.9% (11/19) Basiliximab and in a 42.1% (8/19) of patients. There was a graft loss in 26.3% (5/19), transplanted treated with rATG as induction therapy (DBDt+DCD). rATG was associated with higher dsDNAs rate, especially in DBD treated with rATG. On the best of our knowledge, this data was never observed before. These data, due to the low number of cases, need to be confirmed from larger cohorts. Moreover our study underlines how significant is to develop a personalized approach in order to reduce complications associated to immunosuppressive therapies.

Conclusion: Viral infection and dsDNAs are two paramount aspects in kidney transplantation and demonstrate different incidences depending on donation profile and immunosuppressive induction therapy. Specifically rATG seems to be associated to an higher rate of viral infection and DCD is the more relevant sub-group. Furthermore, rATG was associated with higher dsDNAs.

#6915

POST-TRANSPLANTATION LYMPHOPROLIFERATIVE DISORDER: COMPARISON OF RISK AND PROGNOSTIC FACTORS BETWEEN KIDNEY AND OTHER ORGAN TRANSPLANT RECIPIENTS

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1Medical University of Warsaw, Department of Immunology, Transplantation and Internal Medicine, Warsaw, Poland, 2Medical University of Wrocław, Department of Nephrology and Transplantation Medicine, Wrocław, Poland, 3Medical University of Silesia, Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Zabrze, Poland, 4Medical University of Warsaw, Liver and Internal Medicine Unit, Warsaw, Poland, 5Medical University of Silesia, Department of Biophysics, Division of Laboratory Medicine, Kosnowiec, Poland, 6Medical University of Warsaw, University Clinical Center, Warsaw, Poland, 7Medical University of Warsaw, Department of General and Transplant Surgery, Warsaw, Poland, 8Medical University of Warsaw, Department of General, Transplant and Liver Surgery, Warsaw, Poland and 9Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warszaw, Poland

Background and Aims: Post-transplantation lymphoproliferative disorder (PTLD) is a potentially fatal complication of transplantation, pathogenesis of which remains to be fully understood. In solid organ transplant recipients, the risk of disease development is associated with graft type and is lowest for kidney (KTR), intermediate for liver (ITR) and high for lung (LngTR) transplant recipients. The aim of this study was to investigate the factors contributing to the development and treatment outcomes of PTLD and compare their impact on the populations of KTRs, ITRs and LngTRs.

Figure 1: Incidence of viral infection and dnDSAs in DBDs, DBDt, DCD and rATG.
Method: In this retrospective cohort study we have included all KTRs, LTRs and LngTRs diagnosed with PTLD at four transplantation centers in Poland between 2002 and 2022. The following data were collected from the patients’ medical records: immunosuppression (IS), viral infections, PTLD type, treatment and outcomes. Mann-Whitney U-test was used to assess the differences in group composition, and univariate Cox regression was used to determine the impact of variables upon PTLD time of onset and patient survival. p-values below 0.05 were considered statistically significant.

Results: We identified 31 KTRs, 31 LTRs and 5 LngTRs who fulfilled the inclusion criteria. Among the patients of the transplantation center leading this study, PTLD was diagnosed in 22 (0.82%) out of 2699 KTRs and 29 (2.03%) out of 1386 LTRs. Two thirds of the patients were male, the median age at first transplantation was 39 years and the median age at PTLD diagnosis was 48 years. KTRs and LTRs significantly differed in IS treatment: more KTRs used steroids (GCS, p = 0.042) and cyclosporin (CsA, p = 0.001), more LTRs used tacrolimus (TAC, p < 0.001) and anti-CD25 induction (p = 0.003). KTRs developed PTLD later than LTRs (141 months after transplantation vs 53 months, p = 0.004) and LngTRs (5 months after transplantation, p = 0.001). Monomorphic PTLD was the most frequent in KTRs (80.6%, p = 0.032). Initial IS treatment reduction was used in 91% of all patients. The groups did not significantly differ in the type of PTLD treatment. TAC had the opposite effect on PTLD time of onset in KTRs (HR = 2.92, 95%CI 1.35-6.34, p = 0.007) and LTRs (HR = 0.18, 95%CI 0.04-0.89, p = 0.036). At the end of the observation period 16.7% of KTRs, 51.6% of LTRs and 80% of LngTRs were alive. Complete remission was achieved in 48.4% of KTRs, 61.3% of LTRs and 80% of LngTRs. KTRs had the highest rate of loss to follow up at 41.4%. Patient survival was longer in patients who were treated with anti-CD20 monotherapy (HR = 0.28, 95%CI 0.08-0.96, p = 0.042) and surgery (HR = 0.33, 95%CI 0.12-0.91, p = 0.031).

Conclusion: KTRs develop PTLD significantly later than LTRs and LngTRs, and disease onset is associated with TAC use. Low KTR survival rate is related to the high rate of loss to follow up (e.g. loss of graft function and return to hemodialysis). Surgical treatment, used mainly in focal PTLD improves patients’ survival. The positive effect of anti-CD20 monotherapy on patients’ survival reflects the efficacy of current stratified treatment regimens for PTLD.

#6603
THE ROLE OF ANTICOAGULATION IN KIDNEY TRANSPLANTATIONS FROM UDCD WITH HIGH RESISTANCE INDEX

Maria Molina Gomez1,2, Marina Urrutia3, Gregorio A. Romero-González1, Javier Paíl3, Fredzia Amada Graterol Torres3, Josep Riera2, Carles Cañameras Fugastos1, Ines Perezpaya2, Omar Tác3, Laura Cañas2, Rosely Rodriguez2, Mario Fernandez1, Ester Gonzalez Montes1, Angel Sevillano1, Enrique Morales1, Jimena Cabrera3, Jordi Bover1, Ana Vila2 and Amado Andrés Belmonte1

1Hospital Universitario 12 de Octubre, Madrid, Spain, 2Hospital Universitari Germans Trias i Pujol, Badalona, Spain and 3Hospital Evangélico y Militar. PPTG Centro de Nefrología Hospital de Clínicas Fac de Medicina UDELAR, Montevideo, Uruguay

Background: Kidney transplantations (KT) from uncontrolled donation after cardiac death (uDCD) achieve very good outcomes to short and long follow-up, but the incidence of primary non-function and venous thrombosis (VT) is very high. The resistance index (RI) after kidney transplantation increases in the VT cases and in other kidney diseases.

Aims: To describe the effect of prophylactic anticoagulation in KT from uDCD with RI ≥0.8 to avoid VT and its secondary effect.

Method: Unicentric retrospective cohorts study that included all KT from uDCD with RI ≥0.8 measured by ecodoppler in the first 72 hours post-transplantation. We compared one group, which never received anticoagulation (Group I), and a second one which received prophylactic anticoagulation (Group II). Sodic heparin was the administer anticoagulant to achieve aPTT 1.5-2 time normal range and/or low molecular weight heparin adjusted to patient’s weight and renal function.

Results: We included 107 KT from uDCD with RI ≥0.8, with 36 in Group I and 76 in Group II. In Group I the donors were younger (39 ± 12 vs 46 ± 8; p = 0.003) and there were more men donors (97.2% vs 81.7%; p = 0.032). The prevalence of VT was higher in Group I (19.4% vs 0%; p = 0.001). Patients in Group II needed more red blood transfusions (19.4% vs 39.4%; p = 0.05) and had more macroscopic haematuria (5.6% vs 21.1%; p = 0.049). The competing risk analysis showed a higher probability to develop a VT in non-anticoagulation group (p = 0.00012) than anticoagulation group or other causes of primary non-function (Figure 1).

Conclusion: The prophylactic anticoagulation treatment in KT from uDCD with RI ≥0.8 decreases the VT incidence and it is safe for a donor recipient.

#6128
IMPACT OF MANNOSE-BINDING LECTIN DEFICIENCY ON GRAFT SURVIVAL IN TRANSPLANT RECIPIENTS WITH IGAN

Emma Stea, Francesco Pesce, Rossana Franzin, Elisabetta Sturdà, Ighli Di Bari, Paola Pontrelli and Loreto Gesualdo

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Background and Aims: The progression of IgA nephropathy (IgAN) has been associated with Mannose -Binding Lectin levels (both excess or deficiency). The MBL deficiency, is associated with the rs5030737, the rs1800450 and the rs1800451, who represent the “O” allele. Since lectin pathway deregulation may impact on IgA progression on native kidney we hypothesized that the presence of the “O” allele and therefore MBL deficiency, could influence also the graft survival in recipients with a biopsy-proven diagnosis of IgAN on native kidneys. Therefore we investigated the role of MBL “O” allele in kidney transplant recipients with IgAN.

Method: We enrolled 32 kidney transplant recipients with biopsy-proven IgAN on the native kidney. The region in MBL encompassing the SNPs rs5030737, rs1800450 and rs1800451 were amplified using PCR and analyzed by Sanger sequencing.Clinical data at baseline and during the follow-up were collected from patients’ records. An eGFR ≥60mL/min/1.73m2 (MDRD equation) was considered as main outcome at univariate and multivariate analyses.

Results: The 38% of patients carry the “O” allele and 62% of patients the “A” allele which is associated with the wild genotype. No difference between the two groups as for demographic features, donor and transplant-related variables has been found. Interestingly we found that patients with the “O” allele had a worse graft outcome (P = 0.01) during a mean follow-up of 151 months (Figure 1). The “O” allele was an independent predictor for the graft survival in a Cox survival analysis model adjusted for donor’s and recipient’s age, acute rejection,
Figure 1: Impact of the "A" Vs "O" allele on graft outcome, KM survival curve.

Figure 2: Correlation between genotype and MBL serum levels. "A" allele: Median MBL value = 527.05 ng/ml (interquartile 366.7-1788.5 ng/ml); "O" allele: Median MBL value = 229 ng/ml (interquartile 110.42-296.7). P < 0.001.

and disease recurrence (HR 0.046; 95% I.C. 0.005-0.423; P = 0.01). Moreover we found a link between the genetic background and the MBL serum level (Figure 2).

Conclusion: Our study suggest a potential role of the MBL deficiency in the longterm graft dysfunction in kidney transplant recipient with IgAN.

#4670

HYPERPARATHYROIDISM DURING 1ST YEAR OF RENAL TRANSPLANT IS ASSOCIATED WITH LONG TERM GRAFT LOSS

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Background and Aims: Persistent hyperparathyroidism (HPT) is a frequent problem, especially during the first year after Renal transplant (RTx). We aimed to evaluate the possible association between parathormone (PTH) levels during 1st year of RTx and long-term graft loss (GL) in RTx patients (RTx-p).

Method: We retrospectively evaluated 871 RTx-p, transplanted in our unit from 2004 to 2020. We measured main renal function and mineral metabolism parameters at 1 month (T1), 6 months (T6) and 12 months (T12) after RTx. Renal outcome was intended as GL during the global follow-up (FU) of 103 ± 60 mths.

Results: Mean age at RTx was 49±13 yrs and 58% of RTx-p were male. Most of the RTx-p were on hemodialysis (HD) before RTx (77%) with a mean dialysis vintage of 53±52 months. Most of our cohort (84%) received a kidney from a deceased donor. HPT was highly prevalent during the 1st year of FU; at T1 79% of RTx-p were HPT, of which 63% had secondary HPT (SHPT) and 16% had tertiary HPT (THPT). Comparable prevalence was observed at T6 (HPT 80%; SHPT 64%; THPT 16%) and at T12 (HPT 77%; SHPT 62%; THPT 15%). A strong significant correlation was found between HPT type and GL at every time point [T1 GL: no HPT 6%, SHPT 11% THPT 24%, P < 0.0001 - T6 GL: no HPT 9%, SHPT 9% THPT 22%, P < 0.0001 - T12 GL: no HPT 8%, SHPT 9% THPT 21%, P < 0.001]. Moreover, PTH levels at T1 (GL-: 90.3 [50.6-165.6] vs. GL+: 61.7 [37.4-98.8] < 0.0001), at T6 (GL-: 83.6 [47.1-152.4] vs. GL+: 56.1 [38.3-89.7] < 0.0001) and at T12 (GL-: 69.8 [44-121.9] vs. GL+: 54.6 [36.4-84.1] p = 0.008) were significantly correlated to GL. PTH levels at T1 and T6 were associated with long-term GL [T1, OR: 3.3 (1.3-8.1), p = 0.01 - T6, OR: 3.9 (1.7-9.2), p = 0.01]. Then we considered PTH levels as mean exposure during the first year. Mean PTH exposure alone was strongly associated with GL [OR: 5.7 (2.7-11.9), p < 0.0001]. A multivariate logistic regression analysis was also performed. In the model, we considered 1st year mean PTH exposure and the main factors associated with GL (pre-RTx dialysis vintage, 1st year rejection, T12 uric acid, T12-Proteinuria and T12-MDRD). Mean PTH exposure remained strongly and independently associated with long-term GL (OR 3.1 [1.4-7.1], p = 0.008). We finally performed a ROC curve to calculate the best 1st-year mean PTH cut-off to predict long-term GL. AUC was 0.658, with a p < 0.0001. Using Youden index we identified the best mean PTH cut-off to be 88.6 pg/ml.

Conclusion: In our cohort of 871 RTx-p, the prevalence of HPT during the first year of RTx is quite high. High PTH levels during 1st year of RTx were independently associated with long-term GL. HPT might be considered a therapeutic target to prevent long-term graft failure.

#5256

REACTIVATION OF HEPATITIS B VIRUS IN KIDNEY TRANSPLANT RECIPIENTS WITH RESOLVED INFECTION: A SINGLE-CENTER EXPERIENCE

Gonçalo Pimenta, André Weigert and Sara Querido Conde

Centro Hospitalar Lisboa Ocidental, Nephrology, Lisbon, Portugal

Background and Aims: Patients with end-stage renal disease (ESRD) frequently present serologic evidence of previous contact with hepatitis B virus (HBV). Although uncommon, HBV reactivation after kidney transplantation (KT) may cause serious complications and adverse outcomes in these patients. However, data regarding risk factors for reactivation are still scarce. This study aims to describe a cohort of patients with resolved HBV infection who showed reactivation of the virus after KT.

Method: Retrospective cohort study including patients with resolved HBV infection who underwent KT between August 2007 and December 2021. Resolved HBV infection was defined as being seronegative to HB surface
antigen (HBsAg) and seropositive to HB core antibody (HBcAb), regardless of HB surface antibody (HBeAb) status. HBV reactivation after KT was defined as seropositivity to HBsAg or presence of HBV-DNA in the serum (viremia). Preemptive prophylactic entecavir was not used. Demographic and clinical data were collected from the electronic records.

**Results:** A total of 104 patients (70.2% male) were included with a mean age of 52±10 years. Prior to KT, 93.3% were seropositive to HBsAb. Seropositivity to other viruses was present in 18 patients: human immunodeficiency virus (HIV) alone in 5 patients; hepatitis C virus (HCV) alone in 11 patients; and coinfection in 2 patients. Deceased-donor KT was performed in 94.2% and only 9 patients had a previous KT. Rituximab was used as induction immunosuppressive therapy in 13 patients. Median follow-up time after KT was 75 months (IQR 37-115). HBV reactivation occurred in 6 patients with a median time after KT of 5 months (IQR 3-11.5). At reactivation diagnosis, median HBsAg titer was 83.2 (IQR 34-784.5; reference range < 1) and median viral load was 6.7 × 10^6 copies/mL (IQR 0.4 × 10^6-378 × 10^6). Only one patient presented seropositivity to HBsAg without viremia. Half of these patients were seropositive to HBsAb prior to KT and became seronegative at reactivation diagnosis. No liver enzyme elevation was registered at reactivation diagnosis. Donor HBcAb status, coinfection with HIV or HCV, and recipient HBsAb status were not associated to HBV reactivation after diagnosis. Donor HBcAb status, coinfection with HIV or HCV, and recipient HBsAb status were not associated to HBV reactivation after diagnosis. Half of these patients were seropositive to HBsAb prior to KT and became seronegative at reactivation diagnosis. No liver enzyme elevation was registered at reactivation diagnosis. Donor HBcAb status, coinfection with HIV or HCV, and recipient HBsAb status were not associated to HBV reactivation after diagnosis. Half of these patients were seropositive to HBsAb prior to KT and became seronegative at reactivation diagnosis. No liver enzyme elevation was registered at reactivation diagnosis.

**Conclusion:** Hepatitis B virus reactivation is possible after kidney transplantation and may pose major adjustments to the treatment, namely the immunosuppressive therapy. Careful monitoring of hepatitis B virus serology and viremia could be particularly useful in early diagnosis and prompt approach to its reactivation. Larger and multi-center studies are warranted to identify specific risk factors in this population and prevent reactivation.

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**#3368**

**DIAGNOSTIC YIELD AND CLINICAL SIGNIFICANCE OF SYSTEMATIC CARDIAC SCREENING OF KIDNEY TRANSPLANT CANDIDATES USING CARDIAC COMPUTED TOMOGRAPHY**

Marie Bodilsen Nielsen1,2, Malene Iversen1, Amal Derali1, Jonathan Dahl1, Bente Jespersen1, Per Iversen1, Simon Winther1 and Henrik Birn1,2

1 Aarhus University Hospital, Department of Renal Medicine, Aarhus N, Denmark; 2 Aarhus University, Department of Biomedicine, Aarhus C, Denmark; 3 Gødstrup Hospital, Department of Cardiology, Herning, Denmark and 4 Aarhus University, Department of Clinical Medicine, Aarhus, Denmark

**Background and Aims:** Cardiovascular screening of kidney transplant candidates is currently recommended, although the patient value is presently questioned. The prognostic ability is known, whereas systematic screening may have less recognized effects such as incidental findings, triggering of additional investigations, procedural complications, delay of transplantation and deselection of patients for kidney transplantation. To address this, we characterized the diagnostic yield and clinical implications of systematic screening for cardiovascular disease using cardiac computed tomography (CT) in asymptomatic kidney transplant candidates.

**Method:** In a single-centre, observational study, we included all potential kidney transplant candidates ≥ 40 years or with diabetes or on dialysis treatment ≥ 5 years, who were systematically referred to cardiac CT (a non-contrast enhanced CT scan and a coronary CT angiography) prior to kidney transplantation between March 2014 and September 2019 in North and Central Denmark Regions. Patient records were examined to obtain data on baseline characteristics, additional investigations, incidental findings, conference decisions.

**Results:** In total, 473 patients underwent cardiac CT. The screening programme led to additional cardiac investigations in 155 patients (33%) and viremia could be particularly useful in early diagnosis and prompt approach to its reactivation. Larger and multi-center studies are warranted to identify specific risk factors in this population and prevent reactivation.

**Conclusion:** The clinical significance of the screening by cardiac CT was limited, and one third of patients had to go through additional investigations. Few patients were revascularised and no patients rejected for transplantation. No evidence of contrast-induced acceleration of kidney function decline was observed.

**#4743**

**OMNIGRAF (COMBINED GENE EXPRESSION AND DD-CF DNA) USE IN MONITORING RENAL ALLOGRAFT REJECTION IN MULTIORGAN TRANSPLANT RECIPIENTS**

Ziad Zaky1, James Fleming2 and Juston Weems2

1 Cleveland Clinic, Glickman Urological and Kidney Institute, Cleveland, United States of America and 2 Eurofins, Transplant Genomics, Framingham, MA, United States of America

**Background and Aims:** To date there is no clinically available non-invasive biomarker to monitor for renal allograft rejection in multiorgan transplant recipients. TruGraf (Gene expression profile) and TRAC (dd-cf DNA), as part of the biomarker panel OmniGraf, have shown to be reliable “rule out” tests for subclinical rejection in stable kidney transplant recipients. However, the validity and utility of these tests in monitoring for renal allograft rejections in the setting of multiorgan transplants has yet to be assessed. The aim of this study is to assess the feasibility of using the biomarkers individually, as well as together in the OmniGraf biomarker panel, to assist in making the decision to perform a renal allograft biopsy in multiorgan transplant recipients.

**Method:** This is an ongoing prospective, observational sample collection study in any multiorgan (kidney + non-renal organ) undergoing a renal allograft biopsy. Biopsies were considered positive if they showed rejection in the kidney based on Banff 2019 and included borderline changes as positive results. Copper-Pearson 95% CI were used for sensitivity, specificity, and accuracy; standard logit CIs were used for NPV and PPV. For TruGraf, (TX = negative result) and (not-TX = positive test). For TRAC, 0.7% was used as the threshold for all organs except for those that had a liver transplant, where a threshold of 15% was used to determine positive vs. negative.

**Results:** Paired renal allograft surveillance biopsies and biomarker samples were available for 20 patients. Of the 20, 9 (45%) were liver-kidney transplants, 6 (30%) were heart-kidney transplants, and 5 (25%) were kidney-pancreas transplants. Nine (45%) of the patients were male, 14 (70%) were White, 5 years, who were systematically referred to cardiac CT (a non-contrast enhanced CT scan and a coronary CT angiography) prior to kidney transplantation between March 2014 and September 2019 in North and Central Denmark Regions. Patient records were examined to obtain data on baseline characteristics, additional investigations, incidental findings, conference decisions.

**Results:** In total, 473 patients underwent cardiac CT. The screening programme led to additional cardiac investigations in 155 patients (33%) and viremia could be particularly useful in early diagnosis and prompt approach to its reactivation. Larger and multi-center studies are warranted to identify specific risk factors in this population and prevent reactivation.

**Conclusion:** The clinical significance of the screening by cardiac CT was limited, and one third of patients had to go through additional investigations. Few patients were revascularised and no patients rejected for transplantation. No evidence of contrast-induced acceleration of kidney function decline was observed.

**Table 1: TruGraf Diagnostic Performance.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Balanced Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>TruGraf</td>
<td>66% (9-99)</td>
<td>88% (64-99)</td>
<td>65% (29-90)</td>
<td>100% (100-100)</td>
<td>83% (60-96)</td>
</tr>
</tbody>
</table>

**Table 2: TRAC Diagnostic Performance (0.7% Threshold for SPK, Heart/Kidney; 15% Threshold for Liver/Kidney).**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAC</td>
<td>50% (1-99)</td>
<td>94% (70-100)</td>
<td>73% (20-97)</td>
<td>85% (58-96)</td>
<td>83% (58-96)</td>
</tr>
</tbody>
</table>

**Table 3: OmniGraf Diagnostic Performance (0.7% Threshold for SPK, Heart/Kidney; 15% Threshold for Liver/Kidney).**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>OmniGraf</td>
<td>50% (1-99)</td>
<td>100% (79-100)</td>
<td>100% (100-100)</td>
<td>86% (60-96)</td>
<td>88% (64-98)</td>
</tr>
</tbody>
</table>

*OmniGraf ++ used for positive tests, all others considered negative.

**Table 4: OmniGraf Diagnostic Performance (0.7% Threshold for SPK, Heart/Kidney; 15% Threshold for Liver/Kidney).**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>OmniGraf</td>
<td>100% (16-100)</td>
<td>81% (54-96)</td>
<td>64% (39-83)</td>
<td>100% (100-100)</td>
<td>86% (62-98)</td>
</tr>
</tbody>
</table>

*OmniGraf -/ used for negative tests, any panel with at least one positive test considered positive.
5 (25%) were Black, and 1 patient was Hispanic. The mean age was 50 ± 13 years. Average SrCr was 1.3 ± 0.5 mg/dL. Of the 20 paired biopsies and samples, 2 (10%) had only TruGraf results, while the other 18 (90%) had OmniGraf (TruGraf and TRAC). There were 2 rejections (borderline changes). Diagnostic performance is presented in tables 1–4. Both TruGraf and TRAC individually had NPV of 89% and 85%, respectively, and PPV of 65% and 73%, respectively. When analyzing the performance of the OmniGraf biomarker panel, OmniGraf +/- showed a 100% PPV and OmniGraf -/+ showed a 100% NPV.

Conclusion: In this analysis of renal allograft biopsies in a multiorgan transplant cohort, TruGraf, TRAC (when using organ-dependent thresholds) had reasonable diagnostic performance as a “rule out” test. When the tests are combined into OmniGraf, the PPV and NPV were 100% when both tests agreed with each other. These outcomes justify potential use and the need for continued analysis of the utility of the OmniGraf biomarker panel in monitoring renal allograft in multiorgan transplant recipients.

#4856
HISTOLOGICAL FINDINGS OF ACUTE HUMORAL REJECTION IN PATIENTS WITH STANDARD IMMUNOLOGICAL RISK: ANTIDV-MEDIATED DAMAGE OR MICROVASCULAR INJURY?
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Background and Aims: The development of acute humoral rejection (AHR) is increased in patients with high immunological risk. Taking into account the highly sensitivity from the techniques used to determine anti-HLA antibodies, the histological findings of AHR in the immediate post-transplantation period in patients without preformed anti-HLA antibodies (standard immunological risk) is unexpected. We propose the implication of non-immunological factors as the origin of these findings. Our aim was to evaluate the histological findings of AHR in the immediate post-transplantation period in patients with standard immunological risk and to analyze factors related to its appearance.

Method: A multicenter retrospective study was carried out including renal transplants performed between January-2014 and December-2022, excluding patients with pre-transplant HLA sensitization and failures due to thrombosis. A descriptive analysis of transplant recipients with standard immunological risk who developed histological findings of AHR was made (AHR). In addition, we performed a comparative analysis of this group with the patients who developed AHR with pre-transplant HLA sensitization (AHRs).

Results: Of the 351 patients, 18 (5.1%) presented AHR, all were first transplants without pre-transplant anti-HLA antibodies. Fourteen donors were brain death and four due to controlled circulatory arrest. Banff AHR was grade I in 1 patient, grade II in 13 patients, and III in 3 cases. 50% showed thrombotic microangiopathy (TMA). Seven (38.9%) failed after a mean follow-up of 28.7±26.1 months. The failure etiologies were chronic rejection (3) and primary dysfunction (4). No patient presented anti-HLA antibodies during the follow-up and 3 have received a second transplant without complications. When comparing the AHR group with the AHRs (n = 14), we observed a greater age of the donor in AHR (median 71.5 vs 56.5, p = 0.02) a higher percentage of donor due to controlled circulatory arrest (22% vs 0%, p = 0.005) and with history of Hypertension (66.7% vs 42.9%, p = 0.09). Recipient age was higher in AHRs (median 64.5 vs 51, p = 0.025), with a higher proportion of retransplant in AHRs (42.9% vs 0, p = 0.002). In AHRs, DGF (100% vs 57.1%, p = 0.002) and thrombotic microangiopathy (50% vs 14.3%, p = 0.03) were more frequent. Renal function was worse during the follow-up in AHR (p = 0.05).

Conclusion: The histological finding of RAH in patients with standard immunological risk appears as an aggressive process with negative consequences on graft survival. The absence of anti-HLA antibodies in subsequent follow-up suggests the involvement of non-immunological factors in its developing. Processes related to the maintenance and/or extraction of organs could favor the appearance of microvascular damage, with histological findings suggestive of AHR especially in older grafts and with comorbidity. Studying these cases is essential to identify risk groups and establish appropriate therapeutic strategies.

#5094
PREGNANCY OUTCOME AFTER KIDNEY TRANSPLANTATION AND IMPACT ON GRAFT FUNCTION
Ahmed Alkot, Samir Sally, Mohamed Sakhr, Mahmoud Zahrans and Salwa ElWasif
Egypt

Background and Aims: Within 2 to 3 weeks of a successful renal transplantation, the fertility of women in childbearing age improves; however, pregnancy after kidney transplantation is challenging and may be associated with increased maternal and fetal complications. To study the prevalence of pregnancy and pregnancy related complication after kidney transplantation. Method: A retrospective cohort study conducted on 236 patients out of 3000 kidney transplant recipient who underwent renal transplantation (RT) at Mansoura Urology and Nephrology Centre between March 1976 and December 2019, divided into two groups, group I: 118 kidney transplant recipient who experienced pregnancy at any time after kidney transplantation and Group II: 118 kidney allograft recipients who didn’t experience pregnancy after renal transplantation, they were matched according to age, duration of renal transplantation and they are comparable in primary immunosuppressant drugs. All kidney recipients were reviewed for preoperative, operative, and post-operative details also we record maternal and fetal complication.
Results: Prevalence of pregnancy in our centre is 191 pregnancies in 118 women who had undergone kidney transplantation between 1976 and 2019. We have found that the mean age of pregnancy between (26.27±4.37 - 29.89±4.6), the mean gestational age between (33.69±6.4 - 33.7±7.5) weeks, the live birth rate is 126 (66%). Preterm delivery rate in our study is 85 (44.5%), neonatal death 8 (4.1%), miscarriage 59 (30.9%), intrauterine foetal death 6 (3.1%) and birth defect 4 (2%). The prevalence rates of gestational hypertension is 87 (45.5%), preeclampsia 48 (25.1%), gestational diabetes 19 (9.9%), urinary tract infection 36 (18.8%), and graft rejection 8 (4.1%) during pregnancy. caesarean section is the most common method of delivery in our study 133 (69.6%). Conclusion: The risk of maternal and fetal complications is still high in RT patients and requires multidisciplinary care. All should be considered in patient counseling and clinical decision making. So we recommend educating the transplanted patients to allow for outcome optimization and minimization of complications.

#5548
THE PROGNOSTIC VALUE OF LYMPHOCYTE SUBSETS IN ANTIBODY RESPONSE AFTER SARS-COV2 VACCINATION IN DIALYSIS PATIENTS AND KIDNEY TRANSPLANT RECIPIENTS
Ioannis Mallioras1, Christos Georgopoulos1, Anila Duni2, Georgios Markopoulos3, Ethlymios Pappas2, Gerasimos Baxevanos2, Konstantina Gartzonika4, Eirini Christaki5, Haralampos Milionis6 and Evangelia Nounoumi1
1University Hospital of Ioannina, Department of Nephrology, Ioannina, Greece, 2University Hospital of Ioannina, Laboratory of Haematology - Unit of Molecular Biology, Ioannina, Greece, 3General Hospital of Filipotes, Hemodialysis Unit, Filipotes, Greece, 4Hatzikosta General Hospital of Ioannina, Internal Medicine Department, Ioannina, Greece, 5University Hospital of Ioannina, Microbiology Laboratory, Ioannina, Greece and 6University Hospital of Ioannina, Department of Internal Medicine, Ioannina, Greece

Background and Aims: Mortality due to SARS-COV-2 infection in hemodialysis (HD) patients and kidney transplant recipients (KTRs) is high. Despite intensive vaccination programs in these vulnerable populations, the adequacy of the respective generated immune responses is significantly lower than the general population and additional booster doses have been recommended by multiple health systems and the World Health Organization. The humoral and cellular immune responses to SARS-COV-2 vaccination remain still under further study in HD patients and KTRs. The aim of our study was to determine the predictive value of lymphocyte subpopulations in the production of antibodies against SARS-CoV-2 after the second dose of the vaccine.

Method: The cohort of this prospective study (ClinicalTrials.gov, NCT04932876) included 34 HD patients and 54 KTRs who received two doses of the BNT162b2 (Pfizer–BioNTech). Lymphocyte subpopulations, including B cells, CD4+ and CD8+ T cells as well as naive and memory T lymphocytes subpopulations among others were analyzed by flow cytometry at three time points, before vaccination (T0), before the 2nd dose (T1), 2 weeks after the 2nd dose (T2). Exclusion criteria included previous infection by SARS-CoV2 as well as infection by SARS-CoV2 during study follow-up. The anti-SARS-CoV2 antibody (Ab) response was assessed by using the ARCHITECT IgG II Quant test (Abbott). Titers >50 arbitrary units (AU)/ml were considered positive for seroconversion at T1 and at T2. A multiple linear regression model was applied separately to the two subgroups of patients.

Results: The mean age of the kidney transplanted recipients was 58.5 years of age while the mean age of HD patients was 68.5 years of age. The analysis of KTRs revealed that the populations of CD19+ lymphocytes, CD3+CD16+56+ cells and CD4+CD45RO lymphocytes can predict antibody formation (p-ANOVA <0.001) based on the multiple regression model. Ab = 4669+519*CD19-226*CD3+CD16+56-139* CD4+CD45RO. The analysis of HD patients revealed that the populations
of CD19+ lymphocytes, CD45RA+CD45RO lymphocytes, CD4 to CD8 ratio, CD3-CD16+56+ cells and CD4+CD45RO lymphocytes can predict antibody formation (p-ANOVA<0.001) based on the multiple regression model: Ab = 20267+835.3*CD19-286*CD45RA+375.2*CD4+ CD45RO+851*CD4/CD8-187.3*CD3-CD16+56+. The two regression models explain the variation of the dependent variable (Ab), according to the adjusted R² index, at a rate of 24% and 67% respectively. The 2 models were analyzed for possible residual autocorrelation (DW statistic > DU > DL in both models). No multicollinearity was observed (All VIF< 1). Normality of the residuals and homoscedasticity also met the criteria for both regression models.

Conclusion: Quantification of lymphocyte subpopulations by flow cytometry appears to have a significant prognostic value regarding development of antibodies after vaccination against SARS-CoV-2, especially in KTRs. The above models can predict patients’ response to vaccination based on specific lymphocyte subpopulations. More studies are needed to validate these predictive models.

#2566
THE EFFECT OF ULTRASOUND-GUIDED COMPRESSION IMMEDIATELY AFTER RENAL GRAFT BIOPSY ON POST BIOPSY BLEEDING
Moataz Fathy Abdelnaceem
Faculty of Medicine Cairo University, Nephrology, Cairo, Egypt

Background and Aims: Renal biopsy is the gold standard for pathological diagnosis of graft dysfunction. Minor complications occur as haematuria, arteriovenous fistula (AVF) and/or small hematomas in 17% of cases. Major complications that require additional treatment as blood transfusion, surgical or interventional procedure. Bleeding may be excessive that may deteriorate ending in graft nephrectomy.

Method: For 6 months period, 213 renal biopsy procedure in clinically indicated patients, performed at interventional nephrology unit 144 men and 59 women, mean age 42 years old, were included. Adequate biopsies were considered showing at least ten glomeruli and 2 blood vessels. Immediate after core withdrawal, operator started ultrasound guided compression using 3.5-5 MHZ convex probe for 5 minutes at site of needle entrance compressing biopsy track against the graft. Post biopsy bleeding examined (peri-nephric, sub-capsular, haematuria and urinary bladder hematomas).

Results: Percentage of bleeding complications was compared with bleeding complications of previous 200 biopsies performed at the same centre with same operator using ordinary hand compression technique. Bleeding complications reduction by more than 60% especially percentage of perinephric hematomas.

Conclusion: Ultrasound guided compression technique post renal graft biopsy may reduce incidence of bleeding complications post biopsy.

#3822
POLYOMAVIRUS INFECTION MONITORING BY QUANTITATIVE PCR IN KIDNEY RECIPIENTS AS AN INSTRUMENT FOR PREVENTING POSTTRANSPLANT COMPLICATIONS
Alexandra Arinovich1, Tamara Amrivosieva1, Zoya Bohush1, Natalia Paklonskaya1, Elena Kishkurno1, Kirill Komissarov2 and Aleh Kalachyk3
1 The Republican Research and Practical Center for Epidemiology and Microbiology, The laboratory for infections with a natural reservoir, Minsk, Belarus; 2 State Institution “Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology”, Department of Nephrology, Renal Replacement Therapy and Kidney Transplantation, Minsk, Belarus and 3 State Institution “Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology”, Minsk, Belarus

Background and Aims: Polyomaviruses (PyV) are ubiquitous human viral pathogens. BKV and JCV representing this viral family are common causative agents of viral complications among kidney recipients. Viral load higher than 1 × 10^5 copies/ml in urine (viremia) or 1 × 10^6 copies/ml in serum (viremia) in posttransplantation period may lead to polyomavirus-associated nephropathy (PVAN), hemorrhagic cystitis (HC) or even kidney transplant failure. The aim of the study was to assess PyV reactivation frequency in patients during 12 months after renal transplantation (RT) and to identify molecular subtypes of BKV and JCV.

Method: We examined 3207 samples of biological material (serum and urine) of 763 adult (>18 years) patients who underwent renal transplantation (RT) at the State Institution “Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology”, Healthcare institutions “Brest Regional Clinical Hospital”, “Vitebsk Regional Clinical Hospital Belarus”, “Mogilev Regional Clinical Hospital Belarus”. These patients were divided into 2 groups: group 1 included 394 patients examined only for BKV infection, group 2 – 356 recipients examined for both BKV and JCV infection. Serum and urine samples for regular monitoring were collected from patients before RT, every 2 weeks first 3 months, then at 6, 9, 12 months after RT. In the case of complication development samples from patients were collected later than 1-year monitoring period. PyV DNA was detected by real-time PCR. Viral DNAs from 17 BKV-positive and 11 JCV-positive patients were molecular typed by partial sequencing of VP1 genome region. Confidence intervals for the proportions were calculated using Wald’s method.

Results: Results showed that BKV detection total frequency in the group 1 was 14.47% [11.32%; 18.3%], almost all patients developed viremia, only 2.54% [1.32%; 4.67%] had viremia. In the group 2 PyV DNA was detected in 46.07% [40.96%; 51.26%] of recipients: 19.10% [15.34%; 23.52%] had BKV infection, 19.94% [16.11%; 24.42%] – JCV, 7.02% [4.76%; 10.2%] – BKV+JCV mixed infection. Frequency of viremia was 6.74% [4.53%; 9.87%] in this group. Maximal BKV viral load levels reached 1.2 × 10^12 copies/ml in urine and 5.9 × 10^9 copies/ml in serum. JCV loads were up to 3 × 10^6 copies/ml in urine and 1.2 × 10^8 copies/ml in serum. Then we analyzed frequency of PyV detection before RT and during the first year after RT among the 102 recipients. Results displayed on the Fig. 1 showed that the peak of PyV infection registration and the higher risk for patient had a place on the 1.5-2.5 months after RT. Quantitative monitoring of viral load in posttransplant period was the
basis for the correction of the applied immunosuppressive therapy regimens in relation to the recipients with a high viral load (higher than $1 \times 10^7$ copies/ml in urine or $1 \times 10^4$ copies/ml in serum). The results of molecular typing showed that 17 BKV isolates belonged to subgroups Ib-2 and Iv-c-2 (12 and 5 isolates, respectively). Within subgroups Ib-2 isolates formed 3 clusters corresponding to 3 separate genovariants. JCV isolates belonged to subtype 1A, 1B and 2A (7, 3 and 1 of isolates, respectively). The last one had 99% nucleotide sequence similarity with Greece and South Korea isolates.

**Conclusion:**
Our data demonstrated an importance of PyV DNA monitoring of kidney recipients in the posttransplant period starting from the first days after RT to predict development of PyV complications as PVAN, HC or others by correcting the immunosuppressive therapy.

**OBSERVATIONAL STUDY OF HUMORAL RESPONSE TO SARS-COV-2 MRNA VACCINATION IN A COHORT OF RENAL TRANSPLANTS COMPARED TO PRIMARY IMMUNE DEFICIENCY**

Rahima Hashemi1, Kunigal Shivakumar2, Claire Nicholas3, Malini Bhole4 and Caroline Webber4

1The Dudley Group NHS Foundation Trust, Nephrology, Dudley, United Kingdom, 2The Dudley Group NHS Foundation Trust, Nephrology, United Kingdom, 3Dudley Group NHS Foundation Trust, Nephrology, United Kingdom, 4The Dudley Group NHS Foundation Trust, Immunology, United Kingdom and 5Dudley Group NHS Foundation Trust, Immunology, United Kingdom

**Background and Aims:**
Uraemia in chronic kidney disease impairs both innate and adaptive immune response and is responsible for high failure of vaccination against infection [1]. With a rising global burden of CKD prevalence and mortality, [2] optimising humoral response is important part of management especially in the presence of immunosuppressants in renal transplant patients. There is lacking data in this group and immunosuppressants likely play a bigger role in impairing humoral response hence we compare a group of renal transplant patients (RTs) with a group of patients with primary immunodeficiency (PID).

**Method:**
Non-randomised RTs were recruited between January 2021 to January 2022 and underwent voluntary SARS-CoV-2 vaccination and were tested for immune response. Abbott UK SARS-CoV-2 antibody test was used to identify previous SARS-CoV-2 infection with positive 'N-antibody' titre and immunity with positive 'S-antibody' titre prior to vaccination and 3-8 weeks after each vaccination. Results were analysed with Odds Ratios and Fisher Exact Probability.

**Results:**
A total of 30/51 in the RT group were 'S-antibody' positive; 3 after first vaccination, 21 after second and additional 3 after third vaccination dose (3 patients were 'S-antibody' positive prior to vaccination from previous SARS-CoV-2 infection). In the PID group, 24/30 achieved a significantly positive 'S-antibody' after single vaccination and 27/30 after the second vaccination (Figure 1). No patient tested negative for 'S-antibody' on subsequent testing once they became positive. Compared to PID, transplant patients were much less likely to have positive 'S-antibody' after first vaccination (OR 0.03; 95% CI 0.01 – 0.11, $p < 0.0001$) and second vaccination (OR 0.13; 95% CI 0.03 – 0.46, $p = 0.0012$). Within the transplant group, patients on mycophenolate mofetil (MMF) were less likely (OR 0.12; 95% CI 0.01 – 1.01, $p = 0.036$) to respond to vaccination (Figure 2). Conversely, the patients on azathioprine were more likely to have positive 'S-antibody' response (OR 7.27; 95% CI 0.83 – 63.4). Comparatively patients on tacrolimus were relatively less likely to respond (OR 0.35; 95% CI 0.06 – 1.86). There was no significant difference observed between patients on steroids (OR 0.82 95% CI 0.21 – 3.28), Ciclosporin (OR 1.9; 95% CI 0.33 – 10.88) or patients on two compared to three immunosuppressants (OR 1.6; 95% CI 0.45 – 5.63). Patients within the transplant group who only had single vaccination were less likely to be 'S-antibody' positive (OR 0.21; 95% CI 0.04 – 1.2). There were no significant differences within gender, age, ethnicity, primary renal pathology or co-morbidities.
Conclusion: Renal transplant patients, in particular those on MMF have impaired humoral response to SARS-CoV-2 vaccination compared to PID group which is similar to previous studies [3]. There is significant humoral response to second SARS-CoV-2 vaccination in renal transplant patients which was maintained for the observed study period.

REFERENCES


#3280

PREVALENCE OF POLYPHARMACY AND ASSOCIATED ADVERSE OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

Sungeyeon Kim, Myung-Gyu Kim and Tai Yeon Koo

Department of Internal Medicine, Korea University Anam Hospital, Seoul, Rep. of South Korea

Background and Aims: Polyparmacy (PP) continues to increase, and is associated with numerous adverse clinical outcomes and mortality. Although the burden of medication in kidney transplant recipients (KTRs) is well-known, PP has not been characterized in detail in the KTRs. The aim of this study was to assess the prevalence of PP among KTRs and the association between PP and clinical outcomes in the KTRs.

Method: A total of 1,080 KTRs from multicenter observational cohort study in Korea between 2012 and 2016 (KNOW-KT) were included in the study. PP was defined as the use of more than 10 medications per day.

Results: The PP prevalence at 1, 2, 3, 5, and 8 years after transplantation was 37.9%, 37.3%, 36.5%, 37.1% and 25.4%, respectively. The prevalence of diabetes, dyslipidemia and history of cardiovascular disease was significantly higher in PP group than in non-PP group (the use of fewer than 10 medications). The mean follow-up period was 6.9 years, and there were 69 graft failures, 63 new-onset cardiovascular diseases, and 36 deaths. When the effect of PP prescribed at 1-year post-transplant on clinical outcomes was analyzed, there was no difference in glomerular filtration rate between the non-PP and PP groups, and the hazard ratio of graft failure and death in the PP group was 1.07 (0.718 to 1.59) and 1.37 (0.71 to 2.64), respectively, compared to the non-PP group. However, multivariate analysis adjusted for classical risk factors showed that PP independently increased the risk of new cardiovascular disease (adjusted HR 1.78 (1.07-2.96)) after KT.

Conclusion: These results showed that PP is common in KTRs, and considering the adverse effects of PP on KT outcomes, physician’s attention and efforts are needed to systematically manage and prevent inappropriate PP after KT. Long-term and large-scale research is needed to establish management guidelines for PP in the future.

#3385

A STUDY OF CLINICAL SPECTRUM AND THE OUTCOME IN LIVE KIDNEY TRANSPLANT RECIPIENTS IN A TERTIARY CARE CENTRE OF INDIA

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Background and Aims: Kidney transplantation has become the treatment of choice for end-stage renal disease as it leads to longer survival and superior quality of life. There is a remarkable disparity in the access and outcome of kidney transplant across the world. Limited health care resources, difficulty in access or sometimes non availability of appropriate medications, difficulties with transportation, limited availability of Nephrologists are common challenges in developing countries and also within a country like India due to diverse socioeconomic and cultural backgrounds. We present the pattern of infection, various causative organisms, causes of allograft dysfunction and the clinical outcome of the admitted live kidney transplant recipients in Nephrology department of a tertiary care center from North-East India.

Method: This was a single center retrospective observational study carried out in Nephrology Department of Gauhati Medical College, Guwahati, India. The data were collected from the medical records. All the admissions of live renal allograft recipients during the period May 2017- May 2022, were included in the study.

Results: Out of a total of 156 admissions of renal transplant recipients, male to female ratio was 3:7:1. Among the live KTRs basic disease, most common was chronic glomerulonephritis (44.8%) followed by CTID (23.9%). Infection related complications were present in 72 (46.1%) cases. Among infection UTI (n = 29, 16.6%) was most common followed by pneumonia (n = 24, 15.4%)

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No of patients</strong></td>
</tr>
<tr>
<td>Infections</td>
</tr>
<tr>
<td>UTI</td>
</tr>
<tr>
<td>Pneumonia (all causes)</td>
</tr>
<tr>
<td>Cellulitis</td>
</tr>
<tr>
<td>Diabetic foot</td>
</tr>
<tr>
<td>CMV Diarrhoea</td>
</tr>
<tr>
<td>TB meningitis</td>
</tr>
<tr>
<td>BK Nephropathy</td>
</tr>
<tr>
<td>Bacterial Meningitis</td>
</tr>
<tr>
<td>Esophageal candidiasis</td>
</tr>
<tr>
<td>Perinephric abscess</td>
</tr>
</tbody>
</table>
Table 2: Break up of infections among the patients.

<table>
<thead>
<tr>
<th>Infection Type</th>
<th>No of patients</th>
<th>Percentage (n = 156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI (organisms)</td>
<td>29</td>
<td>n = 29</td>
</tr>
<tr>
<td>E. Coli</td>
<td>11</td>
<td>37.9% (M/C)</td>
</tr>
<tr>
<td>Enterococcus species</td>
<td>7</td>
<td>24.1%</td>
</tr>
<tr>
<td>Klebsiella Species</td>
<td>5</td>
<td>17.2%</td>
</tr>
<tr>
<td>Mixed flora</td>
<td>4</td>
<td>13.7%</td>
</tr>
<tr>
<td>CONS</td>
<td>2</td>
<td>6.9%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>24</td>
<td>n = 24</td>
</tr>
<tr>
<td>Bacterial</td>
<td>11</td>
<td>45.8%</td>
</tr>
<tr>
<td>Fungal</td>
<td>6</td>
<td>25%</td>
</tr>
<tr>
<td>CMV</td>
<td>3</td>
<td>12.5%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3</td>
<td>12.5%</td>
</tr>
<tr>
<td>PCP</td>
<td>1</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

Various causes of graft dysfunction (biopsy proven) were ATI (Acute tubular injury), CNI toxicity, chronic ABMR, acute TCMR and chronic TCMR. NODAT was found in 14 (9%) of the cases. Out of theses 4 cases, 1 had bacterial pneumonia and 3 had UTI. Of 72 admissions with infection, total 8 patients succumbed to their illness with mortality rate of 11.1%. The most common cause of mortality was sepsis due to UTI.

Conclusion: The number of admissions of renal transplant cases has increased significantly in last 5 years, indicating the increased availability and affordability of renal transplantation in our country. Of 156 admitted live KTRs, infection was seen in 46.1% (n = 72) cases. UTI remained the most common infection (n = 29, 16.6%) followed by pneumonia (n = 24, 15.4%). Graft dysfunction was seen in 33.9% (n = 53) cases. Chronic ABMR was the most common cause (n = 30, 19.2%) for graft dysfunction. Neglect of necessary hygiene, ignorance of regular follow up and dysregulated immunosuppressive doses have contributed to high infection rate. Lack of regular follow up in post-transplant period due to logistic issues and lack of access to immunosuppressive drugs, etc. are major contributing factors for graft dysfunction in our set up. The condition worsens with the difficult terrain, repeated floods, and lack of transportation from remote areas in North Eastern part of India.

Table 3: Graft dysfunction in KTRs.

<table>
<thead>
<tr>
<th>Graft Dysfunction</th>
<th>No of patients</th>
<th>Percentage (n = 156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft dysfunction (biopsy proven)</td>
<td>53</td>
<td>33.9%</td>
</tr>
<tr>
<td>Acute Tubular Injury</td>
<td>4</td>
<td>2.6%</td>
</tr>
<tr>
<td>CNI Toxicity</td>
<td>8</td>
<td>5.1%</td>
</tr>
<tr>
<td>Acute ABMR</td>
<td>3</td>
<td>1.9%</td>
</tr>
<tr>
<td>Chronic ABMR</td>
<td>30</td>
<td>19.2%</td>
</tr>
<tr>
<td>Acute TCMR</td>
<td>1</td>
<td>0.6%</td>
</tr>
<tr>
<td>Chronic TCMR</td>
<td>1</td>
<td>0.6%</td>
</tr>
<tr>
<td>Recurrence of basic disease</td>
<td>6</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

EFFECTIVENESS OF ORAL FOSFOMYCIN PROPHYLAXIS IN KIDNEY TRANSPLANT RECIPIENTS

Nancy Daniela Valencia Morales, Isabel Pérez-Flores, Rómulo Katsu Loaya López, María Angeles Moreno de la Higuerá Díaz, Beatriz Rodríguez Cubillo, Natividad Calvo Romero and Ana Sanchez Fructuoso

Hospital Clínico San Carlos, Nefrology, Madrid, Spain

Background and Aims: Urinary tract infections (UTIs) are one of the most common infectious complications in kidney transplant recipients (KTR), which are of great importance due to their high morbidity and recurrent nature. Our main objective was to evaluate the effectiveness of oral fosfomycin prophylaxis in a group of high-risk patients with recurrent/relapsing urinary tract infections.

Method: Retrospective study of a cohort of 60 KTR with frequent UTIs who had been prescribed daily fosfomycin calcium or fosfomycin trometamol every 7-10 days for prophylactic purposes. Demographic, clinical, analytical and microbiological data were collected during a year before and after prophylaxis.

Results: The median age was 61.8 (55.6-71.2) years, 68.3% were men, with 7.4 (2.8-13.6) years since the transplant. The main etiologies of the underlying renal disease were: autosomal dominant polycystic kidney disease 20%, chronic glomerulonephritis 18.3%, chronic tubulointerstitial nephropathy 10%, and diabetic kidney disease 10%. In 51.7% there was chronic pathology of the urinary tract (mainly vesico-prostatic disease, 24.8% and vesico-ureteral reflux, 15%), with a history of urological surgery in 23.3%. Up to 20% of the KTR had some type of endourological device (permanent/intermittent bladder catheter, percutaneous nephrostomy, Bricker, etc.). The most frequently isolated germs were: E. coli and K. pneumoniae, 35.2 and 13.6% pre-prophylaxis and 28.3 and 22.6%, post-prophylaxis, respectively. The median number of UTI pre vs post-prophylaxis was 2 (1-4.75) vs. 1 (0.5-1.6) episode/patient/year (p = 0.001), with a reduction in UTI episodes in 69% of patients. Admissions were also reduced, going from 35% in the pre-prophylaxis year to 10% post (p = 0.001). After prophylaxis, the percentage of resistance to fosfomycin increased from 26 to 54%, and a greater number of multi-resistant germs were isolated, 17.7 pre vs 35% post-. The renal function remained stable during follow-up [CKD-EPI pre - 47.2(20.8) vs 47.2(21.2) ml/min post-].

Conclusion: Oral fosfomycin prophylaxis may be useful in KTR despite the underlying urological pathology, managing to reduce UTI episodes and the need for admission for this reason.
Assessment of Fracture Risk in Kidney Transplant Recipients by FRAX Score Without Bone Mineral Density

Magdy Elsharkawy, Ahmed Emara, Abdelrahman Elbraky and Shaimaa Zaki Abdelmegied

Nephrology and Transplantation Department, Faculty of Medicine, Ain Shams University Hospital, Cairo, Egypt

Background and Aims: Bone disease post-transplantation is a major cause of morbidity in kidney transplant (KT) recipients, with a significantly higher risk of fractures and mortality. This study investigated the added value of calculated 10-year fracture risk for major osteoporotic fracture (MOF) and hip fracture by FRAX score with an assessment of risk factors in KT recipients.

Methods: A cross-sectional study included 71 live-related KT recipients. Demographic, clinical, and laboratory data were recorded. The 10-year fracture risk for MOF and hip fracture were calculated using FRAX score without bone mineral density in recipients who completed at least 1 year after KT.

Results: The prevalence of MOF (>3% risk of fracture) was 14.1% (10 patients), MOF (<3% risk of fracture) was 85.9% (61 patients). A high hip fracture score (>3% risk of hip fracture) was in 10% (1 patient). There was a significant difference between both groups (>3% vs <3% fracture risk) in age, MOF score, hip fracture score, and serum albumin p-value were <0.00001, <0.00001, 0.000134, and 0.043009 respectively. The analysis of demographic data of the patients with a score (>3% fracture risk) showed that 70% were males (7 patients), 50% (5 patients) had BMI >30 and the main cause of ESRD pre-transplant was lupus nephritis and glomerulonephritis in 50% (5 patients) that exposed for long periods of immune suppression pre-transplant. In 80% (8 patients) were 1st transplant, 10% (1 patient) were 2nd transplant, and 10% (1 patient) was a combined liver-kidney transplant. The rejection episode was zero%. There was a significant difference in patients’ fracture risk >3% in phosphorus pre-transplant versus post-transplant p-value 0.01.

Conclusion: FRAX score without bone mineral density has shown a low percent of fracture risk (<3%) in most kidney transplant recipients and high scores were associated with high BMI, phosphorus, and exposure pre-transplant to immune suppression.

Quality of Life as Represented by Physical Activity Was Improving After Full Correction of Post-Transplant Anemia


Hamed Alessa OTC, Nephrology, Kuwait

Background and Aims: Recent studies showed positive impact of correction of post-transplant anemia (PTA) on general health, exercise capacity, and
physical scores. So we conducted this prospective randomized controlled trial (RCT) to assess quality of life after full correction of post-transplant anemia in renal recipients receiving erythropoietin stimulating agents.

**Method:** We recruited 247 kidney transplant recipients with stable graft function in this RCT with 2 groups according to their target hemoglobin (11-12 g/dl, group 1, n = 183) and (13:15 g/dl group 2, n = 64) which was achieved using erythropoietin stimulating agents (ESA). Monthly clinical and laboratory evaluation of kidney graft function was carried out. Quality of life (QOL) was assessed - using 25 and 36 questionnaires at the start and 12 months.

**Results:** We observed more females in group 1 and the original kidney disease was chronic glomerulonephritis was significantly higher in group 2 (37.5%) followed by diabetic nephropathy (15.7%) while in group 1 it came as 25.7% and 22.4% respectively (p < 0.05). The studied groups were comparable regarding pre-transplant co-morbidities. Most patients received thymoglobin as induction and most of them were maintained on cyclosporine. We did not find any significant difference between the two groups concerning post-transplant co-morbidities (p > 0.05), however better graft function was observed in group 2 at 6 months (p < 0.05). At 12 months, the assessment of QOL using the Medical Outcomes Study 36-Item Short-Form Health Survey, group 1 showed better post-transplant physical features and higher emotional factors related inactivity at 12 month (p < 0.05), while group 2 showed significantly higher basal and 12 months activity state (p = 0.05). Basal inactivity was comparable in group 2 with that at 12 months (p > 0.05), emotional factors related inactivity was significantly higher at 12 months in group 1. Graft outcome was comparable between both groups (p = 0.125, (p = 0.005).

**Conclusion:** Quality of life as represented by physical activity was improving by full correction of PTA in renal transplant recipients receiving ESA.

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**#6566**

**A STUDY OF CLINICAL PRESENTATION AND OUTCOME OF COVID 19 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS**

Manzoor Parry1 and Shazad Alam2
1 Sher-i Kashmir Institute of Medical Sciences, Nephrology, Srinagar, India and 2Nephrology, Lucknow, India

**Background and Aims:** Novel coronavirus 19 (coronavirus disease-19 [COVID-19]) disproportionately affects patients with various kidney diseases. Patients with kidney transplant are at higher risk of complications of COVID-19 infection. Our aim of this analysis was to study the clinical profile and outcome of COVID-19 infections in KTRs from Kashmir.

**Method:** Here we present a cohort study of 122 KTRs with polymerase chain reaction-confirmed COVID-19 positivity from March 31, 2020 to October 31, 2022. We detailed demographics, immunosuppression regimen, clinical profile, Covid vaccination status, treatment given, and outcomes (acute kidney injury, graft failure and death) of our study population.

**Table 1: Comparison of study population asper survival.**

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age; mean ± SD</td>
<td>39.5 ± 11.6</td>
<td>46.8 ± 9.7</td>
<td>0.046</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>84/17</td>
<td>17/4</td>
<td>0.7580</td>
</tr>
<tr>
<td>Time since transplant; years, mean ± SD</td>
<td>3.1 ± 2.8</td>
<td>2.5 ± 1.8</td>
<td>0.3488</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>64 (63.4%)</td>
<td>16 (73)</td>
<td>0.267</td>
</tr>
<tr>
<td>Graft dysfunction</td>
<td>29 (28.7%)</td>
<td>12 (55)</td>
<td>0.0121</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>34 (33.7%)</td>
<td>9 (47)</td>
<td>0.4223</td>
</tr>
<tr>
<td>Obesity</td>
<td>15 (14.9%)</td>
<td>07(38)</td>
<td>0.045</td>
</tr>
<tr>
<td>Heart disease</td>
<td>11 (10.9%)</td>
<td>5 (25)</td>
<td>0.111</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>5 (4.9%)</td>
<td>4 (21)</td>
<td>0.0245</td>
</tr>
<tr>
<td>Baseline immunosuppression, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNIs</td>
<td>101 (100)</td>
<td>21 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>101(100)</td>
<td>21 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>mTOR inhibitors</td>
<td>74 (74.7)</td>
<td>16 (76.2)</td>
<td>0.782</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>10 (9)</td>
<td>2 (9.5)</td>
<td>0.958</td>
</tr>
<tr>
<td>17 (17)</td>
<td>3 (14.3)</td>
<td>0.774</td>
<td></td>
</tr>
<tr>
<td>Vaccination status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No dose</td>
<td>28</td>
<td>13</td>
<td>0.002</td>
</tr>
<tr>
<td>Vaccinated</td>
<td>73</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

**Results:** Median age of the patients was 41 years and median age of disease was 2.9 years after transplant. Most common comorbidities included hypertension (65.6%) and diabetes (35.3%); presenting symptoms at the time of COVID-19 included fever (82.7%) and breathlessness (66.4%). Covid-19 vaccination was given to 81 patients (66.4%) with two doses in 26 patients and 55 patients received one dose. Clinical severity ranged from asymptomatic (4.1%), mild (36.1%), and moderate (28.7%), to severe (31.1%). Acute kidney injury developed in 46.7% of patients and mortality in 21 patients. Risk factors for mortality included higher age, severe disease, allograft dysfunction before COVID-19 infection, Obesity, acute kidney injury, absence of covid-19 vaccination. 

**Conclusion:** Mortality rates in COVID-19-positive KTR appear to be higher than those in nonimmunosuppressed patients. Risk factors for mortality included higher age, severe disease, allograft dysfunction before COVID-19 infection, Obesity, acute kidney injury, absence of covid-19 vaccination.

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**#6698**

**THROMBOPROPHYLAXIS IN PEDIATRIC KIDNEY TRANSPLANTATION: A META-ANALYSIS**

MD Azharuddin and Manju Sharma
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**Background and Aims:** Kidney transplant patients are at higher risk for developing renal graft thrombosis, especially in pediatric patients. Renal graft thrombosis mainly causes graft failure leading to high morbidity, mortality, and a significant impact on quality of life. To minimize the risk of renal graft thrombosis, antithrombotic prophylaxis is widely used. However, the effect of antithrombotic prophylaxis for kidney transplantation is still a matter of discussion. Therefore, we carried out a meta-analytic synthesis to determine the effect of antithrombotic prophylaxis in pediatric kidney transplantation patients.

**Method:** We systematically searched MEDLINE, CENTRAL, Cochrane Central Register of Controlled Trials, and Web of Science. The eligible studies were identifying the incidence of renal graft thrombosis, hemorrhagic complication (bleeding and bleeding severity), and adverse outcomes related to antithrombotic prophylaxis compared with control group (placebo, active treatment, and no antithrombotic prophylaxis). Meta-analysis was carried out using Review Manager 5.3. The random-effects model was used to compute the pooled estimates of risk ratio (RR) and 95% confidence intervals (CI).**

**Results:** A total of seven studies with 10,51 patients were included in the meta-analytic synthesis. Heparin was used across all the studies as the preferred antithrombotic prophylaxis. Results from the pooled meta-analysis reported that the overall risk for developing renal graft thrombosis was significantly lower in the antithrombotic prophylaxis group compared with the control group (RR = 0.81, 95% CI = 0.66-0.56, p = 0.003). There is no significant difference was found in incidence of hemorrhagic complications between antithrombotic prophylaxis and control group (RR = 0.81, 95% CI = 0.43-1.54). Similarly, there were no significant deaths were found in antithrombotic prophylaxis group compared with the control group (RR = 0.33, 95% CI = 0.01-22.45).

**Conclusion:** The results showed that antithrombotic prophylaxis significantly reduced the risk of renal graft thrombosis in pediatric kidney transplantation. However, due to limited outcomes, further real-world studies with long-term follow-up are required to generate sufficient data on the use of antithrombotic prophylaxis in pediatric kidney transplantation patients.

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**HYPERTENSION & DIABETES**

**F1 - BASIC SCIENCE & EXPERIMENTAL**

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**#4127**

**MODULATION OF BLOOD PRESSURE THROUGH MICROBIOLOGY EXCHANGE BETWEEN MILAN NORMOTENSIVE AND HYPERTENSIVE STRAINS OF RATS**

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Abstracts
Background and Aims: Hypertension is one of the major health problems contributing to the development of cardiovascular diseases. In contrast to essential hypertension, which often displays complex pathogenesis due to multifactorial aetiology, several monogenic forms of hypertension are caused by mutations in genes associated with renal salt handling. Thus, studies on monogenic forms of hypertension could hold potential for novel therapeutic approaches for essential hypertension. Recently, increasing numbers of studies have demonstrated the alteration of the gut microbiome in pathological states including hypertension. These observations suggest the involvement of the intestinal microbiome in the development and/or maintenance of hypertension. A reciprocal congenic strain of Milan hypertensive rat (NA rat), harbouring a missense mutation in the gene encoding the alpha subunit of the membrane-skeletal protein adducin (Add1), develops hypertension starting from 3 months after birth. Preliminary studies on NA rats and its littermate Milan normotensive (MN) rats showed diverse expression patterns of renal sodium transporters/ion channels in two strains of rats, indicating a putative role of altered renal salt handling on the enhanced blood pressure in NA rats (unpublished data). Based on this background, the aim of this study was to investigate a possible connection between the gut microbiome and blood pressure phenotypes in these two strains. Furthermore, we evaluated whether the exchange of faeces between the two strains could transfer the phenotypes through the gut microbiome. Finally, mechanisms underlying the altered phenotype after microbiome exchange were investigated.

Method: Hypertensive NA rats and normotensive MN rats were subjected to ‘homogenization (HOM)’ of the microbiome after birth, which consisted of the exchange of bedding containing faeces from either strain, followed by co-housing of MN and NA rats in the same cage (MN-HOM and NA-HOM groups). For the baseline (BSL) condition, rats were homogenized within the same strain (MN-BSL and NA-BSL). At the age of 5 months, blood pressure measurement was performed using a non-invasive tail-cuff BP-2000 Blood Pressure Analysis system. Faeces from each rat were collected for microbiota metataxonomic analysis using next generation sequencing of 16S ribosome encoding DNA. At the end of the treatment, rats were sacrificed for the collections of blood and organs to assess the expressions of genes involved in renal salt reabsorption.

Results: Systolic blood pressure (SBP) in MN-BSL was averaged at 143.6 mmHg, while NA-BSL showed average SBP 163.3 mmHg, confirming the hypertensive phenotype in NA rats at baseline (P < 0.001). Interestingly, MN-HOM showed a significantly enhanced SBP compared to MN-BSL, reaching 153.5 mmHg (P = 0.005). On the other hand, the average SBP of NA-HOM was 163.7 mmHg, indicating that homogenization did not significantly impact blood pressure in NA rats. Although the MN-HOM group showed significantly increased SBP compared with MN-BSL group, the average SBP of MN-HOM was still significantly lower than both the NA-BSL and NA-HOM groups.

Different gut microbiota compositions were observed in the two strains of rats at baseline, and HOM altered both.

Conclusion: We have demonstrated that the hypertensive phenotype in NA rats was transferred to normotensive MN rats through the exchange of gut microbiota, indicating that the intestinal microbiota and/or metabolites derived therefrom could eventually modulate blood pressure. Further studies including immunoblotting as well as uremic toxin analyses are required to unveil the molecular mechanisms by which the gut microbiome modulates blood pressure.
blockade versus the monotherapies on top of RAS blockade in experimental diabetes.

Method: Twelve weeks old male and female uninefrectomized (UNx) db/db mice were treated for 8 weeks with an SGLT2i (empagliflozin, 10 mg/Kg/day five days a week) and/or a GLP1-RA (semaglutide, 10.0 nmol/kg twice per week) on top of a RAS blocker (ramipril, 8 mg/Kg/day). Vehicle-treated UNx db/db and non-diabetic (db/m) mice were included as controls. During the experiment weight, food and water intake, blood glucose, blood pressure (BP) and glomerular filtration rate (GFR) were measured. Kidney and heart were collected at the end of the experiment.

Results: The vehicle-treated UNx db/db showed increased body weight, food and water intake and blood glucose as compared to the vehicle-treated UNx db/m (Fig. 1A, B and C, p = 0.03, p<0.001 and p<0.0001, respectively). The GFR slope (ΔGFR, difference between final and basal GFR) was also significantly higher in the vehicle-treated UNx db/db vs the vehicle-treated UNx db/m (Fig. 1D, p = 0.02), a typical feature of incipient DN. All treatments significantly decreased systolic and diastolic BP as compared to vehicle-treated UNx db/db due to its ramipril component (Fig. 1E). Further, both empagliflozin and semaglutide (alone or combined) on top of ramipril lowered blood glucose in UNx db/db (Fig. 1C, p<0.001 vs vehicle UNx db/db in all cases) but semaglutide component maximized this effect. Food and water intake was decreased in UNx db/db treated with semaglutide on top of RAS blockade (alone or combined with empagliflozin) as compared to vehicle-treated UNx db/db (Fig. 1B) although no differences in body weight were noted between treated and untreated UNx db/db (Fig. 1A). A trend towards ΔGFR decline was observed in UNx db/db treated with empagliflozin and semaglutide on top of RAS blockade (Fig. 1D). Finally, heart weight but not kidney weight was significantly lower in all treated UNx db/db as compared to vehicle-treated UNx db/db (Fig. 1F).

Conclusion: Our preliminary results show that addition of semaglutide to empagliflozin therapy on top of RAS blockade could have synergic hypoglycemic effects. Further, although more research is needed, both empagliflozin and semaglutide in combination with ramipril trended to ameliorate diabetic hyperfiltration and decreased heart weight in a DN mouse model which suggests cardiorenal beneficial effects.

#2892

CRITICAL ROLE OF SERUM RESPONSE FACTOR IN PODOCYTE EPITHELIAL–MESENCHYMAI TRANSITION OF DIABETIC NEPHROPATHY

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Background and Aims: To investigate the expression and function of serum response factor (SRF) in podocyte epithelial–mesenchymal transition (EMT) of diabetic nephropathy (DN).

Method: Expression of SRF, pSRF, synaptopodin, P-cadherin, ZO-1, α-SMA, FSP-1, fibronectin and collagen-1 were examined in podocytes or renal cortex following high glucose. SRF was upregulated by SRF plasmids and downregulated by CCG-1423 to investigate how SRF influence podocyte EMT in DN. Streptozocin was used to generate DM in rats.

Results: 1⃝ High glucose induced EMT and SRF upregulation in podocytes (Figure 1). High glucose suppressed synaptopodin and ZO-1 expression, and induced SRF, pSRF, collagen-1, FSP-1, α-SMA and Snail expression. SRF transferred from cytoplasm to nuclei obviously and the level of SRF was also increased in podocytes after high glucose treatment. 2⃝ SRF overexpression mediated EMT, migration and barrier dysfunction of podocytes (Figure 2). Overexpression of exogenous SRF reduced epithelial synaptopodin expression, and increased collagen-1, FSP-1, α-SMA and Snail expression in podocytes. Transwell chamber migration assay showed that overexpression of SRF significantly upregulated the migration of podocytes across the pores of transwell filters. Albumin filtration assay showed that albumin easily diffused across the monolayer of podocytes transfected with SRF cDNA. 3⃝ Inhibition of SRF preserved phenotypes of podocytes in vitro (Figure 3). CCG-1423 selectively

Figure 1:
suppressed the expression of pSRF and SRF in podocytes after high glucose stimulation. Besides, simultaneous treatment of podocytes with CCG-1423 also significantly abolished the reduction of synaptopodin expression and the induction of collagen-1, FSP-1, α-SMA and Snail expression. CCG-1423 also reduced the transfer of SRF from cytoplasm to nucleus in podocytes treated with high glucose.

The effect of CCG-1423 in diabetic rats (Figure 4—5). CCG-1423 significantly abrogated the reduction of synaptopodin expression and the induction of SRF, collagen-1, α-SMA and FSP-1 expression in renal cortex tissues. Masson and PAS staining demonstrated that renal glomerular fibrosis was present in DM group, and after 8 weeks treatment with CCG-1423, renal glomerular fibrosis was dramatically ameliorated. In addition, CCG-1423 significantly preserved P-cadherin expression and suppressed α-SMA and FN expression in DN rats. More importantly, CCG-1423 dramatically decreased 24-h urine protein excretion by about 50%, and increased serum albumin, compared with DM group.

Conclusion: Together, increased SRF activity provokes podocytes EMT and dysfunction in DN. Targeting SRF by small molecule inhibitor may be an attractive therapeutic strategy for DN.
Figure 3:

Figure 4:
RENAL RENIN IS UPREGULATED BY THE COMBINATION TREATMENT OF EMPAGLIFLOZIN AND RAS BLOCKADE IN EXPERIMENTAL DIABETIC NEPHROPATHY

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**Background and Aims:** Sodium-glucose cotransporter 2 (SGLT2) inhibitors have proven to delay diabetic nephropathy (DN) progression on top of renin-angiotensin system (RAS) blockade. This protection is mainly attributed to improvement in renal hemodynamics, although direct effects on the kidney cannot be ruled out. The present study aimed to identify renal proteins differentially expressed between vehicle-treated diabetic mice and mice treated with empagliflozin, ramipril, or their combination, that could help explain the protective mechanisms of the drugs.

**Method:** Twelve weeks old diabetic db/db mice were given empagliflozin (10 mg/Kg/day), ramipril (8 mg/Kg/day), or the combination of both drugs during 8 weeks. Vehicle-treated db/db and db/m mice were used as controls. Serum glucose, blood pressure, GFR, and albuminuria were measured at baseline and at the end of the study. After 8 weeks, mice were euthanized, and the kidneys and serum were saved. A differential high-throughput proteomic analysis by mass spectrometry using isobaric tandem mass tags (TMT labelling) was performed in kidney cortex.

**Results:** Vehicle-treated db/db mice showed increased glycemia during the whole experiment, and empagliflozin reduced blood glucose. Ramipril treatment decreased blood pressure. Vehicle-treated diabetic mice also showed incipient DN with increased mesangial matrix and albuminuria compared to
their non-diabetic littermates. All the treatments reduced mesangial matrix expansion and albuminuria. Only 13 proteins were differentially expressed (false discovery rate $<5\%$ and Log$_2$FC $\geq 1$ or $\leq -1$) when comparing treated mice vs vehicle-treated db/db mice. The differentially expressed proteins were only identified between the mice treated with the combination of empagliflozin and ramipril and the vehicle-treated diabetic mice. Ramipril or empagliflozin alone did not produce significant changes in renal proteins. Kidney renin was evidently increased by the combination therapy with empagliflozin and ramipril, along with the tubular transporter scaffolding protein MAP17. The results were further validated through renin staining and renal renin concentration measurement. Renal renin concentration was increased by ramipril and further increased by the combination therapy with empagliflozin and ramipril when compared to vehicle-treated db/db mice (55 pg/µg (IQR:49–64), 94 pg/µg (IQR:71–102), and 112 pg/µg (IQR 104–116) in the groups treated with vehicle, ramipril and the combination of empagliflozin and ramipril respectively). However, renin serum concentration was similar between mice treated with ramipril and mice treated with the combination. Conclusion: The combined therapy of empagliflozin with ramipril upregulated renin in the kidney of a diabetic mouse model. The increase in kidney renin suggests that other mechanisms different from RAS act in the regulation of glomerular hemodynamics and arteriolar tone. Moreover, the increased sodium delivery to the macula densa does not inhibit renal renin secretion.

#6817

ROLE OF THE CGAS-STING PATHWAY IN THE PROGRESSION OF DIABETIC NEPHROPATHY

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Background and Aims: Diabetic kidney disease (DKD) is the leading cause of chronic renal pathology. Understanding the molecular underpinnings of DKD is critical to designing tailored therapeutic approaches. We have demonstrated previously that type 2 diabetic nephropathy (T2DN) rats develop renal and physiological abnormalities similar to clinical observations in humans with DKD, indicating these rats are an excellent model for studying the progression of renal injury in type 2 DKD [1]. Furthermore, our recent studies revealed sexual dimorphism in this model, indicating that while both male and female T2DN rats developed non-obese DKD phenotype, females had significant protection from the development of severe forms of glomerular and tubular damage [2]. The potential role of the cyclic GMP-AMP synthase (cGAS) / Stimulator of interferon genes (STING) pathway in renal inflammation and fibrosis was also uncovered [3]. Here we focused on sex differences in DKD and the potential mechanisms leading to the progression of DKD.

Method: To explore the sexual dimorphisms in the development of DKD, we utilized young (12-week-old) and aged (>48 weeks old) type 2 diabetic nephropathy (T2DN) rats. To delineate transcriptional changes, RNA-Seq analysis was performed in the kidney cortex of T2DN rats of both sexes at a younger and older age. Western blotting, immunohistochemistry, and flow cytometry analyses were further used to identify specific pathways contributing to sexual dimorphism and disease progression in T2DN rats.

Results: We have revealed that the cGAS/STING signaling pathway is upregulated in T2DN rats compared to non-diabetic Wistar rats and in type 2 diabetic human kidneys. The expression of key proteins in the cGAS/STING pathway, such as cGAS, STING, phospho-IRF, mitTFA, and TREX1, was significantly different between male and female T2DN rats and following the progression of DKD. Proinflammatory genes were also upregulated in male T2DN rats compared to female rats of the same age, and their levels were further elevated in aged rats. RNA-Seq analysis also identified significant changes in genes participating in the cGAS-STING inflammatory pathway. Flow cytometry revealed a significantly greater number of infiltrating leukocytes in the male kidneys compared to their age-matched females. Moreover, the leukocytic count was significantly higher in old males versus young males, while it was almost the same in females of different ages. Approximately 50% of the renal leukocytic population was monocytes/macrophages (CD11b/c$^+$), with fewer CD3$^+$ T cells, both CD3$^+$ CD4$^+$ and CD8$^+$ cytotoxic T cells, and CD45R$^+$ B cells.

Conclusion: Our study provides critical insights into the sexual dimorphism and progression of DKD and identifies the cGAS-STING pathway as an essential contributor to disease development.

REFERENCES


**#4941**

**A METABOLIC FINGERPRINT PERSPECTIVE OF GUT-DERIVED METABOLITES ON EARLY DIABETIC KIDNEY DISEASE IN TYPE 2 DIABETES MELLITUS PATIENTS**

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**Background and Aims:** Type 2 diabetes mellitus (T2DM) is the first cause of end stage renal disease worldwide. Metabolite profiling is an emerging field of great significance, as T2DM prevalence is continuously rising. The subtle dynamics of gut microbiota derived metabolites may have important implications in diabetic kidney disease (DKD) development. Nitrogen metabolic pathway and retinoic acid signaling pathway seem to be rising. The subtle dynamics of gut microbiota derived metabolites may cause of end stage renal disease worldwide. Metabolite profiling is an important approach for understanding the interactions between gut microbiota and the host in the context of DKD.

**Method:** The serum and urine of 90 T2DM patients (P group) and 20 healthy subjects (C group), were assessed in a cross-sectional study, by ultra-high-performance liquid chromatography coupled with electrospray ionization-quadrupole-time of flight-mass spectrometry (UHPLC-QTOF-ESI+MS) techniques. P group was divided in 3 subgroups (normoalbuminuria-P1, microalbuminuria-P2, macroalbuminuria-P3). Statistical analysis was performed by untargeted multivariate (PLSDA, VIP scores, Random Forest, Biomarker analysis) and univariate (One Way ANOVA, Biomarker Analysis) methods. P1 vs. C1, P2 vs. C2, P3 vs. C3.

**Results:** Multivariate analysis, by which the P group vs. C group were compared, displayed: (1) in serum samples: increased levels (P<0.05) of all-trans retinoic acid, cysteine-S-sulfate, oleylglycine, threo-glycine and decreased levels (P<0.05) of phenylalanine, tyrosine, kynurenic acid; (2) in urine samples, there were increased levels of all-trans retinoic acid, indoxyl sulfate, serotonin sulfate and glycylprolylarginine. Subsequently, by applying univariate analysis, the biomarkers derived from gut microbiota were selected: (1) in serum samples: increased levels (P<0.05) of cysteine-S-sulfate, all-trans retinoic acid, cysteine-S-sulfate, and decreased levels (P<0.05) of phenylalanine, tyrosine, kynurenic acid; (2) in urine samples: increased levels (P<0.05) of all-trans retinoic acid, indoxyl sulfate, serotonin sulfate, and decreased levels (P<0.05) of phenylalanine, tyrosine, kynurenic acid.

**Conclusion:** The study suggests that ATRAs dynamic is disturbed in the normoalbuminuric stage of DKD. While its urinary levels correlated significantly with albuminuria, the changes observed in P1 subgroup, in serum and urine, may be correlated to the loss of renal tubular tight junction as a result of claudin downregulation. Phenylalanine and tyrosine, a part of nitrogen metabolic pathway, are indicators of the new-onset DKD. Their levels were upregulated in serum vs. urine, indicating their possible involvement in early DKD when comparing C vs. P1-P2-P3. Kynurenic acid and indoxyl-sulfate rise from tryptophan metabolism. Low levels in serum of kynurenic acid may suggest its possible implication in incipient endothelial dysfunction in DKD. Indoxyl-sulfate (IS) urinary excretion is dependent on albuminuria. The study shows an elevated excretion of IS, in the normoalbuminuric group compared to controls and may suggest a tubular damage that precedes the glomerular modifications in DKD.

**Conclusion:** UHPLC-QTOF-ESI+MS untargeted analysis reveals a particular metabolite fingerprint in early DKD. The study describes all-trans retinoic acid, phenylalanine, tyrosine, kynurenic acid, and indoxyl sulfate, as potential key biomarkers involved in early DKD pathogenesis, their levels being expressed in P1 subgroup compared with C group, and P2, P3 subgroups.

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**#6118**

**ALTERNATIVE SPlicing IN MECHANICALLY STRETCHED PODOCYTES AS A MODEL OF GLOMERULAR HYPERTENSION**

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**Background and Aims:** It has been shown that mRNA splicing plays a relevant role in disease pathophysiology. However, the possible role of alternative splicing (AS) in hypertensive nephropathy (HN) has not been investigated. The purpose of the Sys_CARE (Systems Medicine Investigation of AS in Cardiac and Renal Diseases) project is to investigate the possible implication of AS events in HN development and progression.

**Method:** Differentiated murine podocytes were seeded on a flexible silicone membrane, and mechanically stretched using the Stretchy apparatus (NIPPOKA GmbH, Greifswald). Cells were stretched for 3 days under low and high stretch conditions with a frequency of 0.5 Hz. The mRNA and proteins were isolated and analyzed using RNA_SEQ and LC-MS/MS techniques. Enrichment analysis identified proteins which were classified according to the related biological processes, molecular function and cellular components. Splicing and transcript expression were evaluated with bioinformatical tools (rMATS, leafcutter, Whippet, MAJIO, IsoformSwitchAnalyzer).

**Results:** Proteomic analysis of cultured podocytes revealed significant difference expression levels for 135 proteins (54 increased and 81 decreased) and 424 proteins (195 increased and 229 decreased) under low and high stretch conditions, respectively, compared to unstretched conditions. Interestingly, most of the proteins with decreased intensity upon stretch are cytoskeleton and actin-binding proteins. In contrast, the up-regulated proteins are more associated in clusters affecting mRNA processing and splicing. By RNA_SEQ we identified over 1000 different splicing events including all types of alternative splicing events. We screened for candidates that showed an alternative splicing event in multiple tools, were found in the proteomics, were podocyte-specific, or showed altered expression in glomerulopathies such as diabetic nephropathy. In this regard, we found an isoform switch of My6 and Shroom3 after mechanical stretch.

**Conclusion:** Using mechanically stretched podocytes as a model of HN, we found significant up- and down-regulated proteins. In addition, by RNA_SEQ we identified an isoform switch of My6 and Shroom3 that might be essential for the development of HN.

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**#4375**

**LANOSTEROL SYNTHASE RS2254524 POLYMORPHISM MODULATES SALT SENSITIVITY AND RENAL EXPRESSION IN A NOVEL MICE MODEL, LSSV643LV643L**

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**Background and Aims:** The blood pressure (BP) response to different salt intakes (salt sensitivity-SS), shows variability among individuals, with more frequency in hypertensives compared to the general population. Elevated levels of the Endogenous Oubain (EO) have been associated with hypertension (HT) and SS. We characterized the missense variation rs2254524 (Val642Leu; C>A) of the Lanosterol Synthase gene (LSS) coding for an enzyme in sterol biosynthesis, since AA patients on a low-salt diet showed a greater reduction in BP compared to the LSS CC, with only CC having an increase in plasma EO. Moreover, AKI incidence following cardiovascular surgery was greater among those with the LSS rs2254524 AA genotype than in those with the CC genotype. We aim at dissecting the functional correlation between LSS polymorphism, EO, SS-HT, and renal function.
Method: We generated by CRISPR-Cas9 a knock-in mouse model carrying the Lss V643L (Ls<sup>V635L/V635L</sup>) allele, homologous to Yv6L2 to dissect the functional correlation between LSS polymorphism, EO and salt-sensitive hypertension, and kidney expression. Male mice were fed with a normal-salt diet (0.5% NaCl), high-salt diet (4% NaCl), or low-salt diet (<0.03% Na) and BP was measured every two days by the tail-cuff system.

Results: Ls<sup>V6435L/V643L</sup> mice were viable, healthy, and undistinguishable phenotypically from WT. At baseline, the Ls AA affected kidney weight that was significantly enlarged at 3 (p = 0.02) and 12 months of age, compared to WT (kidney p = 0.04; liver p = 0.003). The Lss V643L mutation did not affect EO and SBP at 3 and 12 months, per se, but affects SBP responsiveness to salt intake. Indeed, we observed an increased SBP upon a high-salt diet only in Ls<sup>V6435L/V643L</sup> mice 12 months old compared to the control diet (p = 0.01). Moreover, the 12-month-old Ls<sup>V635L/V635L</sup> mice in high-salt diet showed labile hypertension and showed a higher incidence of heart fibrosis. At 12 months, in the adrenal gland of Ls<sup>V6435/V643</sup> mice, Lss mRNA level was reduced upon high-salt diet (p = 0.03), while RNA-seq analysis of renal differentially expressed genes revealed a different regulation of multiple Slc genes, both in control and high-salt diet, but also of Cbr2, and Arggap26.

Conclusion: The new Ls<sup>V6435/V643</sup> mouse model resembles the SS-HT phenotype together with EO non-responsiveness observed in HT patients, thus providing a good model of SS-HT. Our results reveal a role of Lss gene in the regulation of BP upon salt stimulus, and its influence at renal level at 3 and 12 months of age.

#5537

**GENETIC VARIABILITY IN THE PROSTAGLANDIN E2 PATHWAY IS RELATED TO SALT SENSITIVITY IN TREATMENT-NAIVE HYPERTENSIVE PATIENTS**

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**Background and Aims:** Hypertensive nephropathy is a common aging-related disorder. One of the main factors that contribute to the development of hypertension is salt intake. Based on blood pressure (BP) variation after sodium intake in an acute salt load test, individuals can be grouped in: sodium sensitive (SS), sodium resistant (SR) or inverse sodium sensitivity (ISS). Prostaglandin E2 (PGE2) is the main renal metabolite of the cyclooxygenase pathway, a major actor mediating renal injury and it has also been related to renal blood flow and hemodynamic changes. Our aim was to determine common, functional variants in genes involved in the PGE2 pathway to identify associations with the sodium sensitivity phenotype of hypertensive patients, as well as with parameters of renal function and BP traits.

**Methods:** We studied 511 treatment-naive hypertensive patients, who were subjected to an acute salt load test and consequently stratified into 173 SR, 172 SS patients and 166 ISS, after they showed an increase in BP values in these patients.

**Results:** In vitro, treatment of HK-2 cells with CoCl<sub>2</sub> decreased the expression of HIF-1<sub>α</sub> and it's translocation from cytoplasm to nucleus. Meanwhile, HIF-1<sub>α</sub> activation induced by CoCl<sub>2</sub> significantly increased lipid accumulation in HK-2 cells. Moreover, TGF-β and CTGF expression in HK-2 cells. The presence of glucose (30mM) made no significant difference to HK-2 cells incubated with CoCl<sub>2</sub>. HIF-1α mRNA expression significantly reduced lipid deposition in HK-2 cells incubated with CoCl<sub>2</sub>. In vivo study showed YC-1 treatment decreased the expression of HIF-1α in renal tubules of diabetic rats, which was accompanied by less lipid accumulation compared with the diabetes mellitus (DM) group. PAS staining showed the desquamation and necrosis of tubular epithelial cells in the YC-1 group were alleviated compared with the DM group. YC-1 treatment did not affect the ratio of kidney weight to body weight, whereas decreased the levels of blood glucose, urine albumin creatinine ratio and NAG creatinine ratio in diabetic rats. The expressions of fibrosis factor TGF-β and CTGF were decreased in the YC-1 group compared with the DM group. Furthermore, the protein expression of CPT1A, the key enzyme of fatty acid oxidation, which was decreased in the DM group compared with the controls, was regained by YC-1 treatment.

**Conclusion:** Our findings demonstrated that HIF-1α activation contributed to interstitial injury in diabetic nephropathy by inducing lipid accumulation.
HIF-1α activation might contribute to lipid nephrotoxicity by downregulating fatty acid oxidation.

**SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS VERSUS DIPEPTIDYL PEPTIDASE 4 INHIBITORS AS STABILIZERS OF HIF PATHWAY IN DIABETIC NEPHROPATHY RATS**

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**Background and Aims:** With the diabetes pandemic, chronic kidney disease is a burden, with diabetic nephropathy (DN) being the primary leading cause of end-stage renal disease. Antidiabetic drugs have shown renoprotective effects via different mechanisms, and among those are SGLT2 inhibitors and DPP-4 inhibitors. Hypoxia-inducible factor (HIF) pathway, a significant contributor to inflammation development in the kidneys, is a major pathway that regulates erythropoietin synthesis. Prolyl hydroxylase domain (PHD) decreases erythropoietin synthesis by inhibiting HIFs. PHD inhibitors are anticipated to have additional effects, such as protection against metabolic diseases, due to HIF’s impact on many genes. The diabetic kidney is characterized by enhanced HIF-1α activation but decreased HIF-2α activity. These actions may significantly contribute to glomerular and renal tubular dysfunction, renal inflammation and fibrosis, and decreased erythropoietin synthesis observed in DN. This work aims to test the renoprotective effect of SGLT2 inhibitors and DPP-4 inhibitors by controlling the proinflammatory and anti-inflammatory domains of the HIF pathway.

**Method:** Type 1 DM rat model was induced in 24-hour-fasted Sprague Dawley rats by a single intraperitoneal injection of 45 mg/kg streptozotocin (STZ). DM was verified by measuring blood glucose seven days following STZ injection, and only animals with glucose levels of ≥15 mM were included (n = 24), randomly and equally distributed, then received either saline or vildagliptin (3 mg/Kg) or empagliflozin (30 mg/Kg) once daily by oral gavage for three months. An additional group was used as a non-diabetic control. At the end of the experiment, rats were placed in metabolic cages for 24-h urine collection, then sacrificed. Blood samples and kidney tissue were collected.

Kidney function was assessed by measuring serum creatinine and urinary albumin: creatinine ratio. Regarding the HIF pathway as a potential mechanism, empagliflozin-treated groups showed a significantly higher HIF2α gene expression in kidney tissue samples (0.98 ± 0.10) than vildagliptin-treated group (0.58 ± 0.05). For the expression of its regulator, PHD3, there was a significant difference between groups (F = 5.694, p = 0.005). However, the vildagliptin-treated group (0.65 ± 0.06) didn’t differ significantly from the untreated group (0.60 ± 0.03), in contrast to the empagliflozin-treated group (2.01 ± 0.50), which showed a significantly higher expression than the other groups (Figure 1).

**Conclusion:** Empagliflozin significantly increased the level of HIF-2α in renal tissue. In addition, it nearly neutralizes the tubular expression of PHD3 compared to non-treated and vildagliptin-treated rats. SGLT2 inhibition is effective for correcting the proinflammatory/anti-inflammatory imbalance in DN.

**Results:** Vildagliptin and empagliflozin could significantly ameliorate the diabetic disturbance of renal function, as demonstrated in serum creatinine (F = 23.518, p < 0.001) with a non-significant difference between both treated groups, and in the significantly reduced albumin/creatinine ratio (F = 14.453, p < 0.001), with a significantly lower ratio for empagliflozin (4.73 ± 0.54) than vildagliptin-treated group (9.09 ± 1.04). Regarding the HIF pathway as a potential mechanism, empagliflozin-treated groups showed a significantly higher HIF2α gene expression in kidney tissue samples (0.98 ± 0.10) than the vildagliptin-treated group (0.58 ± 0.05). For the expression of its regulator, PHD3, there was a significant difference between groups (F = 5.694, p = 0.005). However, the vildagliptin-treated group (0.65 ± 0.06) didn’t differ significantly from the untreated group (0.60 ± 0.03), in contrast to the empagliflozin-treated group (2.01 ± 0.50), which showed a significantly higher expression than the other groups (Figure 1).

**Conclusion:** Empagliflozin significantly increased the level of HIF-2α in renal tissue. In addition, it nearly neutralizes the tubular expression of PHD3 compared to non-treated and vildagliptin-treated rats. SGLT2 inhibition is effective for correcting the proinflammatory/anti-inflammatory imbalance in DN.

**Figure 1:** Immunohistochemical staining of PHD3 in renal tubules. (A) Represents diabetic group with strong staining in about 80% of proximal tubules. (B): Vildagliptin treated diabetic group with moderate staining in about 30% of proximal tubules. (C): empagliflozin treated diabetic group with weak staining in about 20% of proximal tubules. (PHD3 × 400).
ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH COVID-19 DURING ANTIOXIDANT THERAPY
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Background and Aims: In connection with the coronavirus pandemic of 2020, there have been recent discussions about the role of endothelial function in the course and prognosis of the disease. Purpose of the study, study of endothelial function in patients who have had a coronavirus infection.

Methods: Under observation were 60 patients who underwent COVID-19 of moderate severity on the 14th day of therapy at the age of 57 to 67 years. Patients of the 1st group (30 patients), against the background of standard basic therapy, were prescribed L-carnitine at a dose of 5 g/day for 5 days, followed by a maintenance dose of 1 g/day for 5 days. Group II consisted of 30 patients who met the inclusion criteria for the study, were treated for COVID-19 and did not receive metabolic agents. The state of endothelial function was assessed according to Doppler sonography of the brachial artery using the D.S. Celemajer (1992) using a reactive flush test. Changes in the diameter of the right brachial artery were assessed using a 7.5-12 MHz linear transducer with a phase grating ultrasound system En Visor C Philips. The results of the study were processed statistically using Student’s t test for paired and unpaired variables. Differences were considered significant at p<0.05.

Results: After analyzing the data of samples with RG in combination with blood flow velocity indicators, we noted that in response to an increase in blood flow velocity in the control group, the diameter of the brachial artery increased by almost 12%, in patients with COVID-19 from 20 to 25 cm. Male and obese placebo rats showed significantly, and the diameter of the artery practically did not change. Thus, with an increase in the mechanical stimulus, i.e. blood flow velocity in patients with COVID-19 did not occur a commensurate increase in the diameter of the vessel. The results obtained indicate a pronounced dysfunction of the endothelium in patients with COVID-19, in particular, EDV, the indicators of which were two times lower than the control values.

Conclusions: The inclusion of L-carnitine in the regimen of standard therapy for patients with COVID-19 significantly improves the values of EVR compared to the standard basic therapy.

NEXHOPROTECTIVE EFFECTS OF SEMAGLUTIDE IN A MOUSE MODEL OF HYPERTENSION-ACCELERATED DIABETIC KIDNEY DISEASE
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Background and Aims: Obesity, hyperglycemia and hypertension are critical risk factors for development of diabetic kidney disease (DKD). Emerging evidence suggests that glucagon-like peptide-1 receptor (GLP-1R) agonists improve cardiovascular and renal outcomes in type 2 diabetes patients. Here, we characterized the effect of long-acting GLP-1R agonist semaglutide alone and in combination with an ACE inhibitor in a model of hypertension-accelerated, advanced DKD facilitated by adeno-associated virus-mediated renin overexpression (ReninAAV) in uninephrectomized (UNx) female db/db mice.

Method: Seven weeks after ReninAAV administration and six weeks post-UNx, db/db UNx-ReninAAV mice were administered (q.d.) vehicle, semaglutide (30 nmol/kg, s.c.) or semaglutide (30 nmol/kg, s.c.) + lisinopril (30 mg/kg, p.o.) for 11 weeks. Endpoints included tail-cuff blood pressure evaluation at week 1 and 10, plasma/urine biochemistry, kidney histopathology as well as RNA sequencing.

Results: Semaglutide robustly reduced hyperglycemia, hypertension and albuminuria concurrent with notable improvements in glomerulosclerosis severity, urine/renal kidney injury molecule-1 (KIM-1) levels. Furthermore, semaglutide suppressed gene expression markers of extracellular matrix modelling and immune system activation. Co-administration of lisinopril further ameliorated hypertension, glomerulosclerosis as well as markers of fibrogenesis and inflammation.

Conclusion: Semaglutide improves disease hallmarks in the db/db UNx-ReninAAV mouse model of advanced DKD. Renal outcomes were further improved by combined antihypertensive standard-of-care. These data display the translatability of the db/db UNx-ReninAAV mouse model of DKD.

RENAI INJURY IN RELATION TO OBESITY AND THE ADDITIVE EFFECT OF HYPERTENSION IN FEMALE AND MALE OBESE AND LEAN ZSF1 RATS
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Background and Aims: Chronic kidney disease co-exists with heart failure with preserved ejection fraction (HFpEF), which is characterized by the presence of obesity, hypertension, and diabetes mellitus type 2. Obese ZSF1 rats, a model of HFpEF, exhibit multiple of these comorbidities that can disturb cardiac function. Little attention has been paid to how these comorbidities affect renal disease in the ZSF1 rats. HFpEF is found predominantly in women in whom obesity and hypertension are particularly prevalent. Therefore, we aimed to characterize the renal phenotype in female and male, lean and obese, ZSF1 rats and investigated additional effects of worsened hypertension on disease severity.

Method: Systolic blood pressure and renal function were assessed biweekly in female and male, lean and obese, ZSF1 rats from 12 to 26 weeks of age by tail-cuff plethysmography, urine collection via metabolic cages and plasma collection, respectively. From 19 weeks of age, rats were implanted with either a deoxycorticosterone acetate pellet (DOCA) and fed a high salt diet (6% NaCl) or with a placebo pellet and fed a normal salt diet. At 26 weeks of age, terminal GFR was assessed via inulin clearance under isoflurane. Renal sections were processed for histological analysis.

Results: Lean placebo ZSF1 rats, both female and male, were mildly hypertensive (systolic blood pressure 140-150 mmHg). All obese rats showed HFpEF, elevated by a low ratio. In female normoglycemic ZSF1 rats, obesity associates with mild proteinuria, decreased GFR and glomerular hypertrophy. The addition of DOCA-salt worsened hypertension in female obese ZSF1 rats, but not in their lean counterparts. DOCA-salt-worsened hypertension enhanced proteinuria and triggered glomerulosclerosis in female obese rats. Male obese placebo ZSF1 rats were hyperglycemic and showed proteinuria, glomerular hypertrophy and sclerosis, and tubulo-interstitial damage. DOCA-salt worsened hypertension in both male lean and obese rats and further aggravated proteinuria, tubulo-interstitial damage, glomerular hypertrophy and sclerosis in obese male rats. No effect of DOCA-salt was observed on GFR in both male and female ZSF1 rats.

Conclusion: Female obese ZSF1 rats developed mild renal disease and DOCA-salt-worsened hypertension deteriorated renal function and structure in normoglycemic female obese ZSF1 rats similar to hyperglycemic male obese ZSF1 rats.

ACCS2 AGGRAVATES RENAL TUBULAR INFLAMMATION BY INDUCING THE DYSREGULATION OF FATTY ACID METABOLISM AND MITCHONDRIAL OXIDATIVE STRESS IN DIABETIC MICE
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Background and Aims: Treatment options for diabetic nephropathy (DN) are currently limited. Chronic renal inflammation has been widely recognized as a major promoter of DN. The tubular epithelial cells are a major source of IL-1β in diabetic db/db mice. Inhibition of Acetyl CoA Synthase 2 (ACCS2) has been shown to promote high-fat diet-induced liver injuries, but the underlying mechanism of action of ACCS2 in diabetic renal injuries has not been elucidated.

Method: Strepotozocin (STZ) was intraperitoneally injected to establish the diabetic mouse model. We investigated the effects of ACCS2 on diabetes-induced renal tubular injury in transgenic mice with global accs2 knockout (acss2−/−). PAS staining was carried out to evaluate pathological injury of kidneys in mice. The renal tissue immunostaining was conducted to detect IL-1β expression and macrophage distribution in kidney tissues of mice. HK-2 cell culture model was achieved by high glucose stimulation in vitro. Real-time PCR analysis was applied to evaluate gene expression of inflammatory factors IL-1β, TNF-α, and MCP-1. Western Blot and immunofluorescence staining were conducted to detect the activation of the NLRP3 pathway and mitochondrial reactive oxygen species (ROS).

Results: ACCS2 was upregulated in STZ-induced diabetic renal tubular cells, which is significantly co-expressed in IL-1β-positive renal tubular cells of STZ-induced diabetic mice. The mice with acss2−/− exhibited decreased renal tubular inflammation and inhibited NOD-like receptor protein 3 (NLRP3)
Diabetes is a common co-morbidity in patients with end stage renal disease (ESRD) receiving renal replacement therapy (RRT). Glucose-lowering therapies (GLT) such as sulphonylureas and insulin are commonly used treatments in diabetes but increase the risk of hypoglycaemia. Dialysis is also a risk factor for hypoglycaemia due to reduced drug clearance, decreased gluconeogenesis and glucose loss into the dialysate. Guidelines suggest an HbA1c target of 58 mmol/mol for patients with ESRD receiving glucose lowering therapies, given that tight HbA1c control has not been shown to improve cardiovascular risk, and HbA1c <58 mmol/mol will incur risk of hypoglycaemia in a potentially vulnerable population. We evaluated the clinical and demographic features associated with HbA1c <58 mmol/mol in an ESRD cohort aiming to define characteristics that predict the need for closer glycaemic monitoring.

Method: We performed a retrospective observational study of patients receiving RRT and treated with GLT attending a single centre nephrology unit using data collected from a clinically used electronic database. Patients with HbA1c <58 mmol/mol in the last 12 months were identified. Clinical, biochemical and demographic factors were compared between groups. Depreciation was measured using the Scottish Index of Multiple Deprivation (SIMD), whereby 1 represented the most deprived areas within Glasgow, while 5 represented the most affluent. Between group characteristics were analysed using Pearson’s Chi-squared test or Wilcoxon test, and logistic regression was used to evaluate factors contributing to hypoglycaemia.

Results: We identified 607 patients, 51.6% of whom had an HbA1c below 58 mmol/mol. 298 patients were on haemodialysis, 14 on peritoneal dialysis and 291 had a kidney transplant. Patients with HbA1c <58 mmol/mol were older, (58±16.8 vs 60±15.15 years, p = 0.004) but there was no difference in duration of diabetes (9.1±10.2 vs 8.3±12.3 years, p = 0.42) or ESRD vintage (4.6±6.9 vs 4.1±7.5 years, p = 0.44). There was a higher proportion of type 2 diabetes in the group with HbA1c <58 mmol/mol (26% vs 36%, p = 0.04). There was no association between HbA1c and SIMD (p = 0.46) nor gender (p = 0.55). In logistic regression, increasing age (OR 1.19, 95% CI 1.03, 1.38) and ESRD vintage (OR 1.03, 95% CI 1.01, 1.06) increase the likelihood of tight glycaemic control. Transplantation reduced the risk (OR 0.64, 95% CI 0.44, 0.93). There was no association between type of GT and risk of tight glycaemic control. Subgroup analyses of the haemodialysis and transplant populations was also performed with broadly similar findings. In patients on haemodialysis, increasing age and ESRD increased the risk of HbA1c <58 mmol/mol. In patients with a kidney transplant, there was no association between current estimated glomerular filtration rate and HbA1c <58 mmol/mol.

Conclusion: Tight glycaemic control is very common in patients with ESRD on GT. Tight glycaemic control may be beneficial in patients with type 2 diabetes receiving haemodialysis, increasing age, and ESRD vintage, increased risk of tight glycaemic control and hypoglycaemia. Transplantation was a substantial protective factor. In patients with a kidney transplant, no trend was found in eGFR and HbA1c. This is a huge concern and suggests HbA1c checks need to be included as part of regular renal profile monitoring every 3 months. More regular follow-up with the Diabetes team may also be useful in this patient group. Continuous glucose monitoring (CGM) devices have revolutionised diabetes care by allowing easy access to data such as time in range and trends in blood sugar throughout the day, thus making it easier to optimise treatment. These devices also provide the patient with a warning when they are approaching hypoglycaemia. This study provides an argument that existing indications for CGM do not match risk factors for tight glycaemic control in ESRD. Hypoglycaemia is difficult to predict in ESRD patients and access to CGM should be widened.
THE ASSOCIATION BETWEEN HEMOGLOBIN A1C LEVEL AND COMPLICATIONS IN PATIENTS WITH DIABETES AND ADVANCED CHRONIC KIDNEY DISEASE

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Background and Aims: Although the global prevalence of advanced diabetic kidney disease is increasing, the optimum glycemic target remains uncertain. Specifically, data pertaining to the association of hemoglobin A1c (HbA1c) level with micro- and macrovascular outcomes in patients with advanced diabetic kidney disease remain inconclusive. We examined the association between HbA1c levels and complications in patients with diabetes and chronic kidney disease (CKD) stage 4 and 5.

Method: In a Danish nationwide registry-based retrospective cohort study, we included persons ≥18 years of age with diabetes, an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73m2 and a concurrent measured HbA1c between 2010 and 2022. Complications were categorized as 1) major adverse cardiovascular events (MACE) defined as a composite endpoint of acute myocardial infarction, stroke, and all-cause mortality; 2) microvascular complications defined as a composite endpoint of diabetic retinopathy, major lower extremity amputation, and start of dialysis; 3) hospitalization with hypoglycemia. Multiple outcome-specific Cox regressions stratified by HbA1c levels were performed to calculate the 1-year risk of complications standardized to the distribution of risk factors of all patients in the sample. The analyses regarding the risk of hypoglycemia were further stratified according to insulin treatment at baseline.

Results: In total, 34,046 patients were included. The median age was 76.2 (IQR 69.1-82.7) years and 54.6% were men. The median eGFR and HbA1c level was 26.4 (IQR 21.9-28.5) mL/min/1.73m2 and 53 (IQR 46-63) mmol/mol, respectively. Figure 1 depicts the 1-year risks of MACE and microvascular complications stratified by HbA1c level. We found a U-shaped association between HbA1c level and MACE where patients with an HbA1c level between 45-50 mmol/mol had the lowest risk. The risk increased significantly with an HbA1c level below 45 mmol/mol or above 65 mmol/mol compared with 45-50 mmol/mol (P<0.001). The risk of microvascular complications was lowest at an HbA1c level between 35-40 mmol/mol. The risk increased significantly with increasing levels of HbA1c above 50 mmol/mol compared with 35-40 mmol/mol (P<0.05). The 1-year risks of hospitalization with hypoglycemia stratified according to HbA1c level and insulin treatment are illustrated in Figure 2. For both groups, the risk was lowest at an HbA1c level between 30-40 mmol/mol and increased with increasing HbA1c levels.

Conclusion: In patients with diabetes and CKD stage 4 and 5, HbA1c levels >65 mmol/mol and <45 mmol/mol were associated with an increased risk of MACE, whereas HbA1c levels >50 mmol/mol were associated with a higher risk of microvascular complications. Our findings suggest that appropriate glycemic control can reduce adverse outcomes in patients with advanced CKD without increasing the risk of hypoglycemia, but also suggest that intensive glycemic control (HbA1c <45 mmol/mol) might be associated with an increased risk of MACE.
Figure 1: The 1-year risk of major adverse cardiovascular events and microvascular complications with 95% confidence intervals stratified by HbA1c level.

Figure 2: The 1-year risk of hospitalization with hypoglycemia with 95% confidence intervals stratified by HbA1c level and glucose-lowering treatment.
#4682
DOES RENAL ASYMMETRY WITH HYPERTENSION EQUAL RENAL ARTERY STENOSIS?
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Background and Aims: Renal ultrasound (US) is a basic imaging study in renal disease with hypertension (HTN) work up. Asymmetry is a frequent finding but it does not equal renal artery stenosis (RAS). Our aim was to describe the incidence of asymmetry findings in our Diagnostic and Intervisional Nephrology Unit (DINU) and study its correlation with HTN and RAS.

Method:

- Retrospective data collection within our DINU ultrasound database from January 2020 until May 2022. An experienced interventional nephrologist performed all US studies and all US were requested by nephrologists. Search terms included asymmetry, renal atrophy, RAS, stent, kidney malrotation and solitary kidney.
- Control group were all US defined as normal in the same study period. Those with polycystic kidney disease or surgical nephrectomy were excluded.
- Asymmetry was defined as more than 1.5 cm / 10% difference in longitudinal size between both kidneys.
- Demographic data, estimated glomerular filtration rate (eGFR) as per CKD-EPI equation, US request reason and findings were recorded. On those with HTN, number of antihypertensive medications and blood pressure (BP) measurements were also collected.

Results:

2454 US were done in the study period. US was requested due to chronic kidney disease work up in 29%. Urological alterations (hydrenephrosis and kidney scars) were found in 19.7%.
- 78.4% had HTN and 19.7% required more than 3 antihypertensive medications.
- Mean eGFR was 57.61 ± 30 ml/min/1.73 m².
- 51 (2.1%) were diagnosed as renal asymmetry, of which 11 (21.5%) were secondary to RAS confirmed by Doppler US. Doppler US confirmed RAS in 90.9%.
- Mean asymmetry was 2.46 cm and right kidney was the smaller in 67.5%.
- In 37% of those with asymmetry a complementary study was requested (nuclear study or CT angiogram)→ 13.7% had asymmetry without any other related pathology.
- HTN incidence in the asymmetry group without RAS was higher with statistical significance (40 vs 22, p < 0.05), and they required more antihypertensive medications than those in the control group (1 ± 2.09 vs 0.214, p < 0.05) to achieve acceptable BP control as per guidelines.
- Those with asymmetry without RAS had worse hypertension and their BP was toughest to control (32 vs 22, p < 0.05).

Conclusion: Renal asymmetry is infrequent (2%) and in up to a quarter of those this finding is related to RAS. In our experience, asymmetry associates with hypertension even if no RAS is present: renal asymmetry associates with higher hypertension prevalence and higher medication requirements to reach acceptable blood pressure control.

#5147
PREDICTING NON-DIABETIC KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: EXTERNAL VALIDATION OF FOUR PREDICTIVE MODELS
Deborah Soledad Roldán, Angela Rey, Enrique Gruss and Amir Shabaka
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Background and Aims: Several prediction models have been published for estimating the probability of non-diabetic kidney disease in kidney biopsies performed in patients with diabetes mellitus. External validation and comparison of these models is essential prior to their clinical application. The aim of this study was to validate and compare the predictive capacity of four previously described clinical models as a tool to predict non-diabetic kidney disease (NDKD) in diabetic patients.

Method: We retrospectively reviewed kidney biopsies performed in patients with type 2 diabetes mellitus between January 1999 and December 2022 in our centre. The probability of presence of NDKD was calculated by using the clinical and laboratory parameters at the time of the decision to perform a biopsy, according to 4 models: Surinrat’s model, Liu’s model, Li’s model and Garcia-Martin’s model (see Table 1). Overall model fit was assessed, calibration curves were plotted and discrimination for each model was assessed by using the receiver operating characteristic (ROC) curve in line with the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) guidelines.

Results: The study included 280 patients, 68.9% were males and the mean age was 65.4 ± 11.9 years. 172 patients (61.4%) had a diagnosis of non-diabetic kidney disease. On calculating the risk of NDKD, Surinrat’s, Li’s and Garcia-Martin’s models predicted 33.6%, 64.8% and 53.4% of NDKD when using the “probable NDKD” threshold, and 60.7%, 81% and 90.7% respectively when including the “grey zones”. Fleiss’ Kappa test showed a fair agreement between the four models when using the “probable NDKD” threshold, and 64.2% respectively while decreasing in Garcia-Martin’s model to 64.2%. Area under the ROC curve (AUC) was higher in Garcia-Martin’s model (AUC 0.66, 95% CI 0.58-0.74, p < 0.001) compared to Lin’s model (AUC 0.59, 95% CI 0.50-0.67, p = 0.044), while Surinrat’s and Liu’s models did not discriminate (AUC 0.55, 95% CI 0.47-0.64, p = 0.214 and AUC 0.58, 95% CI 0.49-0.63, p = 0.084).

Conclusion: There is a fair agreement between the four models for predicting non-diabetic kidney disease in type 2 diabetic patients. Of the models studied, Garcia-Martin’s model most accurately predicted non-diabetic kidney disease in type 2 diabetes patients, although discrimination remained poor. These models may not be suitable for guiding clinicians on indicating a kidney biopsy in diabetic patients in our population.
**Table 1: Performance of models for predicting the risk of NDRD.**

<table>
<thead>
<tr>
<th>Training set (N = 2244)</th>
<th>Clinical model</th>
<th>LASSO model</th>
<th>XGBoost model</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROC-AUC (95% CI)</td>
<td>0.713 (0.690-0.736)</td>
<td>0.853 (0.837-0.869)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.889 (0.875-0.902)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>PR-AUC (95% CI)</td>
<td>0.792 (0.768-0.816)</td>
<td>0.903 (0.885-0.920)</td>
<td>0.937 (0.939-0.957)</td>
</tr>
<tr>
<td>NRI (95% CI)</td>
<td>Ref</td>
<td>0.598 (0.543-0.648)</td>
<td>0.922 (0.872-0.973)</td>
</tr>
<tr>
<td>NRI (NDRD)</td>
<td>Ref</td>
<td>0.428 (0.396-0.457)</td>
<td>0.550 (0.518-0.579)</td>
</tr>
<tr>
<td>NRI (isolated DN)</td>
<td>Ref</td>
<td>0.170 (0.127-0.215)</td>
<td>0.372 (0.330-0.413)</td>
</tr>
<tr>
<td>IDI (95% CI)</td>
<td>Ref</td>
<td>0.188 (0.161-0.216)</td>
<td>0.327 (0.297-0.357)</td>
</tr>
<tr>
<td>Testing set (N = 961)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROC-AUC (95% CI)</td>
<td>0.737 (0.705-0.771)</td>
<td>0.845 (0.820-0.871)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.905 (0.886-0.923)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>PR-AUC (95% CI)</td>
<td>0.816 (0.783-0.850)</td>
<td>0.911 (0.891-0.931)</td>
<td>0.948 (0.938-0.964)</td>
</tr>
<tr>
<td>NRI (95% CI)</td>
<td>Ref</td>
<td>0.550 (0.469-0.626)</td>
<td>0.968 (0.894-1.045)</td>
</tr>
<tr>
<td>NRI (NDRD)</td>
<td>Ref</td>
<td>0.413 (0.367-0.457)</td>
<td>0.550 (0.506-0.593)</td>
</tr>
<tr>
<td>NRI (isolated DN)</td>
<td>Ref</td>
<td>0.136 (0.067-0.201)</td>
<td>0.418 (0.356-0.487)</td>
</tr>
<tr>
<td>IDI (95% CI)</td>
<td>Ref</td>
<td>0.173 (0.130-0.216)</td>
<td>0.354 (0.310-0.398)</td>
</tr>
</tbody>
</table>

<sup>a</sup>P < 2.2e-16 for comparison of LASSO model versus Clinical model.

<sup>b</sup>P < 2.2e-16 for comparison of XGBoost model versus Clinical model.

**Abreviations:** DN, diabetic nephropathy; NDRD, non-diabetic renal disease; ROC-AUC, receiver operating characteristic curves with area under curves; PR-AUC, precision and recall curves with area under curves; NRI, net reclassification improvement; IDI, integrated discrimination improvement; Ref, reference.
KIDNEY BIOPSY IN PATIENTS WITH TYPE 2 DIABETES: A SINGLE CENTER OBSERVATIONAL STUDY

Inês Alexandre, Andreia Curto, Fábio Henriques, Mariana Ramos, Catarina Brás, Afonso Santos, Pedro Campos, Fernando Domingos and Ana Pires

Hospital Prof. Dr. Fernando Fonseca, Portugal

Background and Aims: Patients with type 2 diabetes mellitus (T2DM), may have various underlying causes contributing to kidney disease beyond diabetic nephropathy (DN). In such cases, a kidney biopsy (KB) can provide a definite diagnosis and allow for tailored treatment options. The aim of this study is to evaluate non diabetic kidney disease (NDKD) in T2DM patients and identify data to support KB indications.

Method: This is a retrospective observational study that included patients with T2DM who were submitted to a native KB between 2011 and 2022. We collected demographic, clinical and laboratory data at the date of biopsy. KB indication was considered in order to include the patients in the first encountered criteria defined sequentially as the presence of (1) nephrotic syndrome, (2) low or rapidly declining estimated glomerular filtration rate (eGFR), (3) nephrotic proteinuria and (4) hematuria.

Results: We analysed 72 patients with T2DM that were submitted to KB (Table 1). All except one patient had hypertension and 38 patients were screened for diabetic retinopathy (DR), which was present in 23 patients.

Table 1: Demographic and clinical characteristics of patients submitted to KB.

<table>
<thead>
<tr>
<th></th>
<th>DKD</th>
<th>NDKD</th>
<th>NDKD and DKD</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>36 (50)</td>
<td>27 (37.5)</td>
<td>9 (12.5)</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>66.7</td>
<td>55.6</td>
<td>77.8</td>
<td>63.9</td>
<td>ns</td>
</tr>
<tr>
<td>Median age, [IQR], years</td>
<td>64 [50-72]</td>
<td>65 [41-76]</td>
<td>68 [58-80]</td>
<td>66 [56-70]</td>
<td>ns</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>81</td>
<td>89</td>
<td>89</td>
<td>85</td>
<td>ns</td>
</tr>
<tr>
<td>Median HbA1c, [IQR], %</td>
<td>6.9 [6.0-8.0]</td>
<td>6.2 [5.7-7.0]</td>
<td>6.6 [6.1-7.2]</td>
<td>6.6 [5.9-7.8]</td>
<td>ns</td>
</tr>
<tr>
<td>Median CKD-EPI eGFR, [IQR], mL/min/1.73m²</td>
<td>21.3 [15-38]</td>
<td>24 [14-28]</td>
<td>19.5 [10-41]</td>
<td>22.2 [14-35]</td>
<td>ns</td>
</tr>
<tr>
<td>Median albumin to creatinine ratio, [IQR], g/g</td>
<td>4.01 [2.2-5.0]</td>
<td>1.0 [0.1-3.5]</td>
<td>4.14 [0.5-6.9]</td>
<td>2.65 [0.9-4.8]</td>
<td>0.006</td>
</tr>
<tr>
<td>Hematuria (%)</td>
<td>58.3</td>
<td>51.9</td>
<td>55.6</td>
<td>55.6</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetic retinopathy (%)</td>
<td>76.2</td>
<td>23</td>
<td>100</td>
<td>60.5</td>
<td>0.002</td>
</tr>
<tr>
<td>KB criteria nephrotic syndrome (%)</td>
<td>22.2</td>
<td>7.4</td>
<td>22.2</td>
<td>16.7</td>
<td>ns</td>
</tr>
<tr>
<td>KB criteria low or rapidly declining eGFR (%)</td>
<td>50.0</td>
<td>77.8</td>
<td>44.4</td>
<td>59.7</td>
<td>0.05</td>
</tr>
<tr>
<td>KB criteria nephrotic proteinuria (%)</td>
<td>25.0</td>
<td>11.1</td>
<td>22.2</td>
<td>19.4</td>
<td>ns</td>
</tr>
<tr>
<td>KB criteria hematuria (%)</td>
<td>2.8</td>
<td>3.7</td>
<td>11.1</td>
<td>4.2</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns – not significant (p-value > 0.05)
Diabetic kidney disease (DKD) is a common complication of type 2 diabetes (T2DM) and is associated with increased mortality and morbidity. The diagnosis of DKD is based on the presence of proteinuria (with a protein-to-creatinine ratio (pPCR) ≥ 30 mg/mmol) and declining estimated glomerular filtration rate (eGFR) (≤ 60 mL/min/1.73 m²). However, the absence of DKD does not exclude the presence of diabetic kidney disease (DKD) with or without non-diabetic kidney disease (NDKD) in T2DM patients.

### #3505 DIAGNOSING HYPERTENSION IN HEMODIALYSIS PATIENTS USING HOME VERSUS ROUTINE PERIDIALYTIC BP MEASUREMENTS

**Kallitheni Leonidou1, Panagiotis Georgiannos1, Anastasios Kollias2, Ioannis Kontogiorgos3, Vasilios Vaios1, Apostolos Karligkiotis1, Konstantinos Mavromatis3, Pantelis Zebekakis2, George Stergiou2 and Vassilios Liakopoulos4**

1AHEPA Hospital, Aristotle University of Thessaloniki, 1st Department of Medicine, Thessaloniki, Greece, 2Sotiria Hospital, National and Kapodistrian University of Athens, Hypertension Center STRIDE-7, 3rd Department of Medicine, Athens, Greece, 3Therapeutiki Dialysis Center, Thessaloniki, Greece and 4AHEPA Hospital, Aristotle University of Thessaloniki, 1st Department of Medicine, Thessaloniki, Greece

**Background and Aims:** Although routine blood pressure (BP) measurements taken shortly before or after dialysis provide imprecise reflection of interdialytic ambulatory BP, this method continues to form the basis for the diagnosis of hypertension among patients on hemodialysis. Home BP monitoring (HBPM) is a guideline-recommended technique that may improve the diagnosis of hypertension in this population. Using 44-hour ambulatory BP monitoring (ABPM) as the reference-standard method, this study aimed to compare the diagnostic performance of home versus routine pre- and postdialysis BP recordings in hemodialysis patients.

**Method:** In 70 stable patients with end-stage kidney disease receiving thrice-weekly hemodialysis, BP was assessed with the following methods: (i) routine predialysis and postdialysis BP measurements averaged over 2 weeks; (ii) HBPM for 7 days (dublate morning and evening measurements, Microlife WatchBP Home N); (iii) ABPM (20 min intervals over an entire interdialytic interval - 44 hours, Microlife WatchBPO3).

**Results:** The mean age of the patients was 65±3.13 years; 45 patients (64%) were males, and 62 (88.7%) had a known history of hypertension. The mean 95% confidence interval (CI) of the difference between ambulatory systolic BP (SBP) and (i) predialysis SBP was 11.43 (8.24, 14.62) mmHg, (ii) postdialysis SBP was 3.9 (0.37, 7.56) mmHg, and (iii) home SBP was 8.61 (6.05, 11.17). The area under the receiver operating characteristic curve for the detection of an ambulatory daytime SBP ≥ 135 mmHg was significantly higher for home BP measurements 0.934 (95% CI: 0.871-0.996) as compared to predialysis 0.778 (95% CI: 0.643-0.913) and postdialysis 0.766 (95% CI: 0.623-0.909) BP recordings (P = 0.02 for both comparisons). 1-week average home SBP at the cut-off point of 141.0 mmHg provided the best combination of high sensitivity (85.7%) and high specificity (92.9%) in diagnosing systolic ambulatory hypertension.

**Conclusion:** The present study shows that among patients on hemodialysis, HBPM for 1 week provides greater accuracy than 2-week averaged routine pre- and postdialysis BP recordings in the diagnosis of hypertension confirmed by the reference-standard method of interdialytic ABPM.

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**ANTIHYPERTENSIVE PRESCRIBING PATTERNS IN CKD: FINDINGS FROM THE SALFORD KIDNEY STUDY**

**Rajkumar Chinnadurai1,2, Hon Lin Henry Wu1, Jones Abumara1,2, Sharmilee Renganarajan1, Darren Green1,2 and Philip A. Kalra1,2**

1Salford Care Organisation, Northern care Alliance NHS Foundation Trust, Department of Renal Medicine, Salford, United Kingdom and 2Faculty of Medicine, Medicine and Health, University of Manchester, Manchester, United Kingdom

**Background and Aims:** Hypertension is the second leading cause of chronic kidney disease (CKD) following diabetes and occurs in most patients with CKD. Finding an optimal treatment regime for hypertension remains challenging due to the complex bidirectional cause-and-effect relationship between hypertension and CKD, and hypertensive CKD patients may require treatment with multiple antihypertensive drugs. Database studies and practice guidelines have continued to demonstrate international variability in antihypertensive treatment practices. We analysed data from the Salford Kidney Study (SKS) database in relation to antihypertensive prescribing patterns among study patients.

**Method:** The SKS is an ongoing prospective study recruiting patients with CKD since the year 2002. Data including patient demographics, comorbidities, physical parameters, concurrent medications, and biochemical results are collected at baseline (study enrolment). All patients are followed up annually until they reach their endpoints [reaching end-stage kidney disease (ESKD), death, or discharge from follow-up] individually, with updates in their medical records including a list of medications. We have used Cox regression analysis and Kaplan Meier charts to investigate the associations between Renin-Angiotensin-Aldosterone System inhibitor (RAASi) use and the number of antihypertensive agents (binary groups of ≤ 3 or > 3), and clinical outcomes (ESKD and all-cause mortality).

**Results:** A total of 3230 patients recruited between October 2002 and December 2019 were included in this analysis. At baseline, the median age of the cohort was 67 years with a predominance of males (62%) and those of white ethnicity (96%), 90% had a history of hypertension and 32% were diabetic. The median blood pressure was 138/75 mmHg. Previous myocardial infarction was recorded in 15%, congestive cardiac failure in 17% and cerebrovascular disease in 7.7% of the patients. The median estimated glomerular filtration rate (eGFR) was 30 ml/min/1.73 m² and the median urine protein creatinine ratio (uPCR) was 35 mg/mmol. RAASi agents (ACEi & ARB) (56%) were the most common antihypertensive medications to be prescribed, followed by diuretics (50%), calcium channel blockers (45%), and beta blockers (34%). The proportion of patients prescribed RAASi was associated with greater proteinuria (43 vs 33%, p < 0.001). CKD patients with preexisting cardiovascular comorbidities were more likely to be prescribed beta blockers (44 vs 27%, p < 0.001), diuretics (58 vs 39%, p < 0.001) and mineralocorticoid antagonists (6.4 vs 1.85%, p < 0.001). An increasing number of CKD patients were being prescribed ARBs over 24-month follow-up (34 vs 28%, p = 0.02). In a multivariable Cox-regression analysis, RAASi intake was not associated with reaching ESKD (HR 0.91; p = 0.49) but was associated with a significant survival benefit (HR 0.84; p = 0.001) (Figure 1). Use of a higher number of antihypertensive agents (i.e. > 3) was associated with both greater mortality (HR 1.28; p = 0.02) and worse dialysis-free survival (HR 1.46; p = 0.007) (Figure 2).

**Conclusion:** Antihypertensive prescribing patterns in the SKS were consistent with current guidelines in the U.K. (e.g. NICE guidance 2022), with RAASi being predominantly prescribed as the first-line antihypertensive agent. An overall survival benefit was noted with RAASi use, although there was no signal for reducing progression towards ESRD. Outcomes were poor in patients with resistant hypertension needing multiple antihypertensive agents. Considering existing variations between the U.K. and other international guidelines regarding antihypertensive treatment in CKD, continued research is indicated to bridge the gaps between these recommendations and optimise patient outcomes.
ENVIRONMENTAL MELAMINE EXPOSURE AND ADVERSE KIDNEY OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Yi-Chun Tsai¹,² and Ming-Tsang Wu³

¹Kaohsiung, Taiwan, Rep. of China, ²Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, Rep. of China and ³Kaohsiung Medical University, Kaohsiung, Taiwan, Rep. of China

Background and Aims: The impact of environmental melamine exposure on kidney outcomes in type 2 diabetes (T2D) remains unclear. The aim of this study is to evaluate the relationship between melamine and adverse kidney progression in T2D population.

Method: This longitudinal study enrolled 561 T2D patients during October 2016 and June 2020 and followed until December 2021. Baseline urinary melamine levels were measured by LC-MS/MS, and average daily intake (ADI) of melamine was estimated. Primary kidney outcomes were defined as doubling of serum creatinine levels or end stage kidney disease (ESKD), and secondary kidney outcomes included rapid decline in kidney function as estimated glomerular filtration rate (eGFR) decline > 5 ml/min/1.73m²/year.

Results: Baseline median urinary corrected melamine levels and estimated DI of melamine were 0.8 μg/mmol and 0.3 μg/kg/day in 561 T2D patients. During 3.7 years of follow-up, urinary corrected melamine level was positively correlated with reaching composite outcomes of either doubling of serum creatinine levels or ESKD and rapid decline in kidney function. Those with the highest quartile of urinary corrected melamine had 2.96-fold risk of composite outcomes of either doubling of serum creatinine levels or ESKD and 2.47-fold risk of eGFR decline > 5 ml/min/1.73m²/year. Estimated ADI of melamine also had significant correlation with adverse kidney outcomes. Furthermore, the positive relationship between melamine exposure and rapid decline in kidney function was only found in T2D patients with male, baseline eGFR ≥ 60 ml/min/1.73m² or glycated hemoglobin ≤ 7%.

Conclusion: Melamine exposure is significantly associated with kidney outcomes in T2D patients, especially in those with male, well sugar control or preserved baseline kidney function.

PREVALENCE, AWARENESS, TREATMENT, AND CONTROL OF HYPERTENSION IN OLDER ADULTS WITH CHRONIC KIDNEY DISEASE: THE IRISH LONGITUDINAL STUDY ON AGEING

Mohammed Alamin¹, Hamidi Miri¹, Mary Byrne², Robert Gilligan³, Leonard Browne¹,², Donal Sexton¹,²,³ and Austin Stack¹,²,⁶

¹University of Limerick, School of Medicine, Limerick, Ireland, ²University of Limerick, Health Research Institute, Limerick, Ireland, ³Trinity College Dublin, School of Medicine, Dublin, Ireland, ⁴Trinity College Dublin, Department of Medical Gerontology, School of Medicine, Dublin, Ireland, ⁵Trinity College Dublin, Trinity Health Kidney Centre, Dublin, Ireland and ⁶University Hospital Limerick, Department of Nephrology, Limerick, Ireland

Background and Aims: Hypertension is a well-known modifiable risk factor for chronic kidney disease (CKD) yet effective management remains a challenge. Data on hypertension awareness, treatment and control among CKD patients in Ireland is limited. Therefore, the objective of this study was to determine the prevalence, extent of awareness, treatment and control of hypertension among older adults with CKD in the Irish population.

Method: We utilised cross sectional data from the first wave of The Irish Longitudinal Study on Ageing (TILDA) conducted between 2009 and 2011. Participants aged 50 years or more with complete measurements on serum creatinine and blood pressure (BP) were included (n = 5,356). CKD was defined as eGFR <60ml/min/1.72m². Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or self-reported use of antihypertensive medication. Participants' awareness and treatment of hypertension were defined using self-report and hypertension control was evaluated as systolic/diastolic blood pressure <140/90 mmHg. We determined the weighted prevalence of hypertension, awareness, treatment, and control using sample weights, and multivariable logistic regression explored associations of demographic, clinical and behavioural characteristics with control of hypertension. Associations were expressed using adjusted odds ratios (OR) with 95% confidence intervals (CIs). Analyses were conducted in Stata and R.
Method: There were 639/5,356 participants (13.3% (95% CI: 12.3-14.4)) with CKD. The weighted prevalence of hypertension was significantly higher in participants with CKD than without CKD (81.8% versus 59.8% respectively, P<0.001). Among those with CKD and hypertension, 70.8% (95% CI: 66.5-74.7) were aware of hypertension, and 83.4% (95% CI: 79.9-86.5) were treated with antihypertensive medication. Despite higher levels of awareness and treatment of hypertension in those with CKD, only 50.4% (95% CI 45.4-55.5) of treated subjects had BP <140/90 mmHg. BP control was similarly poor for non-CKD participants at 49.4% (95% CI: 46.9-51.8). The most commonly used medications among treated CKD participants were β-blockers 41.8% (95% CI 36.7-47.1), angiotensin-converting enzyme inhibitors 34.0% (95% CI 29.2-39.2), and angiotensin receptor blockers 33.7% (95% CI: 28.9-38.8). Over half [54.8% (95% CI: 49.5-60.0)] of CKD participants were treated with ≥2 antihypertensive medications. In multivariable analysis, the likelihood of BP control (<140/90 mmHg) was lower for older CKD patients [OR: 0.94 (95% CI: 0.90-0.98) per 1 year increase in age], greater for those on combination therapy [OR: 1.87 (95% CI: 1.13-3.1)] and for those with history of cardiovascular disease [OR: 2.33 (95% CI: 1.43-3.82)].

Conclusion: Despite established evidence that control of hypertension can slow the progression of CKD and reduce cardiovascular complications, our results indicate that the prevalence of hypertension in older adults with CKD is high and the control of hypertension is poor and worsens with advancing age. Approximately, one third of participants with CKD were unaware of their hypertensive status and approximately one fifth of participants were untreated.

#6530
WHAT IS IMPORTANT IN PRIMARY CARDIORENAL INTERACTION SYNDROME
Danijela Tasic1, Zorica Dimitrijevic1, Sonja Radenkovic2 and Gordana Kocić3
1University of Niš, Faculty of Medicine, UCC, Clinic of Nephrology, Niš, Serbia, 2University of Niš, Faculty of medicine, Institute of Pachophysiology, Niš, Serbia and 3University of Niš, Faculty of Medicine, Niš, Serbia

Background and Aims: Renal function is important in congestive heart failure syndrome because existing or secondary-induced renal weakness contributes to the worsening and progression of heart failure. Decreased ejection fraction in acute heart failure leads to more acute kidney damage compared to patients with preserved ejection fraction. Also, heart failure with a drop in the ejection fraction of the left ventricle is not a dominant characteristic of patients with cardiorenal syndrome type 2. A significant risk factor in the first type of cardiorenal syndrome is, among others, age and diabetes. The prevalence of heart failure with preserved ejection fraction and increased left ventricular mass is higher in the elderly. The aim of the work is how to differentiate and which factors predispose the occurrence of the first and second types of primary cardiorenal syndrome.

Method: 42 subjects, 24 men and 18 women, with an average age of 70.72±9.26 years, with a diagnosis of worsening heart function that led to kidney dysfunction, were analyzed. The first type of cardiorenal syndrome accounted for 57.14% and the second type of cardiorenal syndrome accounted for 42.86%. The study was designed as a cross-sectional comparative study, and the main criterion for the inclusion of subjects was the existence of a new or previously diagnosed clinically manifest cardiovascular disease. Continuous variables are presented with mean values, standard deviations and medians, and categorical variables with frequencies and percentages. The normality of the distribution of continuous variables was determined by the Shapiro-Wilk test. Depending on the normality of the distribution of continuous variables, the comparison of continuous variables between two groups was performed by the Student’s t-test of unknown samples in the case of normality, or by the Mann-Whitney test in the case that the distribution deviates from normality. Determining the difference in the representation of categorical variable modalities between groups was determined by the chi-squared test. Values of p<0.05 were considered statistically significant.

Results: Based on everything is done, the following was determined as statistically significant: Patients with CRS2 are statistically significantly older than patients with CRS1 (p<0.05, Student’s t-test of independent samples), and they also have a statistically significantly higher value of HDL-C (p<0.05), Patients with diabetes (p = 0.0488) and with sinus rhythm (p = 0.0442) were statistically significantly more represented in patients with CRS1. Patients with CRS1 had statistically significantly higher values of serum urea and serum creatinine compared to patients with CRS2 (p<0.05, Mann Whitney test). In patients with CRS2, the value of AOPP was statistically significantly higher than in patients with CRS1 (p<0.01, Student’s t-test of independent samples).

Conclusion: The results obtained in our study are related to the assessment of the functional state of the heart and kidneys in primary cardiorenal syndrome type one and two in which the main predisposing factors are age, diabetes and reduction of renal function. By correlation analysis in the second type of cardiorenal syndrome, HDL-C particles were significantly elevated. Although the values of nitrogen products were lower in the second type of cardiorenal syndrome, AOPP stood out as statistically significant in the lower functional class.

#3420
CLINICAL CHARACTERISTICS AND PRIMARY OUTCOMES OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND CENTRAL DIABETES INSIPIDUS
Xin Chen1, Shuo Zhang1, Peng Xia3, Xiaoxiao Shi3, Wuhai Ting1, Yu-Bing Wen1, Yan Qin1, Xingping Tian1, Huijuan Zhu2 and Limeng Chen1
1Peking Union Medical College Hospital, Nephrology, Dongcheng-qu, P.R. China, 2Peking Union Medical College Hospital, Rheumatology, Dongcheng-qu, P.R. China and 3Peking Union Medical College Hospital, Endocrinology, Dongcheng-qu, P.R. China
**Background and Aims:** Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by systemic small-vessel vasculitis and may rarely present as central diabetes insipidus (CDI). AAV-associated CDI should be recognized to avoid unnecessary biopsies of the pituitary gland and minimize the risk of irreversible loss of pituitary function. In this study, we aimed to determine the clinical characteristics and prognosis of patients with AAV-associated CDI.

**Method:** This was a nested case-control study where AAV patients with CDI at the Peking Union Medical College Hospital were followed from January 2012 to April 2022. Case-control matching with AAV patients without CDI was performed (1:2), and participants were matched by age, sex, and AAV classification. We collected clinical data every 3–6 months and conducted a literature review using PubMed to identify relevant articles published from 1983–2022.

**Results:** Among 1203 hospitalized AAV patients, 16 patients with CDI were included (1.3%). The average age was 49 years, and men accounted for 56.3%. Granulomatosis with polyangiitis (GPA) accounted for 87.5% of patients. AAV patients with CDI had more ear, nose, and throat (ENT) (81.3%) involvement and less renal impairment than those in the control group (P < 0.05). After a mean follow-up of four years, 50% of patients were in remission, 37.5% relapsed, and 12.5% died. Our literature review suggested that patients in Asian countries tend to be older men and have higher MPO-ANCA positivity than those in European countries. Furthermore, PR3-ANCA positivity may predict disease recurrence.

**Conclusion:** AAV patients with CDI had more ENT involvement and a higher eGFR. MPO-ANCA positivity is more commonly observed in Asian countries than in European countries, and PR3-ANCA positivity may predict recurrence.

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**ASSOCIATION OF DEMENTIA AND EXPOSURE OF PROTON PUMP INHIBITORS IN DIABETIC PATIENTS**

Yi-Hsin Chen

Taichung Tzuchi Hospital, Nephrology, Taichung City, Taiwan, Rep. of China

**Background and Aims:** Dementia is characterized by a decline in cognition and an increasing inability to live independently. Proton pump inhibitors (PPI) are commonly used to treat gastric or duodenal ulcers. Recently, concern about the risk of dementia and exposure to PPI was noted. However, no known association has previously been reported in patients with diabetes.

**Method:** We analyzed data from the Taiwan National Health Insurance Research Database between January 1st, 2002 and December 31st, 2013. A total of 526920 diabetic patients were selected as the study cohort. A 1 to 4 propensity score was used for matching.

**Results:** During the follow-up period, 169 (2.2%) patients experienced newly diagnosed dementia compared to 1.7% of the control group. According to univariate analysis, the hazard ratio of dementia when exposed to PPI was 1.98 (p = 0.0007). In multivariate analysis, the hazard ratio of exposure to PPI was 1.11 (p = 0.0008). In the sensitivity test, greater than 180 cDDDs were associated with a hazard ratio of 1.5 (p = 0.0006).

**Conclusion:** The association between PPI use and dementia was significant in diabetic patients. Therefore, PPI use should be cautious in this population. Further study is needed to clarify the mechanism.

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**Table 1: Baseline characteristics.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Exposure</th>
<th>No Exposure</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
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<td>30332</td>
<td>NA</td>
</tr>
<tr>
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<td>58.7±11.8</td>
<td>58.7±11.8</td>
<td>NA</td>
</tr>
<tr>
<td>CCIS (mean±SD)</td>
<td>0.6±1.0</td>
<td>0.6±1.0</td>
<td>0.339</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Male</td>
<td>4550(60.0)</td>
<td>18200(60.0)</td>
<td>NA</td>
</tr>
<tr>
<td>Female</td>
<td>3033(40.0)</td>
<td>12132(40.0)</td>
<td>NA</td>
</tr>
<tr>
<td>CCIS group</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>0</td>
<td>4872(64.2)</td>
<td>19488(64.2)</td>
<td>NA</td>
</tr>
<tr>
<td>1-2</td>
<td>2349(31.0)</td>
<td>9396(31.0)</td>
<td>NA</td>
</tr>
<tr>
<td>3-4</td>
<td>310(4.1)</td>
<td>1240(4.1)</td>
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</tr>
<tr>
<td>&gt;4</td>
<td>52(0.7)</td>
<td>208(0.7)</td>
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</tr>
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<td>Comorbidities</td>
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<tr>
<td>Hypertension</td>
<td>2775(36.6)</td>
<td>11100(36.6)</td>
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</tr>
<tr>
<td>Lipid disorders</td>
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<td>4168(13.7)</td>
<td>NA</td>
</tr>
<tr>
<td>Stroke</td>
<td>368(4.9)</td>
<td>1472(4.9)</td>
<td>NA</td>
</tr>
<tr>
<td>Depression</td>
<td>49(0.6)</td>
<td>196(0.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Insomnia</td>
<td>460(6.1)</td>
<td>1840(6.1)</td>
<td>NA</td>
</tr>
<tr>
<td>Anxiety</td>
<td>396(5.2)</td>
<td>1584(5.2)</td>
<td>NA</td>
</tr>
<tr>
<td>SES</td>
<td></td>
<td></td>
<td>0.425</td>
</tr>
<tr>
<td>Low</td>
<td>2397(31.6)</td>
<td>9870(32.5)</td>
<td>NA</td>
</tr>
<tr>
<td>Moderate and high</td>
<td>5186(68.4)</td>
<td>20462(67.5)</td>
<td>NA</td>
</tr>
<tr>
<td>Urbanization</td>
<td></td>
<td></td>
<td>0.011</td>
</tr>
<tr>
<td>Urban</td>
<td>2130(28.1)</td>
<td>8381(27.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Un-urban</td>
<td>5453(71.9)</td>
<td>21951(72.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Geographic region</td>
<td></td>
<td></td>
<td>0.011</td>
</tr>
<tr>
<td>Northern/Central</td>
<td>4778(63.0)</td>
<td>19589(64.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Southern/Eastern</td>
<td>2805(37.0)</td>
<td>10743(35.4)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviation: SES, socioeconomic status
**Table 2: Multivariable Cox proportional hazard model hazard ratios of dementia in exposure and no exposure group in diabetes patients.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Event, n</th>
<th>Rate (per 100 persons)</th>
<th>Univariate HR [95% CI]</th>
<th>Multivariate HR [95% CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI Usage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Exposure</td>
<td>503/30332</td>
<td>1.7</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure</td>
<td>169/7583</td>
<td>2.2</td>
<td>1.98(1.66-2.35)</td>
<td>1.90(1.60-2.27)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>356/2180</td>
<td>1.3</td>
<td>1.23(1.11-1.38)</td>
<td>1.16(1.04-1.30)</td>
<td>0.0016</td>
</tr>
<tr>
<td>Female</td>
<td>147/1383</td>
<td>1.5</td>
<td>1.31(1.13-1.51)</td>
<td>1.25(1.05-1.48)</td>
<td>0.012</td>
</tr>
<tr>
<td>CCIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>250/12267</td>
<td>2.0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate and high</td>
<td>422/25648</td>
<td>1.6</td>
<td>0.78(0.67-0.92)</td>
<td>0.95(0.81-1.12)</td>
<td>0.565</td>
</tr>
<tr>
<td>SES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>250/12267</td>
<td>2.0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
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<td>422/25648</td>
<td>1.6</td>
<td>0.78(0.67-0.92)</td>
<td>0.95(0.81-1.12)</td>
<td>0.565</td>
</tr>
<tr>
<td>Geographic region</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern/Central</td>
<td>432/24367</td>
<td>1.8</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern/Eastern</td>
<td>240/13548</td>
<td>1.8</td>
<td>0.97(0.83-1.13)</td>
<td>0.91(0.77-1.07)</td>
<td>0.259</td>
</tr>
</tbody>
</table>

The adjusted HRs were calculated after controlling for age, gender, CCIS, hypertension, lipid disorders, stroke, depression, insomnia, anxiety, socioeconomic status, urbanization and region.

HR is abbreviation for hazard ratio. CI is for confidence interval and CCI is for Charlson comorbidity index.

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**#6373**

**EFFECT ON BLOOD PRESSURE AND CARDIOVASCULAR RISK FACTORS IN PEDIATRIC PATIENTS DURING COVID-19 PANDEMIC CONFINEMENT (COBECOR STUDY)**

Elena Codina Sampera1, Pedro Arango Sancho1, Ana Cristina Aguilar Rodríguez2, Bernat Gómez Herrera1, Marta Jiménez Moreno1, Yolanda Calzáda Baños1, Raquel Jiménez García1, Verónica Coll Brito1, Osmar David González3 and Álvaro Madrid Aris1

1Hospital Sant Joan de Déu, Pediatric Nephrology, Esplugues de Llobregat, Spain, 2Fundació Puigvert, Barcelona, Spain and 3Pontificia Universidad Católica de Chile, Santiago, Chile

**Background and Aims:** Patients monitored in the cardiovascular risk (CVR) consultation usually present overweight/obesity, metabolic syndrome, tendency to hypertension (HTN), poor eating habits and sedentary lifestyle, with great resistance to change, great influence of the environment and, frequently, psychosocial limitations. We asked whether home confinement for COVID-19 (March-May 2020) could have negative effects in relation to CVR in these patients. The main objective of this work is to assess this hypothesis with respect to HTN and the use of antihypertensive drugs in these patients. As a secondary objective, we assessed changes in other parameters: body mass index (BMI), level of physical activity and diet.

**Method:** Retrospective cohort study with review of 738 ambulatory blood pressure monitoring (ABPM) between 2019-2022 obtaining, after applying the exclusion criteria (no overweight/obesity, poor therapeutic compliance, underlying renal pathology or failure to perform two ABPM in the study period), a final cohort of 46 patients divided into two groups (23 each): one group exposed to home confinement (G1) with one ABPM before and after home confinement and another group not exposed to confinement (G2) with two ABPM in different periods between 2021-2022. Blood pressure (BP) percentile values, dipper pattern, variability and blood pressure load, as well as the rest of the CVR parameters were compared in both periods.

**Results:** The mean age was 13 years (13.8 G1/13.2 G2) with a mean time between the 1st and 2nd ABPM of 11 months (11.08 G1/10.95 G2) and a greater reduction in BMI in G2 than in G1 (1.05 G1/1.21 G2). Despite this, the results were not statistically significant. Nor were the results significant in terms of differences in AT or worsening of the dipper pattern (30.4% in G1 and 21.7% in G2). We did observe differences (p < 0.022) in the use of antihypertensive drugs, although contrary to our initial hypothesis, with greater use of drugs in G2.

**Conclusion:** Although the low sample size, the biases inherent in the design and the lack of previous studies make the interpretability and statistical significance of some results difficult, they reinforce that the measures during confinement did not contemplate all spheres of health and the need to implement specific CVR consultations. Obesity and its associated pathologies are an important public health problem that pediatricians have the responsibility to address.

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**#4869**

**ULTRASOUND IMAGING PATTERNS OF KIDNEY DISEASE IN PATIENTS WITH METABOLIC SYNDROME**

Rostyslav Bubnov

Clinical Hospital ‘Pheophania’ of State Affairs Department, Ultrasound, Kyiv, Ukraine

**Background and Aims:** Meeting definition of metabolic syndrome (MetS) requires detection of central obesity (increasing waist circumference, WC) plus any two of the other four factors (hyperglycemia, dyslipidemia, cardiovascular disease, hypertension) [1]. Up to date, kidney evaluation is not fully reflected in MetS evaluation. Multiparameter ultrasound (US) can provide accurate information on every MetS sign [2] and for specific detecting type of chronic kidney disease (CKD) [3]. The Aim was to study added diagnostic value of ultrasound diagnosis of chronic kidney disease in patients with MetS for precise diagnosis and patients stratification.

**Method:** We included 48 overweight subjects patients (27–75 years; 25 women) with signs of MetS, BMI > 30, waist circumference (WC) > 110. The control group included 50 healthy individuals (26 women), mean age 43 ± 7 years without clinical, laboratory signs of MetS, nephropathy and liver pathology. All patients underwent general clinical, lab tests; abdominal US including precise multiparameter US of kidneys as in [3] measuring shear wave elastography (SWE), Doppler in parenchyma and vessels. We determined fat accumulations measuring VF and subcutaneous (SF) fat thickness (cm) and areas (cm²) on US.

**Results:** We detected hypertension (in 62%); hypercholesterolemia (in 45%); hyperuricemia (in 28%); hyperglycemia (in 32%); nephropathy (in 37%), portal hypertension (in 32%) in obese individuals (vs controls p < 0.05). In all patients we found increasing of visceral fat and various abnormalities in kidneys on US, we distinguished patterns in according to constituents of MetS by its definition follows:
Diabetic nephropathy included mild decreasing or normal kidneys size, thinning parenchyma, low differentiation, clear smooth margins, Doppler showed mild decreasing velocities, increasing of RI in segmental arteries over 0.7 (Figure 1).

Ischemic pattern associated with advanced atherosclerosis included severe decreasing of size, thinned, hyperechoic parenchyma; decreasing velocities under 25 cm/s., severe increasing of RI over 0.8.

Hypertension associated nephropathy: mild changes in structure, normal velocities, increased RI (Figure 2). Hypertension correlated with levels of RI.

Nephropathy in hyperuricemia and gout: signs as in [3] included thinning, increasing echogenicity of kidney parenchyma (P < 0.05), detection of fibrotic changes and small hyperechoic inclusions, hilly margins, anechoic strips under the capsule, RI increasing in segmental arteries over 0.7.

“Circular pyramids pattern” included hyperechoic circles around pyramids (white pyramids sign, hyperdense renal pyramids sign) with normal size, normal / mild increase of RI. SWE showed increased parenchyma stiffness to 10 ± 1.7 kPa (6–17 kPa) versus 4.2 ± 1.2 kPa (P < .05), showed differences among patterns, highest values were in nephropathy in gout and ischemia.

Conclusion: Multiparameter ultrasound is effective for detecting and distinguishing patterns of kidney disease in MetS provides additional value for differentiation and modification treatment and targeted prevention. Kidney involvement should be considered in management of MetS.
interdialytic interval. The parameters evaluated by the Mobil-o-graph device were peripheral and central systolic (pSBP and cSBP) and diastolic (pDBP and cDBP) blood pressure and pulse wave velocity (PWV). All patients were screened for hydration status with lung ultrasound before entering the study and body weight was actively monitored before each session.

Results: Overall, 29 patients with a mean age of 57.9±14.9 years were included in this prospective interventional study. Body weight did not change significantly between the 3 dialysate concentrations. There was a significant increase of 6 mmHg in the mean pSBP with the change in sodium concentration from 137 to 139 and to 141 meq/l (from 122.7 to 125.6 and to 128.3 mmHg respectively, p = 0.032). Mean cSBP was also significantly increased by 5 mmHg (from 110.3 to 112.6 and to 115.1 mmHg respectively, p = 0.02). Peripheral and central DBP did not change significantly (from 71.4 to 73.2 and to 74.1 mmHg, p = ns and from 73.9 to 74.8 and to 75.3 mmHg, p = ns, respectively), as well as PWV (from 8.4 to 8.2 cm/sec, p = ns).

Conclusion: The increasing sodium concentration in the dialysate causes a significant increase in systolic blood pressure and body weight, without a change in PWV.

#5690
COMBINED USE OF SOLUBLE ST2 AND NT-PROBNP FOR PREDICTING MAJOR ADVERSE CARDIOVASCULAR EVENTS IN TYPE 2 DIABETES AND DIVERSE RENAL FUNCTION

Xabier Irazusta Olloquegui1, Jose Maria Mora Gutierrez2,3, Laura Juliana Castaneda-Infante2, Saioa Echeverria Andueza4, Marina Pascual Icoz1,3, Susanna Ravassa1,3, Agnes Diaz-Dorronsoro1, Maria A Fernandez-Seara5, Francisco Javier Escalada1,4 and Nuria Garcia-Fernandez1,3

Background and Aims: Plasma levels of soluble ST2 protein (sST2), a biomarker associated with fibrosis and inflammation, have been related with an increased risk of adverse events in patients with heart failure (HF) [1,2]; however, data is limited on the prognostic value of sST2 in patients with type 2 diabetes mellitus (T2DM) [3], particularly in association with chronic kidney disease (CKD) [4]. We aimed to evaluate the impact on cardiovascular (CV) prognosis of sST2 in a population of T2DM with diverse renal function.

Method: A prospective observational study was conducted in patients with T2DM. Demographic, clinical and analytical data were collected. The main objective was to analyze a composite of combined CV events (major adverse cardiovascular events; MACE) including: CV death, acute myocardial infarction, stroke, coronary revascularization, hospitalization for heart failure, atrial fibrillation, significant valvular heart disease, and hospitalization for any other CV cause). The levels of sST2 and NT-proBNP were analyzed in association with the primary endpoint, as well as with each event separately by survival analysis (log-rank test).

Results: Ninety-three patients were included with a mean follow-up of 3.5 (3.4-4.2) years. Median sST2 concentrations were 29.8 ng/mL. Table 1 shows the baseline characteristics of patients according to sST2 levels. Univariate analysis showed that higher sST2 levels independently predicted the occurrence of MACE (HR = 2.92; 95% CI: 1.35-6.33) (Figure 1). These results persisted after adjusting for age, sex, and glomerular filtration rate. In addition, a significant interaction was found between sST2 and NT-proBNP, showing a

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total n = 93</th>
<th>sST2 (&lt;29.8 ng/mL, n = 47)</th>
<th>sST2 (&gt;29.8 ng/mL, n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66 ± 10.2</td>
<td>67 ± 9.2</td>
<td>65.5 ± 11.4</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>23 (24.5)</td>
<td>11 (12.2)</td>
<td>12 (12.2)</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>27.9 ± 4</td>
<td>27.8 ± 4</td>
<td>28.1 ± 4</td>
</tr>
<tr>
<td>Active smoking, n (%)</td>
<td>25 (25.6)</td>
<td>16 (16.3)</td>
<td>9 (9.2)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>64 (65.3)</td>
<td>25 (25.5)</td>
<td>39 (39.8)</td>
</tr>
<tr>
<td>Dyslipemia, n (%)</td>
<td>57 (58.1)</td>
<td>26 (26.5)</td>
<td>31 (31.6)</td>
</tr>
<tr>
<td>Lab analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GFR, mL/min/1.73 m²</td>
<td>81.8 ± 21.3</td>
<td>82.5 ± 16.9</td>
<td>80.5 ± 24.9</td>
</tr>
<tr>
<td>NT-ProBNP, pg/ml</td>
<td>195.1 ± 366.1</td>
<td>112.3 ± 129.5</td>
<td>277.2 ± 488.9</td>
</tr>
<tr>
<td>Troponine T, ng/mL</td>
<td>12.8 ± 9.6</td>
<td>11.5 ± 7.1</td>
<td>13.5 ± 11</td>
</tr>
<tr>
<td>Concomitant therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>50 (50.2)</td>
<td>23 (23.5)</td>
<td>27 (27.6)</td>
</tr>
<tr>
<td>Statins, n (%)</td>
<td>80 (81.6)</td>
<td>36 (36.7)</td>
<td>44 (44.9)</td>
</tr>
<tr>
<td>ACEI/ARB, n (%)</td>
<td>46 (46.7)</td>
<td>24 (24.5)</td>
<td>22 (22.3)</td>
</tr>
</tbody>
</table>

BMI: Body mass index; GFR: Glomerular filtration rate; ACEI/ARB: angiotensin converting enzyme inhibitors/angiotensin receptor blocker.

Figure 1: Panel (A): Combined target results of MACE events in patients with sST2 above the median (sST2 ≥ 29.8 ng/mL) (red line), compared with patients with sST2 below the median (blue line). Panel (B): Combined target results of MACE events in patients with NT-proBNP and sST2 below their medians (blue line), patients with only one of the parameters above the median (red line), and patients with both biomarkers above their medians (green line).
significant relationship between the combination of both biomarkers and the main event (Figure 1).

Conclusion: Elevated ST2 levels are associated with the occurrence of long-term major cardiovascular events in patients with T2DM, independently of renal function. These findings could allow stratification of patients with T2DM according to their cardiovascular risk in order to develop therapeutic strategies based on precision medicine.

REFERENCES

#5805

ACCURACY OF FIXED 24-H AMBULATORY BLOOD PRESSURE RECORDINGS FOR DIAGNOSING HIGH 48-H AMBULATORY BLOOD PRESSURE IN HEMODIALYSIS PATIENTS

Marieta Theodorakopoulou1, Foteini Iatridi1, Eva Pella1, Antonios Karpetas2, Areti Georgiou1, Erasmia Sampani1, Eleni Karkamani1, Alexandros Tsiotouridis1, Aikaterini Papagianni1 and Pantelis Sarafidis1

1Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, Greece and 2Therapeutiki Hemodialysis Unit, Θεσσαλονίκη, Greece.

Background and Aims: Hypertension is highly prevalent in hemodialysis patients. Ambulatory-BP-monitoring (ABPM) during the 44-h interdialytic interval is recommended for hypertension diagnosis and management in these subjects. This study assessed the diagnostic accuracy of fixed 24-h ABPM recordings with 44-h BP in hemodialysis patients.

Method: 242 Greek hemodialysis patients that underwent valid 48-h ABPM (Mobil-O-Graph NG device) were included in the analysis. We used 44-h BP used as reference method and tested the accuracy of the following BP metrics: 1st 24-h without HD period (20h-1st), 1st 24-h including HD period (24h-1st) and 2nd 24-h (24h-2nd).

Results: All studied metrics showed strong correlations with 44-h SBP/DBP (20h-1st: r = 0.973/0.978, 24h-1st: r = 0.964/0.972 and 24h-2nd: r = 0.978/0.977, respectively). In Bland-Altman analysis, small between-method differences (−1.70, −1.19 and +1.45 mmHg) with good 95% limits-of-agreement ([−10.83 to 7.43], [−11.12 to 8.74] and [−6.33 to 9.23] mmHg, respectively) for 20h-1st, 24h-1st and 24h-2nd SBP were observed. The sensitivity/specificity and κ-statistic for diagnosing 44-h SBP ≥ 130 mmHg were high for 20h-1st SBP (87.2%/96.0%, κ-statistic = 0.817), 24h-1st SBP (88.7%/96.0%, κ-statistic = 0.833) and 24h-2nd SBP (95.0%/88.1%, κ-statistic = 0.837). Similar observations were made for DBP In ROC-analyses, all studied BP metrics showed excellent performance with high Area-Under-the-Curve values (20h-1st: 0.983/0.992, 24h-1st: 0.984/0.987 and 24h-2nd: 0.982/0.989 for SBP/DBP respectively).

Conclusion: Fixed 24-h ABPM recordings during either the first or the second day of interdialytic interval have high accuracy and strong agreement with 44-h BP in hemodialysis patients. Thus, ABPM recordings of either the first or the second interdialytic day could be used for hypertension diagnosis and management in these subjects.

#3584

COMPLIANCE OF DIABETIC MONITORING IN PATIENTS WITH END-STAGE RENAL DISEASE ON MAINTENANCE HEMODIALYSIS

Alwyn Yung Zhuang Choo1,2, Thatoe Aung3 and Vivian Yiu4,5

1United Kingdom, 2Norfolk & Norwich University Hospital, Norwich, United Kingdom, 3Eastbourne District General Hospital, Eastbourne, United Kingdom, 4Bury St. Edmonds, United Kingdom and 5West Suffolk Hospital, Bury St Edmunds, United Kingdom.

Background and Aims: Diabetic nephropathy is a major cause of end-stage kidney disease (ESKD) in the UK, accounting for nearly 30% of patients requiring dialysis and in some units over 40% of the people on dialysis have diabetes. The national reviewing and benchmarking committee (GRFt NHS) had highlighted the disjointed and variable care received by these patients, with increasing risk of complications including blindness, foot ulcers and amputations from suboptimal care. Increased monitoring is shown to be cost-effective and co-ordination of a multi-disciplinary team focus can reduce complications especially lower limb amputation rates. Hence, we aimed to review the quality of care on our setting and compare it to national recommendations.

Method: We performed a cross-sectional review on patients with diabetes on haemodialysis in the satellite unit at a district general hospital to assess compliance with the Joint British Diabetes Societies (JBDS) and the UK Kidney Association (UKKA) recommendations on management of adults with diabetes. Subsequently we introduced monitoring protocols for the relevant key areas of diabetes monitoring (pre and post-dialysis glucose checks, Hba1c checks, check boxes for once weekly feet inspections, criteria for inpatient podiatry review), highlighted potential complications including hypoglycaemia, re-emphasised the importance of adequate documentation to allied healthcare teams, and updated the haemodialysis monitoring sheets. We worked with the unit manager to highlight the rationale for monitoring and provided brief education on complications to the team, and over repeated visits, gained the confidence and support of staff for the changes suggested despite an increased workload.

Results: We reviewed data from January to April 2021 followed by re-evaluation 12 months later after implementation of changes. Data for 25 patients were reviewed and re-assessed after a year. 7 patients passed away during this period. Initial review recognised the lack of awareness of good practice management of diabetic patients in the haemodialysis unit. Most patients have type 2 diabetes which carries a higher risk of ESKD. After a year of change in protocols there were significant improvements in monitoring parameters, with greatest improvements seen in glucose monitoring and routine feet inspections.

Conclusion: The review was based on care standards that included diabetes parameters as part of the recommended national care processes, and individualised treatment approach. The aims included were performing annual reviews, adequate glucose monitoring and rational glycaemic targets, and earlier targeted involvement of the diabetes specialist team. There was improvement in most of the monitoring parameters and clearer documentations from allied healthcare teams. Implementation of recommendations was initially challenging due to the COVID-19 pandemic and staff workload on the unit however with persistence we were able to obtain co-operation from the team. As expected, patients on insulin/sulphonylureas (SUs) had proper blood glucose monitoring methods. Most were on insulin, and the remaining were on SU and DPP-IV inhibitor, and those with Hba1c <58 mmol/mol declined. One-third of these patients used flash glucose monitoring and with increasing recognition and recommendation by the NHS hopefully more patients will benefit from this. This audit showed that simple interventions such as staff engagement and education can improve care and monitoring of patients in this population. With recovery of service provisions, more interventions can be put in place. Following this, we can reaudit amputation rates and gather patient feedback, plan interventions with the community team, and encourage involvement from general practitioners and their trainees to deliver better care to these patients. Hence, we emphasise the importance of clear protocols for the management and monitoring of each patient with diabetes mellitus in haemodialysis units to ensure care standards are met.
CLINICAL PROFILE OF PATIENTS WITH DIABETIC KIDNEY DISEASE ATTENDING NEPHROLOGY CLINICS IN A LOW-MIDDLE INCOME COUNTRY

Sonia Yaqub1, Marwah Saeed2, Safia Awan2 and Sanam Bano2

1Aga Khan University Hospital (AKUH), Medicine, Karachi, Pakistan and
2Aga Khan University Hospital (AKUH), Karachi, Pakistan

Background and Aims: Chronic kidney disease secondary to diabetes is a significant contributor to the global burden of disease, both financially and through a marked deterioration in the quality of life. Diabetic kidney disease (DKD) increases the likelihood of adverse outcomes such as infirmity, cardiovascular events, progressive multi-organ damage, impaired quality of life and reduced life expectancy. Pakistan, a low-middle income country, is ranked among the top 10 countries for absolute diabetes prevalence. Over 19 million Pakistani adults have diabetes, which amounts to 17.1% of the adult population in the country. There is a dearth of literature examining the quality of care of diabetic kidney disease (DKD) patients in Pakistan. The aim of the current study is to evaluate the clinical profile and the quality of care delivered to patients with DKD attending nephrology clinics at a large tertiary care hospital in Karachi, Pakistan.

Method: It was a cross-sectional observational study at Aga Khan University Hospital (AKUH), a private tertiary-care facility located in Karachi, Pakistan. The data used in the study was acquired from the Diabetic Kidney Disease outpatient-database, a registry of patients managed by AKUH. It was used to identify a cohort of patients, with DKD presenting to the nephrology clinic at AKUH from December 2018-January 2021 (n = 553).

Results: Mean age of the study participants was 61.7 ± 11.0 years and 60.9% of the study participants were male. 80.5% (n = 445) were non-smokers and over three-quarters (n = 400) had a body mass index (BMI) > 25 which according to the Asian-Pacific BMI cut-offs classified them as obese. These patients had been living with diabetes for an average of 15 years (median IQR = 10-21) and 99% had type 2 diabetes mellitus. A total of 519 study participants (93.9%) had hypertension while 34.2% and 30.9% had dyslipidemia and ischemic heart disease (IHD), respectively. Almost two third of the participants (68.4%) had advanced CKD (stages 3b, 4 and 5) at the time of presentation. Less than half of the study population (43.6%) had HbA1c < 7.0 percentage and only 34.9% attained systolic blood pressure (BP) target <130mm Hg while optimal diastolic BP (<80 mmHg) targets were achieved in 72.7%. Almost 70% of the study population were on insulin while 49.7% were receiving oral anti-diabetics. The most prescribed oral anti-diabetic was DPP4 followed by metformin and two thirds were on statins. Calcium channel blockers and beta-blockers were the most used antihypertensive drugs 53.5% and 52.6% respectively; half of the population was on diuretics, while 47.4% were taking Renin-angiotensin system (RAAS) blockers. Those who had eGFR > 60, only 60% of them were receiving RAAS blockade therapy. Women were more likely to be obese and to have higher systolic BP compared to men. Diastolic BP and HbA1c were similar in men and women. The use of statins was higher in men and use of calcium channel blockers and RAAS blockers was significantly higher in women.

Conclusion: The basis for DKD management is multifactorial risk factor reduction which is achieved by optimizing care through modifiable risk factors. In our study we identified potential gaps in the quality of care related to risk factor control, optimal glycemic and/or blood pressure targets and pharmacotherapy to delay the progression of DKD and minimize cardiovascular events. This highlights a major treatment gap in DKD prevention and management calling for greater quality improvement effort in Pakistan, which now has the third highest number of people living with diabetes in the world.
Background and Aims: Hypertension and type 2 diabetes mellitus (T2DM) are important, intertwined issues in public health. People with both conditions face significantly elevated risks of complications, particularly albuminuria, which is an independent risk factor for cardiovascular (CV) events, kidney failure and all-cause mortality, and thus deserves more attention among physicians and patients. The purpose of this study is to describe the development of recommendations for the management of hypertension and T2DM by a multidisciplinary expert panel.

Method: The panel included eight specialists (three cardiologists, three endocrinologists and two nephrologists) experienced treating patients with T2DM. The panel followed an evidence-based, multidisciplinary approach to synthesise evidence from the literature, including randomised controlled clinical trials, large observational studies and expert consultations. The final recommendations were agreed upon by all panel members through a series of consensus meetings.

Results: The final recommendations for the management of hypertension and T2DM were divided into five sections: diagnostic and classification, treatment, monitoring, patient education and lifestyle modifications. The recommendations were designed to be applicable to all patients with hypertension and T2DM, regardless of age, gender or comorbidities. Key recommendations included the importance of early detection and aggressive management of hypertension and T2DM, the use of evidence-based antihypertensive and antihyperglycaemic therapies, regular monitoring of blood pressure and glycaemic control, patient education and lifestyle modifications, and the integration of comprehensive care for patients with hypertension and T2DM.

Conclusion: The consensus recommendations developed by this multidisciplinary expert panel provide a comprehensive framework for the management of hypertension and T2DM in patients with these conditions. The recommendations are designed to be adaptable to the specific needs of individual patients, taking into account their age, gender, comorbidities and preferences. The recommendations are intended to improve the outcomes of patients with hypertension and T2DM, reduce the risk of complications and improve the quality of life for these patients.
hypertension or T2DM. The panel reviewed clinical trials, meta-analyses, observational studies and clinical guidelines that were obtained by searching PubMed for the publication period from January 2015 to June 2021, to address five discussion areas: (i) blood pressure (BP) targets based on CV/renal benefits; (ii) management of isolated systolic or diastolic hypertension; (iii) roles of angiotensin II receptor blockers (ARBs); (iv) implications of albuminuria for CV/renal events and treatment choices; and (v) roles and tools of screening for microalbuminuria. The panel held three virtual meetings using a modified Delphi method to discuss the literature and their experience regarding the discussion areas. After each meeting, consensus statements were derived and anonymously voted on by every panelist. A consensus statement was accepted only if ≥ 80% of the panelists selected ‘accept completely’ or ‘accept with some reservation’.

Results: A total of 17 consensus statements were formulated.

Conclusion: The key messages include: (i) home BP is considered as important as office BP in treatment decision-making; (ii) in patients with T2DM and hypertension on antihypertensive drug treatment, the targets important as office BP in treatment decision-making; (ii) in patients with T2DM and hypertension, the targets should be < 130/80 mmHg for office BP and < 125/75 mmHg for home BP; (iii) albuminuria is an important therapeutic goal and should be screened for regularly in people with T2DM or hypertension; and (iv) an ARB with proven cardioprotective and renoprotective effects is the preferred drug treatment for patients with T2DM and hypertension.

#4540
LONG-TERM OUTCOMES AFTER RENAL DENERVATION: A FOLLOW-UP OF 5 YEARS

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Background and Aims: Arterial hypertension is a significant cause of cardiovascular morbimortality worldwide. Adequate blood pressure control constitutes a crucial tool to prevent the enduring end-organ damage inflicted by hypertension and, consequently, its high burden of disease. Resistant hypertension may be particularly challenging to address: in this field, denervation of the renal sympathetic nerves is developing as a promising
despite controversial therapy. Our goal was to study long-term outcomes in a cohort of patients with resistant hypertension who underwent renal denervation between July 2011 and July 2022. All patients routinely underwent blood and urine testing, 24-hour ambulatory blood pressure monitoring (ABPM) and echocardiographic evaluation every 6 to 12 months after the procedure. We collected several demographic, clinical and laboratory variables, and analysed outcomes at 5 years of follow-up using SPSS software.

Results: 78 patients were submitted to renal denervation in our centre, 53% of which (n = 41) were male. There were no reported complications related to the procedure. At 5 years of follow-up, there were different types of responders. In ABPM, 61% of the patients showed a decrease in mean systolic blood pressure (SBP), with a median reduction of 16 mmHg (IQR 16.5). In 46% of patients, there was a reduction in albumin/creatinine ratio (ACR), with a median decrease of 17.63 mg/g (IQR 120.67). Before renal denervation, 30 patients (38.5%) had an ACR above 30 mg/g, while after 5 years the number of patients with ACR in this range was 21 (26.9%). In echocardiographic evaluation, 70% of the patients evidenced a decrease in left ventricular mass index (LVMI) with a median reduction of 20 g/m² (IQR 41). These results are summarised in Figure 1. In total, 70% of the patients were considered responders to renal denervation, either through a reduction in mean SBP in ABPM, in LVMI, in ACR or simultaneously in all three variables. Additionally, the reduction in mean SBP in ABPM, LVMI and ACR proved to be independent variables, both in Spearman tests and binary logistic linear regression (nonsignificant p-values). 77% of the patients were prescribed less antihypertensive drugs after follow-up, with a median reduction of 2 drugs (IQR 2).

Conclusion: Our study identified a significant percentage of responders to renal denervation, evidenced by an improvement in one or more variables associated with blood pressure control and hypertension-mediated end-organ damage, without any safety issues to report. It is also important to emphasize that the observed reduction in ACR and LVMI was independent of the reduction in SBP. This finding suggests that renal denervation might have a direct effect on albuminuria and left ventricular hypertrophy, instead of solely as an indirect result of the control of blood pressure. Hence, while further studies are necessary to support this evidence, the results nevertheless raise hope for the therapeutic potential of renal denervation in patients with resistant hypertension.

Figure 1: Descriptive analysis of the reduction in mSBP in ABPM, RAC and LVMI in responders, before DRSN and 5 years after the procedure (ACR: albumin/creatinine ratio; DRSN: denervation of the renal sympathetic nerves; IQR: interquartile range; LVMI: left ventricular mass index; mSBP in ABPM: mean systolic blood pressure in 24-hour ambulatory blood pressure monitoring).
MITOCHONDRIAL DNA Deregulated Pattern Parallels Inflammation in Early Diabetic Kidney Disease of Type 2 Diabetes Mellitus Patients

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Background and Aims: Mitochondrial DNA (mtDNA) abnormalities, as well as complex inflammatory processes involved in the pathogenesis of DKD may be detected early in the course of DKD. The aim of the study was to evaluate a potential relation of mtDNA modifications in blood and urine with podocyte injury and proximal tubule (PT) dysfunction in early DKD of type 2 diabetes mellitus (DM) patients. The hypothesis according to which mtDNA changes may be related to a specific inflammatory response in normoalbuminuric DKD of type 2 DM patients was also questioned.

Method: A total of 150 patients [52 patients with normoalbuminuria, 48 patients with microalbuminuria, and 50 patients with macroalbuminuria] and 30 age- and gender-matched healthy controls were enrolled in this case series study. All patients were assessed concerning urinary albumin/creatinine ratio (UACR), biomarkers of podocyte damage (synaptopodin, podocylaxyin) and of PT dysfunction (kidney injury molecule-1-KIM-1, N-acetyl-D-glucosaminidase-NAG), serum and urinary interleukins (IL-17A, IL-18, IL-10), and eGFR (creatinine-cystatin C). MtDNA-CN and nuclear DNA (nDNA) was quantified in peripheral blood and urine by qRT-PCR (ABI 7900 HT–Applied Biosystem). TaqMan assays were utilized for the assessment of cytochrome b (CYTB), gene subunit 2 of NADH dehydrogenase (ND2), and of beta 2 microglobulin gene nuclear (B2M). mtDNA-CN was defined as the ratio of the number of mtDNA/nDNA copies, through analysis of the CYTB/B2M and ND2/B2M ratio. DNA standards were created by plasmidial cloning vectors. Cloning was verified by PCR sequencing and validation.

Results: Serum mtDNA was decreased, while urinary mtDNA was increased in all study groups as compared to healthy controls. In univariable linear analysis, serum mtDNA correlated directly with UACR, synaptopodin, podocylaxyin, KIM-1, and urinary KIM-1, and urinary NAG. Also, serum mtDNA correlated negatively with serum IL-17A and urinary IL-17A, and with serum IL-18 and urinary IL-18, and directly with serum IL-10 and urinary IL-10. Urinary mtDNA correlated directly with UACR, synaptopodin, IL-17A, and IL-18, and showed an inverse correlation with IL-10, and eGFR. Multivariable linear analysis provided models in which serum mtDNA correlated directly with IL-10, and indirectly with UACR, IL-17A, and KIM-1 (R2 = 0.626; p = 0.0001). Urinary mtDNA correlated directly with UACR, podocalyxin, IL-18, and NAG, and negatively with IL-10 and eGFR (R2 = 0.631; p = 0.0001). This data suggests that increased urinary mtDNA levels may be attributed to increased filtration of circulating DNA and that this may derive from filtered and circulating mtDNA due to lesions to the glomerular and tubular structures. The correlations of mtDNA with proinflammatory cytokines IL-17A and IL-18, as well as with the anti-inflammatory cytokine IL-10 could explain the association of these cytokines with mtDNA variations and with the expression of podocyte damage and PT dysfunction biomarkers in all studied groups, even in normoalbuminuric type 2 DM patients.

Conclusion: MtDNA abnormalities and inflammatory processes occur early in the course of type 2 DM. MtDNA displays a specific profile in relation to inflammation both at podocyte and tubular level in normoalbuminuric patients with type 2 DM. These observations are independent of renal function decline.

BLOOD PRESSURE RESPONSE TO A LOW SODIUM DIET IN NORMOTENSIVE SUBJECTS

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Background and Aims: The term salt sensitivity (SS) has been used to show an increase in BP in response to saline overload in both normotensive and hypertensive patients. Age, sex, and obesity have been proposed as predisposing factors. The objective of our work was to evaluate the response of office BP (OBP) and ambulatory BP (ABP) to changes in salt intake in healthy normotensive subjects.

Method: We analyzed 193 subjects who participated in the evaluation as potential kidney donors; none had a history of hypertension, diabetes, renal or cardiovascular disease. They received two consecutive standardized diets, one with 300 mEq and the other with 30 mEq of Na+ /day. On the last day of each diet, a 24-h urine collection was obtained and an ambulatory BP monitor was placed for 24 h in the non-dominant arm, following recording of OBP. Data were expressed as mean and standard deviation (SD). Student’s test and one-way ANOVA were used to compare means, values of p < 0.05 were considered statistically significant differences.

Results: In the study group there were 120 females (62%) and 71 were salt sensitive (SS) (37%). The mean age was 46.9 ± 10 years (20 – 72) without significant gender differences (F = 46.7 ± 10 vs M = 47.3 ± 9 p = 0.704). The group was salt sensitive (SS) and significantly higher than the salt resistant (SR) (49.8 ± 9 vs 45.3 ± 10 p = 0.002). BMI was found to be increased (27.7 ± 4) without significant gender or incidence of SS differences. We found no association between gender and SS (p = 0.509). After the high sodium and before low sodium diets, the mean difference in urine Na+ excretion was 165.2 ± 83 mEq/24h, significantly higher among men than women (201.6 ± 84 vs 142.3 ± 75 p = 0.0001). There were no differences based on SS. We did not find significant gender differences in the variation of OBP or ABP, with the changes in the diet. The mean reduction of systolic pressure OBP for the group was 6.13 ± 10 and of diastolic pressure OBP 0.35 ± 5 mmHg. In separate analysis, systolic and diastolic OBP drops were significantly higher in the SS than in the SR (9.69 ± 12 vs 2.57 ± 8 and 2.24 ± 7 vs – 0.95 ± 5 mmHg respectively, p = 0.001). The average reduction in systolic ABP was 7.13 ± 8 and in diastolic ABP 3.33 ± 5 mmHg. In separate group analysis we also observed a significantly greater reduction in SS than in SR (12.83 ± 7 vs 1.8 ± 5 and 6.56 ± 5 vs 0.12 ± 3 mmHg respectively, p = 0.001).

Conclusion: In our study group, the reduction of both OBP and ABP following a low sodium diet in normotensive subjects depends on salt sensitivity and is independent of gender and body weight.
A DEEP LEARNING APPROACH TO PERSONALISED ANTI-HYPERTENSIVE MEDICATION TITRATION

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Background and Aims: Hypertension is the number one risk factor for premature death worldwide. Artificial Intelligence (AI) Clinical Decision Support Systems are an important next step for hypertension management but require rigorous evaluation before assimilation into routine clinical practice. Our aim is to develop and evaluate an AI clinical decision support tool for hypertension management trained on randomised clinical trial data.

Method: The Systolic Blood Pressure Intervention Trial (SPRINT) trial showed that intensive BP control to SBP <120 mm Hg results in significant cardiovascular benefit in high-risk patients with hypertension compared with routine BP control to <140 mm Hg. We trained a feed-forward neural network using Keras and Tensorflow for R and data from 9361 persons in the SPRINT randomized clinical trial to predict the probability of increase, reduce or no-change in total number of anti-hypertensive medications at each visit. The network is designed to model SPRINT investigator deviations from the protocol. Six baseline patient variables (age, sex, race, aspirin use, eGFR, group assignment (intensive or standard)), two visit patient variables (Systolic and Diastolic Blood Pressure), and two previous visit variables (Systolic and Diastolic Blood Pressure) were inputted into the model after data normalisation and centering. Hyperparameters were tuned using a grid search method. We conducted internal validation using a 20% validation set. Clinical validation was performed using an unseen test set of typical hypertension scenarios (n = 50). An R Shiny app was developed to enter new patient information and display a sensitivity analysis of probabilities calculated after changing each baseline variable by plus and minus 10 (Figure 1). To avoid poor performance on new out of distribution cases we tested five methods for Out of Distribution (OOD) detector, 1. Autoencoders, 2. Normalizing flow, 3. Local Outlier Factor (LOF), 4. Probabilistic Principal Component Analysis (PPCA) and Kernel Density Estimation (KDE).

Results: The accuracy was 76.7% on the validation dataset after 1000 Epochs. Clinical validation revealed suboptimal performance for unseen Out of Distribution data (e.g. recommending reduction of medication when SBP > 160 and number of medications was zero). This poor performance on OOD samples prompted the creation of an OOD detector to use in series with the AI Decision Support System for Hypertension. The AUROCs were 0.77 for AE, 0.96 for Normalizing Flow, 0.82 for LOF, 0.88 for PPCA and 0.96 for the Kernel Density Estimation.

Conclusion: Artificial Intelligence (AI) Clinical Decision Support Systems for Hypertension are feasible and an important next step for hypertension management but generalisability and safety require rigorous evaluation before assimilation into routine clinical practice.

STATIN INITIATION AND RISK OF INCIDENT KIDNEY DISEASE IN PATIENTS WITH DIABETES

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Background and Aims: The role of statin therapy in the development of kidney disease in patients with type 2 diabetes mellitus (T2DM) remains uncertain. We aim to determine the relationships between statin initiation and kidney outcomes in patients with T2DM.

Method: Using deidentified electronic health record data and new-user design, we conducted a nationwide retrospective cohort of patients with T2DM aged 40 years or older across China. The study outcomes included the development of diabetic kidney disease (DKD) and a sustained ≥40% decline in estimated glomerular filtration rate (eGFR). Cox proportional hazards regression was used to evaluate the relationships between statin initiation and kidney outcomes. Analyses were conducted using propensity overlap weighting to balance the characteristics.

Results: Among 7272 statin initiators and 12 586 noninitiators in the weighted cohort, statin initiation was associated with lower risks of incident DKD (hazard ratio [HR], 0.72; 95% confidence interval [CI] 0.62-0.83), new-onset eGFR <60 ml/min/1.73 m² (HR 0.63, 95% CI 0.50-0.79), new-onset proteinuria (HR, 0.70; 95% CI 0.59-0.84) and kidney function decline (HR 0.60, 95% CI 0.44-0.81). Among statin initiators, intensive control of LDL-C (<1.8 mmol/L) had a lower risk of incident DKD (HR 0.51, 95% CI 0.32-0.81) than that in non-control group (LDL-C ≥ 3.4 mmol/L). Similar results were obtained for participants with differing patterns of dyslipidemia, those using different statins, and after stratification according to the characteristics of the participants.

Conclusion: Statin initiation is significantly associated with a lower risk of kidney disease development in patients with diabetes. This renoprotective effect was more prominent in patients with intensive control of LDL-C.

Figure 1: An R Shiny application for inputting data into the AI decision support tool. In sensitivity analysis, red bar represents probability of an increase in antihypertensive medications, green bar represents probability of no change in antihypertensive medications and blue bar represents probability of decrease in antihypertensive medications.
Figure 1: Statin initiation and weighted cumulative incidence of kidney outcomes in patients with T2DM DKD: diabetic kidney disease, eGFR: estimated glomerular filtration rate.

Figure 2: Adjusted hazard ratio of statin initiation associated with kidney outcomes among the total populations and patients with or without dyslipidemia.

Abstracts
Efficacy and Safety of GLP1 Analogues in Advanced CKD Patients: A Potential Strategy for Weight Loss and Inclusion in Renal Transplant Waiting List

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Background and Aims: Diabetes mellitus (DM) is one of the main causes of chronic kidney disease (CKD) and the need for renal replacement therapy. New antidiabetic drugs such as glucagon-like peptide 1 receptor analogues (aGLP1) improve glycemic control and cardiovascular risk and promote weight loss. Our main objective was to analyze the efficacy and safety of aGLP1 agonists in patients with advanced chronic kidney disease (ACKD).

Method: Prospective cohort study of CKD (estimated glomerular filtration rate (eGFR) ≤ 30 ml/min) and DM2 patients who started treatment with aGLP1 between April 2018 and November 2022. We analyzed clinical and demographic variables. We collected aGLP1 type and dose, eGFR and weight at baseline and after 6 and 12 months of treatment. We analyzed glycemic and lipid control and blood pressure (BP). We documented adverse effects. Descriptive analysis was performed and we compared eGFR before and after aGLP1 initiation.

Results: During the period 36 patients with ACKD started treatment with aGLP1 in our center, 30 with a minimum follow-up of 6 months. 66.7% were male and the mean age was 67. 88.9% were hypertensive and 91.7% dyslipidemic. 33.3% had a history of ischemic heart disease, 11.1% heart failure, 41.7% peripheral arterial disease and 8.3% stroke. The mean eGFR at drug initiation was 20.7 mL/min. The most frequent cause of CKD was diabetic nephropathy (66.7%) followed by glomerulonephritis (11.1%). Mean weight was 92.7 ± 9.7 kg and BMI 33.15 ± 3.2 kg/m2. The most prescribed aGLP1 was Semaglutide (83.4%) followed by Liraglutide (13.9%) and Dulaglutide (2.8%). Maximum drug dose was reached in 69.4% of patients. After initiation, eGFR remained stable at 6 months and 1 year (p = .424). We observed a 12% reduction in weight at one year after treatment (94Kg vs 83Kg; p < .001). We found no differences in glycosylated hemoglobin, lipid control and BP at 6th month and first year. Two patients suffered gastrointestinal adverse effects and one discontinued the drug because of this. One patient died during follow-up of independent cause.

Conclusion: aGLP1 in patients with ACKD are safe. Adverse effects do not occur more frequently than in the non-CKD population. In addition to improving cardiovascular risk of patients, they can produce a weight loss that can independently help patients to be included in the waiting list for renal transplantation.

SGLT2-Inhibition Improves Vascular Function in Type 2 Diabetes: A Double Blind, Randomized, Placebo Controlled Crossover Trial

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Background and Aims: Sodium glucose cotransporter 2 inhibitors (SGLT2i) reduce cardiovascular events and protects kidney function in type 2 diabetes (DM2) patients. These benefits may partly be related to improvement of vascular function. In this study we examined the effects of SGLT2i treatment on vasodilatory capacity in patients with DM2.

Method: Using a double-blind, randomized, placebo-controlled cross-over study design, we included 15 patients with DM2 and preserved kidney function (eGFR > 60 ml/min/1.73 m²). Each participant received four weeks of SGLT2i treatment (empagliflozin 10 mg once daily) or matching placebo. After a two-week wash-out period, each participant was cross over to four weeks of the opposite treatment. At the end of each treatment period, vascular function was evaluated by venous occlusion plethysmography. Forearm blood flow (FBF) was measured during intra-arterial infusion of increasing concentrations of acetylcholine (ACh) and sodium nitroprusside (SNP), assessing endothelium-dependent and independent vasodilation, respectively. Repeated measures two-way ANOVA was performed to compare absolute FBF between groups.

Results: 11/15 (73%) of participants were male. Mean age was 68 ± 9 (SD) years (range 49-82), eGFR was 81 ± 10 ml/min/1.73 m² and duration of diabetes was 15.8 ± 9 years. 11/15 (73%) had hypertension and 9/15 (60%) received treatment with an ACE-inhibitor or Angiotensin-II blocker. 4/15 (27%) had cardiovascular disease. The median albumin-to-creatinine ratio was 29 mg/g (range: 4-1293). Both ACh and SNP dose-dependently increased FBF (Figure 1 and 2). FBF during SNP infusion was significantly higher during empagliflozin treatment as compared to placebo (p = 0.004), whereas there was no difference between empagliflozin and placebo in FBF during ACh infusion (P = 0.399).

Conclusion: Empagliflozin improves endothelium-independent vasodilata-

tion in patients with DM2, whereas no changes could be observed in endothelium-dependent vasodilation. These results suggest that SGLT2i positively affects vascular function and that the effect is not related to nitric oxide from the endothelium.
EFFECTS OF SGLT-2 INHIBITORS VERSUS DPP-4 INHIBITORS ON ANEMIA IN PATIENTS WITH TYPE 2 DIABETES

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Background and Aims: The number of people suffering from diabetes has exceeded 400 million worldwide. The incidence of anemia in type 2 diabetes mellitus (T2D) patients is about twice that of non-diabetic patients. Moreover, patients with T2D who have chronic kidney disease are at higher risk of developing anemia and it also occurs earlier. Therefore it is worth investigating the problem of anemia in T2D patients. This study was conducted to compare the effects of the new oral hypoglycemic agents (sodium-glucose cotransporter-2 inhibitors, SGLT-2i and dipeptidyl peptidase-4 inhibitors, DPP-4i) on anemia in patients with T2D.

Method: This study was designed as a retrospective cohort study and analyzed using the Kaohsiung Medical University Hospital Research Database (KMUHRD). Study inclusion criteria: (1) patients start using SGLT-2i or DPP-4i from January 1, 2015 to December 31, 2020 (first prescription is defined as not used within 180 days prior to the activation date, and cases are screened from the year prior to the starting intake date), and (2) patients with T2D who meet the diagnosis of anemia (according to the World Health Organization definition of hemoglobin <13 g/ dL in men and <12 g/ dL in women) at the time of initial dosing. Patients without hemoglobin data within 180 days before and after treatment were excluded. The outcome will evaluate the effect of SGLT-2i and DPP-4i on erythropoietic parameters including erythrocyte, reticulocyte count, hemoglobin, and hematocrit.

Results: In total 4,555 patients were enrolled in this study. Of these patients, 4,251 were treated with DPP-4i and 304 with SGLT-2i. Using propensity score matching, 303 patients each from the DPP-4i and SGLT-2i groups were selected based on patient characteristics. There were no difference in hemoglobin values (Median: 11.30 vs. 11.20 g/ dL, P = 0.328) and renal function (expressed as...
eGFR, 83.30 vs. 81.84 mL/min, P = 0.255) between the DPP-4i and SGLT-2i groups before treatment. After six months of follow-up, only the SGLT-2i group showed a statistically significant increase in erythrocyte count (3.88 to 4.19 × 10^6/uL, P < 0.001), hemoglobin (11.20 to 11.70 g/dL, P < 0.001), and hematocrit values (34.4 to 36.5%, P < 0.001). However, the same changes were not observed in the DPP-4i group: erythrocyte count (3.87 to 3.91 × 10^6/uL, P = 0.051), hemoglobin (11.30 to 11.40 g/dL, P = 0.315), and hematocrit values (34.4 to 34.7%, P = 0.102). The Δhemoglobin showed a significant correlation with the SGLT-2i use, metformin use, erythrocyte count, hematocrit, hemoglobin and eGFR levels at baseline. Multiple regression analyses showed that use of SGLT-2i might be the main influencing factor.

Conclusion: Our study compared the effects of SGLT-2i and DPP-4i on erythropoietic parameters in T2D patients, and only the SGLT-2i group showed significant increase in erythrocyte count, hemoglobin, and hematocrit. The use of SGLT-2i may be the major factor affecting the improvement of erythropoietic parameters. Therefore the hypoglycemic effect of SGLT-2i may be accompanied by the improvement of anemia.

#3802
ROLE OF NEUTROPHIL EXTRACELLULAR TRAPS IN DIABETIC KIDNEY DISEASE: DATA FROM INTEGRATION OF BULK RNA AND SINGLE-NUCLEUS RNA SEQUENCING ANALYSES
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Background and Aims: Neutrophil extracellular traps (NETs) is an important immune response against infections that is implicated in various immune-mediated conditions. Growing evidence shows that inflammation has key pathogenic contributions in diabetic kidney disease (DKD) but the role of NETs remains unclear.

Method: We evaluated the differentially expressed genes (DEGs) of NETs in human DKD using the bulk RNA sequencing datasets of kidney biopsy from DKD patients (GSE30528 and GSE30529). The candidate genes were further selected based on the machine learning algorithms (LASSO and SVM-RFE). The single-nucleus RNA sequencing (GSE195460 and GSE131882) and DKD bulk RNA sequencing (GSE30122) were used to validate the results. Receiver Operating Characteristics (ROC) curve were constructed to assess the diagnostic performance of the identified genes for DKD. Candidate drugs were further screened from the DSigDB database.

Results: Three characteristic genes (ITGAM, ITGB2 and TLR7) were selected using machine learning approach, which all were upregulated in human DKD glomerular and tubulointerstitial portion compared to healthy controls (all P < 0.05). Single-cell analysis further demonstrated that ITGAM, ITGB2 and TLR7 were mainly overexpressed in leucocytes. ITGAM, ITGB2 and TLR7 expression in tubulointerstitial compartment also showed good diagnostic performance for DKD (ROC AUC 0.983, 0.975 and 0.958 respectively). Candidate drugs that target ITGAM, ITGB2 or TLR7 genes in DKD include ropivacaine, lidocaine and sulfasalazine.

Conclusion: ITGAM, ITGB2 and TLR7 may serve as biomarkers for DKD and drugs that target these genes may have therapeutic potential for DKD.

Figure 1: Intersected neutrophil extracellular traps (NETs) associated genes in human diabetic kidney disease (DKD) datasets. *p<0.05, **p<0.01, ***p<0.001.
Figure 2: Three identified NETs related genes (ITGAM, ITGB2 and TLR7) expression validated in in human DKD bulk and single-nucleus RNA datasets.

#3873

UTILITY OF BLOOD KETONE MONITORING IN HAEMODIALYSIS PATIENTS UNDER INPATIENT NEPHROLOGY CARE

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Background and Aims: There is a lack of evidence regarding the relationship between capillary blood glucose (CBG) >15 mmol/L and blood ketones in maintenance haemodialysis dialysis patients meaning the utility of ketone measurement in this group is uncertain. Despite this, guidance published by the Joint British Diabetes Society for Inpatient Care (JBDS-IP) in 2022 states that blood ketones should be measured in patients on maintenance haemodialysis with diabetes mellitus (DM) who have pre- or post-dialysis CBG >15mmol/L and symptoms consistent with diabetic ketoacidosis (DKA), acknowledging that these can be non-specific [1]. We sought to identify if there is a relationship between elevated CBG and blood ketone levels in haemodialysis patients, and if haemodialysis affects blood ketone levels.

Method: Maintenance haemodialysis patients with DM admitted to a single ward over 2 separate 2 month periods were included. Nursing staff recorded CBG and blood ketone levels pre- and post-dialysis using a FreeStyle PrecisionPro ketone meter. For each patient, further demographic data were collected from the electronic patient record.

Results: 79 measures were collected from 30 patients, with between 1 and 7 measures for each patient. 57% patients (n = 17) were male, 37% (n = 11) had T1DM, and 80% (n = 24) were on insulin therapy. The median pre-HD CBG for all measures was 10.5mmol/L (IQR 8.15-15.05), median post-HD CBG was 9.1mmol/L (IQR 6.8-12.95), median pre-HD ketones were 0.1mmol/L (IQR 0.1-0.2) and median post-HD ketones were 0.1mmol/L (IQR 0.1-0.3). There was no significant difference in blood ketones pre-and post-HD for all measures (p = 0.09) (Figure 1). For measures where pre-HD CBG was >15mmol/L (n = 21) median pre-HD and post-HD ketones were 0.1 (IQR 0.1-0.2) and 0.2mmol/L (IQR 0.1-0.2) respectively (p = 0.45). For measures where pre-HD CBG was >20mmol/L (n = 6) median pre-HD and post-HD ketones were 0.1 mmol/L (IQR 0.1-0.13) and 0.2 mmol/L (IQR 0.1-0.2) respectively (p = 0.13). For measures where pre-HD CBG was <15mmol/L, median pre-HD ketones were 0.1 (IQR 0.1-0.2). There was no significant difference in blood ketones pre-HD between those with a pre-HD CBG >15mmol/L and those with a pre-HD CBG <15mmol/L (p = 0.69).

Conclusion: These results demonstrate no significant relationship between elevated CBG measures (>15mmol/L) and blood ketone levels in haemodialysis patients, nor do they demonstrate a significant change in blood ketone levels post haemodialysis. Unwell haemodialysis patients with elevated CBG clearly warrant medical assessment, but there is a lack of evidence that blood ketones are useful to aid assessment and guide management of these patients.

REFERENCE

#6682

RENAAL ARTERY STENOSIS: A SINGLE CENTRE STUDY
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Background and Aims: Renal artery stenosis (RAS) is present from 1% to 5% in people affected by arterial hypertension and it is often associated with peripheral artery disease and coronary artery disease; as the matter of fact, it is commonly found in people undergoing cardiac catheterization (18-20%) or angiography for aorto-iliac and lower extremities diseases. The major cause of renal artery stenosis is an atherosclerotic lesion localized in the proximal segment or to the ostium. Clinical presentations are renovascular hypertension and ischemic nephropathy. The aim of the study is to define either endovascular treatment gives a significant benefit on renal function and blood pressure control, when associated to medical therapy.

Method: This is a retrospective study focused on patients who underwent renal artery angioplasty and stenting in the last ten years, from November 2011 to April 2021 in the Nephrology Department, at Sant’Andrea Hospital, La Spezia (Italy). The primary outcome was kidney function, while secondary outcomes were blood pressure and the number of antihypertensive drugs one year after the revascularization. Patients included in the study had uncontrolled and refractory arterial hypertension (PA ≥ 140/90 mmHg) and/or progressive worsening of renal function, secondary to bilateral or unilateral stenosis in one functional kidney, that was identified at the color-doppler ultrasound examination by a peak systolic velocity (PSV) > 200 ml/min and an aortic-renal ratio > 3.5. We found 36 patients who had these characteristics. They were all affected by chronic kidney disease (CKD) (mean ± SD eGFR 25.3 ± 15.3 ml/min/1.73 m²) equally divided into stage 3 (33%, eGFR 30-60 ml/min/1.73 m²), stage IV (31% eGFR 15-29 ml/min/1.73 m²) and stage V (36%, eGFR <15 ml/min/1.73 m²).

Results: Kidney function, measured as serum creatinine (Scr) (mg/dl), improved immediately after the revascularization (mean ± SD Scr after vs before 2.52 ± 1.61 vs 3.31 ± 2.47 mg/dl p < 0.05), after 30 days (mean ± SD Scr after vs before creat. 2.36 ± 1.53 vs 3.19 ± 2.39 mg/dl p < 0.05) and after one year (mean ± SD Scr after vs before creat. 2.04 ± 1.16 vs 2.99 ± 2.40 mg/dl p < 0.05) (Fig. 1). Regarding arterial hypertension, a significant reduction of both systolic (SBP) and diastolic (DBP) blood pressure was detected in...
the subgroup of people under 75 years old (mean ± SD SBP after vs before, 144,62 ± 12,55 vs 168,18 ± 36,40 mmHg, p<0.01; after one year vs before, 143,93 ± 21,10 vs 167,83 ± 38,16 mmHg, p<0.05) (mean ± SD DBP after vs before, 73,62 ± 9,62 vs 83,07 ± 21,75 mmHg, p<0.05; after one year vs before 75,20 ± 9.02 vs 83,33 ± 23,10 mmHg, p = 0.07) (Fig. 2). The number of antihypertensive drugs dropped immediately after the angioplasty (mean ± SD tablets after vs before, 2,28 ± 1,11 vs 3,21 ± 1,43, p<0.01), while after one year there was not a significant increase of therapy (mean ± SD tablets after one year vs before, 3,00 ± 1,41 vs 3,23 ± 1,42, p = 0.47), even if blood pressure was better controlled than before the procedure with the same amount of tablets (Fig. 3).

Conclusion: Although our population was quite small, we demonstrated the advantages of renal artery revascularization in atherosclerotic renovascular disease, as demonstrated by kidney function and blood pressure control. Our results contrast the larger studies considered, that found no relevant clinical benefit on renal function and incidence of major adverse cardiovascular and renal events by comparing patients treated with medical therapy alone or with medical therapy plus angioplasty. The different conclusions are probably due to our strict adherence to the endovascular treatment indications, which consider the revascularization as the optimal strategy for a well-defined population.

#2967

CALCULATION OF THE RISK OF CONTRAST-INDUCED ACUTE KIDNEY DAMAGE IN THE CUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH DIABETES MELLITUS

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Background and Aims: Analysis of the pathogenetic mechanisms of the development of contrast nephropathy in patients with coronary artery disease on the background of type 2 diabetes mellitus and the effectiveness of the proposed preventive measures.

Method: The study took place in two stages. The study included 56 patients with type 2 diabetes, the average age of the patients was 58 years, the CG consisted of 20 healthy persons. In most patients, the reason for which the endovascular radiopaque procedure (EVRCP) was performed was associated with atherosclerotic lesions: coronary artery disease, chronic lower limb ischemia (CLLI), atherosclerosis of the brachiocephalic arteries (BCA). EVRCP was performed on the vessels of the coronary basin, BCA, abdominal aorta and its branches, lower extremities. A retrospective analysis included a comparative analysis of two groups of diabetic patients who underwent EVRCP: 29 patients who developed CI-AKI (CI-AKI+ group) and 27 patients in whom the post-procedure period was uneventful. CI-AKI was defined as an increase in venous creatinine concentration of more than 25% by the end of 48 hours after EVRCP. During this phase of the study, the patient's medical history was analyzed - their anamnestic data, glycemic status, general urinalysis, kidneys, estimated glomerular filtration rate (eGFR) initially, 2,4,6,8 and 10 days after the procedure. The first stage, a retrospective one, included a comparative analysis of two groups of diabetic patients who underwent an endovascular radiopaque procedure (EVRCP): 29 patients who developed CI-AKI (CI-AKI+ group) and 27 patients in whom the post-procedure period was uneventful. CI-AKI was defined as an increase in venous creatinine concentration of more than 25% by the end of 48 hours after EVRD.
Results: Based on the analysis, we developed a risk scale for the development of CI-AKI in patients with DM. In the process of compiling the scale, the value of RR for the development of CI-AKI in the presence of the corresponding factor, rounded to the nearest whole number, was used as risk coefficients. According to the developed scale, in the presence of a risk factor, the patient is assigned a certain score. The score determines the risk of CI-AKI.

Conclusion: Thus, the present study showed that in patients with DM, compared with healthy volunteers, there is a change in kidney function, which is more pronounced in individuals prone to the development of CI-AKI. Changes in the cellular and biochemical blood composition in patients with DM are characteristic of diabetic nephropathy and are also more pronounced in patients at risk of CI-AKI.

#3421
MRI PREDICTORS OF DIASTOLIC DYSFUNCTION OF THE LEFT VENTRICLE
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Background and Aims: Non-invasive assessment of diastolic dysfunction remains challenging, this study aims to identify the most informative cardiac magnetic resonance imaging (CMR) parameters for assessing left ventricular diastolic dysfunction (LVDD).

Objective: To study MRI parameters as predictors of left ventricular diastolic dysfunction (LVDD) in patients with suspected heart failure.

Method: The study included 239 patients cases with heart failure were identified during the study. The CMR measurements of the patients’ heart chambers were obtained from an independent manual examination using an image archiving and transmission system. CMR measurements were performed as follows. The patients were examined with a 1.5 Tesla MRI machine and eight-channel cardiac coils were used to acquire the image. The position and orientation of the heart in the chest were determined after cardiac reference images of the chest were taken. Using stationary free precession sequences, a two-chamber image of the left ventricle was obtained with a breath hold of 10 – 15 seconds at the end of exhalation (image parameters: repetition time 3.6 ms; echo time 1.6 ms; 350 mm; slice thickness 6 mm; gap 2 mm; angle of rotation 45°, 14 projections per segment, matrix 224 160). Four-chamber short axes and three-chamber sequences were then obtained. The right ventricular end-diastolic size (EDD) diameter was measured between the right ventricular endocardium and the interventricular septum, parallel to the tricuspid valve and 1 cm distal to the valve on four-chamber sinusoids with free precession (SSFP).

Results: As a result the left atrial enlargement is the most prognostic factor for diastolic dysfunction (DD) among the assessed complex MRI parameters. TBI and tissue tracking reflect internal aberration, revealing abnormal deformity patterns in the basolateral segments compared to patients with normal diastolic function. Based on the quantitative assessment of the size of the LA, it is possible to determine the threshold value for the detection of DD. In addition, it was found that the quantitative assessment of LV diastolic deformity is predictive for identifying patients with DD. Increased LA dimensions have a diagnostic accuracy according to our data for detecting diastolic dysfunction (DD).

Conclusion: Tissue tracking and TRM reveal impaired diastolic deformity of the basal-lateral wall in DD as a direct sign of DD.

#5867
EFFECT OF SGLT2I ON URIC ACID AND GLUCOSE URINARY FRACTIONAL EXCRETION IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND TYPE 2 DIABETES MELLITUS
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Background and Aims: Sodium-glucose cotransporter type 2 inhibitors (SGLT2i) have demonstrated broad benefits beyond glycemic control, including hypouricemic effects. However, this fact has not been completely validated in chronic kidney disease (CKD). The mechanism by which SGLT2i produces an increase in uric acid elimination is not fully understood and appears to be mediated in part by increased glucose in the renal tubule, which would compete in reabsorption with uric acid through GLUTb transporter. The aim of this study is to analyse the effect of SGLT2i on uric acid and glucose urinary fractional excretion (FE) in type 2 diabetes mellitus (T2DM) + CKD patients.

Method: Retrospective observational single-center study conducted between January 18 and December 22 in T2DM-CKD patients on SGLT2i. Subjects on renal replacement therapy, treatment with GLP1 analogues and those for whom we did not have uricosuria prior to the start of ISGLT2 were excluded. Urinary uric acid and glucose FE were analysed at baseline and during follow-up of up to 24 months, with 3, 6 and 12 months cut-offs. Data are described as mean and standard deviation (SD). Statistical analysis was performed using STATA v14 with statistics for paired samples.

Results: 82 patients were included in the study, with a mean follow-up of 1.2 years. During follow-up, 23 patients left the study (arGLP1 initiation (n = 9), adverse reactions (n = 4), exitus (n = 2) and loss to follow-up (n = 8). 78.1% were male, mean age 72.7 years (SD 8.5), and main co-morbidities were: obesity 76.8%, arterial hypertension 95%, hyperuricemia 75.6% and congestive heart failure 25.6%. Distribution according SGLT2i drug was: 65.6% dapagliflozin, 25% canagliflozin and 9.4% empagliflozin. eGFR decreased immediately after initiation of SGLT2i with ulterior stabilization as described elsewhere (Table 1). We observed a significant increase on urinary uric acid FE that remained stable along the follow-up: basal 7.4%, 3 months 9.4% (p < 0.001). However, serum uric acid levels did not show significant differences along the study. Urinary glucose FE increase remained stable along the whole observation period in spite of no significant differences from a clinical point of view on % of glycosylated haemoglobin (Table 1).

Conclusion: Despite decreased GFR, T2DM-CKD patients exhibited significant urinary uric acid and glucose FE increase after starting SGLT2i. This increase remained stable for at least 2 years. However, we did not observe significant reductions on uricemia in these patients, implying that increase on urinary uric acid excretion is not enough in this setting to obtain significant modifications on uricemia.
### Abstracts

**Background and Aims:** The use of GLP-1 receptor agonist (ra) has become one of the cornerstones for CKD type 2 diabetic patients (T2DM) treatment. Oral formulation of semaglutide appeared as new therapeutic tool to increase the use of drugs with proved renal benefit. However, method of administration of the oral formulation and oral absorption limitations in CKD patients could adversely affect drug efficacy. The aim of this study was to compare the efficacy of semaglutide sbc vs oral in CKD patients.

**Method:** Prospective, real-world study performed in T2DM-CKD patients with indication of initiation of GLP-1ra therapy in which semaglutide sbc or oral was initiated. Patients were assigned to sbc or oral formulation according to drug accessibility and patient preferences. Patients previously treated with any other GLP-1ra were excluded.

**Results:** 70 patients were included, 50 with sbc and 20 with oral semaglutide with mean follow up time of 407 [180-753] and 154 [75.5-205] days respectively.

**Conclusion:** Oral formulation of semaglutide was equally effective in terms of glucose control and body weight in patients with T2DM and CKD even with more patients on the low-medium doses. Gi side effects were similar with both formulations though the lower number of patients on the higher oral dose does not allow further conclusions.

### Table 1: Laboratory data expressed as mean and standard deviation (SD) with paired statistical analysis.

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>0 (baseline)</th>
<th>3</th>
<th>6</th>
<th>12</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>82</td>
<td>64</td>
<td>46</td>
<td>46</td>
<td>22</td>
</tr>
<tr>
<td>Uric fractional excretion (%)</td>
<td>7.4 (4.5)</td>
<td>9.4 (4.3)*</td>
<td>9.0 (4.4)*</td>
<td>9.0 (3.9)*</td>
<td>10.5 (5.0)*</td>
</tr>
<tr>
<td>Glucose fractional excretion (%)</td>
<td>0.01 (0.08)</td>
<td>21.8 (16.1)*</td>
<td>24.1 (15.2)*</td>
<td>22.9 (14.0)*</td>
<td>27.5 (14.4)*</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m²)</td>
<td>48.9 (14.6)</td>
<td>44.4 (16.1)*</td>
<td>40.4 (13.6)*</td>
<td>43.1 (17.4)*</td>
<td>45.9 (17.7)*</td>
</tr>
<tr>
<td>Serum uric acid (mg/dL)</td>
<td>6.6 (1.7)</td>
<td>6.4 (1.8)</td>
<td>6.2 (1.6)</td>
<td>6.3 (1.7)</td>
<td>6.2 (1.4)</td>
</tr>
<tr>
<td>Glycosylated haemoglobin (%)</td>
<td>6.7 (0.8)</td>
<td>6.7 (0.8)</td>
<td>7.1 (1.2)**</td>
<td>6.8 (1.0)***</td>
<td>6.7 (0.7)</td>
</tr>
<tr>
<td>Serum glucose (g/dl)</td>
<td>133.7 (29.5)</td>
<td>129.6 (27.4)</td>
<td>137.6 (45.5)</td>
<td>134.3 (28.2)</td>
<td>130 (27.0)</td>
</tr>
</tbody>
</table>

vs basal

\*pvalue < 0.001

\*pvalue 0.008

\*pvalue 0.01. No statistically differences between other values.
Conclusion: The data suggest that in diabetic nephropathy, the eNOS T786C allele may be involved in endothelial dysfunction. Azerbaijani patients showed dominance of the C allele and a mutant homozygous genotype CC of the T786C gene of eNOS.

#2965
DYNAMICS OF THE FUNCTIONAL STATE OF THE KIDNEYS IN PATIENTS WITH DIABETES MELLITUS AND A HIGH RISK OF CI-AKI AND THE USE OF PREVENTIVE MEASURES
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Background and Aims: Analysis of the pathogenetic mechanisms of the development of contrast nephropathy in patients with coronary artery disease on the background of type 2 diabetes mellitus and the effectiveness of the proposed preventive measures.

Method: The study included 56 patients with type 2 diabetes, the average age of the patients was 58 years, the CG consisted of 20 healthy persons. In most patients, the reason for which the endovascular radiopaque procedure (EVRCP) was performed was associated with atherosclerotic lesions: coronary artery disease, chronic lower limb ischemia (CLLI), atherosclerosis of the brachiocephalic arteries (BCA). EVRCP was performed on the vessels of the coronary basin, BCA, abdominal aorta and its branches, lower extremities. A retrospective analysis included a comparative analysis of two groups of patients with type 2 diabetes who underwent (EVRCP): 29 patients who developed CI-AKI (CI-AKI+ group) and 27 patients in whom the post-procedure period was uneventful. CI-AKI was defined as an increase in venous creatinine concentration of more than 25% by the end of 48 hours after EVRCP. During this phase of the study, the patient's medical history was analyzed - their anamnestic data, glycemic status, general urinalysis, kidneys, estimated glomerular filtration rate (eGFR) initially, 2,4,6,8 and 10 days after the procedure.

Results: The CI-AKI+ and CI-AKI- groups were compared in terms of clinical and anamnestic, hematological, urological data and the results of echocardiography and renal ultrasound with each other and with representatives of the CG. The CI-AKI+ and CI-AKI- groups did not differ in nosological distribution (Fig. 1): in both groups, half of the patients with EVRCP were performed due to the presence of coronary pathology (51.72% and 48.15%, respectively), the rest in patients it was comparable for CCI and CVD (27.59% and 26.09% in the CI-AKI+ group and 25.93% each in the CI-AKI- group).

Conclusion: Taking into account the OR of CI-AKI in patients with DM in the presence of identified predictors, a risk scale was developed. A risk score of 28 points or more demonstrates a predictive sensitivity in terms of the development of CI-AKI of 96.55% (p<0.001).

#3423
DIAGNOSTIC SIGNIFICANCE MAGNETIC RESONANCE IMAGING IN CHRONIC HEART FAILURE OF VARIOUS GENESIS
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Background and Aims: Based on a comparative assessment of radiological, ultrasound, clinical and laboratory studies, to determine the diagnostic significance of magnetic resonance imaging (MRI) in the heart disease.

Method: We analyzed echocardiographic and magnetic resonance imaging of the heart in 40 patients who were examined and treated in the cardiology departments of the Republican Medical Specialized Scientific and Practical Center for Therapy and Medical Rehabilitation. The information content of the use of instrumental research methods in patients with chronic heart failure was evaluated. Information on demographic characteristics, including age, gender, education, occupation, was collected from doctors visits using a standard questionnaire.

Results: The average age of patients was 57 years. 40% of the surveyed were made up of men. When studying risk factors for the disease, 49% of all patients had arterial hypertension, 18% had type 2 diabetes mellitus, 21% of patients were active smokers, and 11% had a family history of risk of cardiovascular disease. 36% of patients had a history of myocardial infarction, percutaneous coronary interventions. The mean LV EF was 42% and the mean right ventricular EF (RV EF) was 48%. In patients with CHF of ischemic origin, in the vast majority of cases, the results of echocardiographic and MRI examinations of the heart were comparable. The conducted MRI of the heart had an additional informative value in case of doubtful ECG and EchoCG data, as well as in differential diagnosis. The results of MRI were more accurate in determining the etiology of myocardial hypertrophy, in particular hypertrophic cardiomyopathy.

Conclusion: The diagnostic value of cardio-MRI showed great diagnostic value in the diagnosis of ischemic damage and non-coronary diseases of the myocardium.

#5490
GENERATIVE ARTIFICIAL INTELLIGENCE FOR CREATION OF SYNTHETIC HYPERTENSION TRIAL DATA
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University of Galway, Galway, Ireland

Background and Aims: Synthetic data can be an effective supplement or alternative to real data for the training of machine learning models. Synthetic data may also be used to evaluate new tools, develop educational curricula, or remove undesirable biases in datasets. We aim to evaluate four synthetic data generation methods applied to hypertension randomized clinical trial data.

Method: The Systolic Blood Pressure Intervention Trial (SPRINT) trial data showed that intensive BP control to SBP <120 mm Hg results in significant cardiovascular benefits in high-risk patients with hypertension compared with routine BP control to <140 mm Hg. The Synthetic Data Vault (SDV) is a Synthetic Data Generation ecosystem of libraries that allows users to easily generate new Synthetic Data that has the same format and statistical properties as the original dataset. SDV supports multiple types of data, including date-times, discrete-ordinal, categorical, and numerical. SPRINT data was pre-processed to create a single table of 140,000 patient visits with baseline variables (age, sex, race, aspirin use, estimated Glomerular Filtration Rate (eGFR)) and visit level variables (systolic and diastolic blood pressure, heart rate and total number of antihypertensive medications at end of visit). Using the SDV library for python, we used four generative models to create synthetic SPRINT data, 1) Gaussian copula model, 2) Conditional Tabular Generative adversarial network (CTGAN), 3) CopulaGAN model, and 4) Tabular Variational Auto-encoder (TVAE). We evaluated the results using the SMetrics library which includes the shapes of the columns (marginal distributions), the pairwise trends between the columns (correlations), reproduce mathematical properties from your original data and new row synthesis. Finally, an overall quality score which represents an amalgamation of the marginal distribution and correlations was computed, where 0 indicates the lowest quality and 1 indicates the highest.

Results: Two hundred thousand synthetic patient visits were created for each method. The overall quality scores in order were 90.67% for Gaussian copula, 86.77% for TVAE, 81.03% for CTGAN, and 79.7% for CopulaGAN. The column shape score which represents the marginal distribution was highest for Gaussian Copula (94.54%), followed by TVAE (88.44%), CTGAN (82.35%), and Copula GAN (80.27%). The column pair trend which corresponds to correlations was highest for Gaussian Copula (86.8%), followed by TAVE (85.1%), CTGAN (79.72%), and Copula GAN (79.12%).

Conclusion: Gaussian copula created the highest scoring synthetic SPRINT data based on the marginal distribution, correlations, and overall score. The Synthetic Data Vault is a feasible collection of methods for generation of synthetic clinical trial data for training future machine learning and AI models.

F4 - HYPERTENSIVE & KIDNEY DISEASES IN PREGNANCY

#4482
PREGNANCY AND RENAL OUTCOMES IN WOMEN WITH CHRONIC KIDNEY DISEASE: A POPULATION STUDY
Elizabeth Ralston 1, Yanzhong Wang 1, Chris Farmer 2, Steve Childs 3, Ranjit Akolekar 4 and Kate Bramham 1

1King’s College London, School of Life Course and Population Sciences, London, United Kingdom, 2Centre for Health Services Studies, University of Kent, United Kingdom and 3Medway NHS Foundation Trust, Medway Fetal and Obstetric Medicine Centre, United Kingdom

Abstracts
Table 1: Summary of pregnancy outcomes according to pre-conception eGFR.

<table>
<thead>
<tr>
<th>Age at conception (mean (SD))</th>
<th>eGFR &gt;90 ml/min/1.73 m² (N = 12852)</th>
<th>eGFR &gt; 90 ml/min/1.73 m² with proteinuria (N = 221)</th>
<th>eGFR 60-89 ml/min/1.73 m² (N = 1170)</th>
<th>eGFR ≤59 ml/min/1.73 m² (N = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth (%)</td>
<td>27.5 (5.5)</td>
<td>27.7 (5.9)</td>
<td>30.8 (5.4)</td>
<td>28.4 (6.4)</td>
</tr>
<tr>
<td>Gestation at delivery (days)</td>
<td>278 [271, 284]</td>
<td>274 [265, 281]</td>
<td>277 [271, 284]</td>
<td>278 [270.5, 283]</td>
</tr>
<tr>
<td>Birthweight (mean (SD))</td>
<td>3385 (706)</td>
<td>3355 (653)</td>
<td>3368 (615)</td>
<td>3073 (663)</td>
</tr>
<tr>
<td>Preterm birth &lt;34 weeks (%)</td>
<td>241 (2.3)</td>
<td>6 (2.9)</td>
<td>19 (2.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Small for gestational age 3rd centile (%)</td>
<td>128 (1.4)</td>
<td>2 (1.2)</td>
<td>16 (1.8)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Background and Aims: Women with CKD stages 3-5 are at higher risk of adverse pregnancy outcomes, including preterm delivery and low birthweight and progression of kidney disease. However, data describing outcomes of women with less severe kidney disease are limited, and few compare with women normal renal function. Furthermore, most studies report cohorts recruited from specialist clinics and may not be representative. This study aimed to describe pregnancy outcomes in a UK population cohort according to pre-conception eGFR <90 ml/min/1.73 m² compared with women with eGFR ≥90 ml/min/1.73 m².

Method: Routinely collected pregnancy data from three NHS Trust hospitals in Kent (UK) between 2010 and 2020 were extracted with Research Ethics Committee approval (19/LO/1242 and 18/SC/0158). Local laboratory and clinical data were linked to identify women with eGFR measured within two years of conception. Women without preconception creatinine were excluded from analysis. Baseline characteristics were described and comparisons between eGFR and adverse pregnancy and renal outcomes were tested.

Results: A total of 14,243 pregnancies with confirmed pre-pregnancy creatinine were included, of which 1,405/14,243 (9.9%) had CKD stages 1-4 (stage 1: 221/14,243 (1.6%), stage 2: 1,170/14,243 (8.2%), stage 3: 12/14,243 (0.1%), stage 4: 2/14,243 (0.01%) (Table 1). Women with pre-pregnancy eGFR 60-89 ml/min/1.73 m² (stage 2) were significantly older at conception than women without CKD (eGFR >90 ml/min/1.73 m²) but there were no significant differences in live birth rates, small for gestational age, gestation at delivery, and preterm birth. In pregnancies with CKD (1,405, stages 1-4), pre-pregnancy eGFR was weakly correlated with birthweight (r = 0.05, p = 0.05), and gestational age (r = 0.06, p = 0.05).

Conclusion: To our knowledge, this is the largest population cohort to describe pregnancy outcomes between women with eGFR 60-89 ml/min/1.73 m² compared with eGFR ≥90 ml/min/1.73 m². Women with eGFR 60-89 ml/min/1.73 m² did not have worse renal or pregnancy outcomes compared to eGFR >90 ml/min/1.73 m². Limitations include lack of proteinuria data and details of structural CKD (Class 1 CKD), and only one eGFR measurement prior to pregnancy may have led to some women with temporary reduction in function being included in the cohort. Overall, the findings suggest that women with eGFR 60-89 ml/min/1.73 m² should not be discouraged from pregnancy.

#4180

HYPERTENSION, HYPOKALEMIA AND PREGNANCY: A CASE OF GELLER SYNDROME

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Background and Aims: Hypokalemia is not a common laboratory finding in pregnancy, with a recent study revealing a prevalence of less than 1%, nationwide [1]. In a pregnant patient with newfound hypertension and hypokalemia, it is important to consider causes that would affect the Renin-Angiotension-Aldosterone pathway. Although these causes are usually suspected in patients with a triad of hypertension, hypokalemia and metabolic alkalosis, the latter finding may not be present in pregnant patients given metabolic compensation for their respiratory alkalosis of pregnancy.

Method: A 27 year old, 36 week and 5 day pregnant female presented to her OBGYN follow up appointment at the beginning of the year. At that time, she was found to be hypokalemic and was admitted overnight for potassium repletion, consisting of 40 mEq of oral potassium chloride and 40 mEq of intravenous potassium. She was discharged after that with a follow up appointment scheduled the next month. At that clinic visit, her potassium was 2.6 mmol/L and she was admitted for further workup. The patient was also hypertensive, with a blood pressure markedly increased from her baseline value. The patient endorsed having elevated blood pressures during her previous pregnancy with normalization after delivery. She stated that she was followed at a different outpatient clinic at that time, so she did not have all the records, however was told she suffered from pre-eclampsia. During this current admission, patient did note dyspnea, fatigue and generalized weakness. She denied any diarrhea or gastrointestinal distress. Her physical examination was unremarkable. Spot urine potassium was 19 with a serum potassium of 2.8 mmol/L after 40 mEq of potassium supplementation. Aldosterone was <3 ng/dL and renin was 4.8 pg/mL. Urine protein to creatinine ratio was 167 mg/g with normal liver enzymes. Her magnesium level was 1.8 mg/dL. The patient had a vaginal delivery with improvement in blood pressure. No antihypertensive agents were required. During subsequent outpatient visits, her potassium also started to improve and she was eventually weaned off supplementation. Given an unremarkable physical examination along with hypokalemia and hypertension which resolved after delivery, a diagnosis of Geller syndrome was made. Genetic testing was considered but could not be performed.

Results: In Geller syndrome, a gain-of-function mutation allows progesterone to bind and stimulate the mineralocorticoid receptor. Clinically, this presents as a patient who develops hypertension and hypokalemia during states of high circulating progesterone, such as pregnancy. Often these derangements resolve after cessation of high levels of progesterone, such as delivery of fetus, without major intervention.

Conclusion: High clinical suspicion is needed for pregnant patients who present with hypertension and hypokalemia. Reviewing records of past pregnancies can often shed light in this patient population, specifically the resolution of the blood pressure and potassium derangements after delivery of fetus. Newer evaluation techniques, such as genetic testing, can also play an important role with identifying this condition and allowing for counselling prior to subsequent pregnancies. Treatment typically consists of electrolyte supplementation and blood pressure control until birth occurs.
#6868
MACHINE LEARNING-BASED HYPERTENSION DISEASE RISK CLASSIFICATION USING LEARNING VECTOR QUANTIZATION ALGORITHM

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Yogyakarta State University, Computational Biology and Medicine Laboratory, Sleman, Indonesia

Background and Aims: According to the World Health Organization, the disease dubbed as the silent killer of death is the number one cause of death in the world. Hypertension is a disease that does not show certain symptoms. There are about 95% of hypertension cases have no known cause, while the rest are caused by other diseases. Therefore, an early detection system for hypertension is needed. In this research, the Learning Vector Quantization (LVQ) algorithm is used to perform the classification process.

Method: In this research, the LVQ machine learning algorithm is used. LVQ is an algorithm that is a type of artificial neural network and uses neural computation. The data in this study is hypertension patient data from Sultan Daeng Radja Hospital which is divided into four classes. In the system design stage using the LVQ algorithm, the process in this system is by entering input data in the form of medical records consisting of 12 attributes based on their weights which will then be carried out by the LVQ process to produce classification results. If the classification results have been obtained, the system will stop. After the classification testing process is carried out, the accuracy calculation process is carried out.

Results: Based on six test scenarios that have been carried out, the system produces recommendations for a value of 0.1 for the learning rate, a value of 0.2 for the learning rate multiplier, the amount of training data of as much as 50%, the maximum epoch value of six, the minimum value of alpha 0.001. From these values, the average accuracy result obtained is 94%.

Conclusion: Based on the value of accuracy results obtained exceeding 90%, these values, the average accuracy result obtained is 94%.

#4808
DIFFERENTIATING POSTPARTUM HELLP SYNDROME FROM ATYPICAL HEMOLYTIC UREMIC SYNDROME

Michael Che1, Sarah Moran2, Richard Smith3, Sara Gastoldi4 and Jocelyn Garland5

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Background and Aims: HELLP (hemolysis, elevated liver enzymes, low platelets) is a severe variant of preeclampsia whose pathogenesis remains unknown but likely involves abnormal placentalation, endothelial dysfunction and release of vasoactive substances. Complement dysregulation is implicated in the pathogenesis of atypical hemolytic uremic syndrome (aHUS) and there is growing evidence to support its role in HELLP syndrome. Here we present a case of postpartum thrombotic microangiopathy (TMA) in the setting of HELLP syndrome.

Method: We present a case report. Ethics approval was obtained by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

Results: A 22 year old G1P1 Caucasian woman presents at 37 weeks gestation with abdominal pain and severe hypertension. Labs demonstrated TMA including hemoglobin 95, platelets 30, LDH 2397, and schistocytes. She had severe transaminitis with AST 1845 and ALT 830, and proteinuric acute kidney injury. She was diagnosed with HELLP syndrome and treated with anti-hypertensives and emergency Caesarean section. Unfortunately, the infant did not survive, and there was no placental abruption. Platelets recovered by day 5 postpartum, LDH by day 7. However, renal function worsened and by day 6 postpartum, she required hemodialysis. A renal biopsy revealed acute and chronic TMA. She did not have cortical necrosis. Further workup revealed normal C3, C4 and ADAMTS13 levels. Dialysis was stopped after two weeks. By 6 months, her renal function and proteinuria returned to normal. Complement function testing revealed negative complement factor H autoantibody, but elevated soluble CsA-9 (sCsA-9) level (0.42 mg/L, normal <0.3). Ex-vivo serum CsA-9 deposition on human microvascular endothelial cells was assessed both on resting (182%, normal <150%) and on ADP-activated endothelial cells (273%, normal <150%). This test was repeated 6 months postpartum when renal function had normalized, and results were persistently abnormal both on resting (215%, normal <150%) and on ADP-activated endothelial cells (282%, normal <150%). aHUS genetic testing was negative.

Conclusion: Results from Burwick et al suggest that this patient had a very high likelihood of clinical aHUS in association with HELLP syndrome (elevated LDH >1832 U/L and creatinine >1.9 mg/dL) [1]. Identifiable aHUS genetic mutations only occur in 50% of aHUS patients. Complement function testing is not routinely assessed for postpartum HELLP; however, the severity of her HELLP syndrome prompted further investigation (C5b-9 deposition testing). The persistence of increased C5b-9 deposition 6 months postpartum for this patient mimics the findings of patients who have confirmed aHUS [2]. Our patient’s unique results suggest the patient may be at risk for recurrent TMA/aHUS in her lifetime, particularly if another pregnancy is being considered. Future research should explore which pregnancy associated TMA patients may benefit from anti-complement therapy.

Table 1: Blood pressure, laboratory values and potassium supplementation prior, during and post hospitalization.

<table>
<thead>
<tr>
<th>BP (mmHg)</th>
<th>Serum HCO3 (mmol/L)</th>
<th>Serum K (mmol/L)</th>
<th>Supplementation of K (mEq/L/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>98/56</td>
<td>23</td>
<td>3.9</td>
</tr>
<tr>
<td>2020</td>
<td>103/75</td>
<td>21</td>
<td>4.0</td>
</tr>
<tr>
<td>2021</td>
<td>108/73</td>
<td>23</td>
<td>3.6</td>
</tr>
<tr>
<td>2022</td>
<td>134/90</td>
<td>20</td>
<td>2.7</td>
</tr>
<tr>
<td>HD 1</td>
<td>132/81</td>
<td>19</td>
<td>2.6</td>
</tr>
<tr>
<td>HD 2</td>
<td>139/92</td>
<td>18</td>
<td>2.8</td>
</tr>
<tr>
<td>HD 3</td>
<td>137/97</td>
<td>19</td>
<td>3.5</td>
</tr>
<tr>
<td>HD 4</td>
<td>137/91</td>
<td>17</td>
<td>4.4</td>
</tr>
<tr>
<td>HD 5</td>
<td>130/76</td>
<td>18</td>
<td>4.1</td>
</tr>
<tr>
<td>HD 6</td>
<td>125/80</td>
<td>17</td>
<td>4.5</td>
</tr>
<tr>
<td>Post Discharge Day 11</td>
<td>122/83</td>
<td>22</td>
<td>4.2</td>
</tr>
<tr>
<td>Post Discharge Day 44</td>
<td>120/82</td>
<td>23</td>
<td>4.0</td>
</tr>
<tr>
<td>Post Discharge Day 70</td>
<td>109/72</td>
<td>23</td>
<td>3.9</td>
</tr>
</tbody>
</table>

HD: Hospital Day, NA: not applicable

REFERENCE

#4808
DIFFERENTIATING POSTPARTUM HELLP SYNDROME FROM ATYPICAL HEMOLYTIC UREMIC SYNDROME
REFERENCES


#5113
THE MULTIVERSE OF PREGNANCY-ASSOCIATED AHUS: TRIGGERS, TIMING AND OUTCOMES – A SINGLE CENTER EXPERIENCE
Andrea Spasiano1,2, Daniela Palazzetti1,2, Anna Petrosino1,2, Chiara Tacente1,2, Gianmarco De Luca1,2, Alessandro Naticchia1, Francesca Bruno1,2, Rocco Baccaro1,2, Pietro Manuel Ferraro1,2 and Giuseppe Grandaliano1,2

1Università Cattolica del Sacro Cuore, Dipartimento di Chirurgia e Medicina Traslazionale, Rome, Italy, 2Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Unità Operativa Complessa Nefrologia, Dialisi e Trapianto, Rome, Italy and 3Azienda Ospedaliera Cardinale Giovanni Panico, Unità Operativa Complessa di Nefrologia, Tricase, Italy

Background and Aims: Atypical hemolytic uremic syndrome (aHUS) is a rare disease caused by dysregulation of the alternative pathway of complement, characterized by hemolytic microangiopathic anemia, thrombocytopenia and acute kidney injury. Incidence is ~ 0.23 per year per million people and about 7% of aHUS diagnoses occur in the setting of pregnancy, determining the so-called “pregnancy associated aHUS” (PaHUS). It could occur during gestation, in the immediate postpartum period or up to 12 weeks after delivery. Maternal exposure to semiallogenic fetoplacental material represents a complement triggering condition, worsened over gestation, with a climax at the delivery. Despite the attempt of solute and membrane regulators to mitigate the immune overactivation, an exaggerated inflammatory response, a decrease in the amount of regulatory proteins or some inherited or de novo mutations in complement factors’ genes, predispose to complement dysregulation. Its diagnosis is often delayed due to a multif orm manifestation and similarity with HELLP syndrome or other thrombotic microangiopathy disorders (TMA), such as thrombotic thrombocytopenic purpura. It results in a delayed treatment, consequently threatening mother and fetus life. PaHUS is linked to high rates of end stage kidney disease, nearly achieving 78% at 24 months’ postpartum without eculizumab therapy. Indeed, anti-C5 therapy is effective and universally considered the best choice to treat aHUS.

Method: In this case series, we report our experience about the management of PaHUS during the last 2 years. An internal hospital protocol points out suspected TMA patients semi-automatically, thanks to a structured teamwork among emergency department and laboratory, hematology, nephrology and intensive care units. Treatment protocol applied was standard eculizumab

Figure 1: Progressive normalization of serum values for each patient.

Table 1: Patients’ clinical features.

<table>
<thead>
<tr>
<th>Trigger</th>
<th>A - 36 yrs</th>
<th>B - 27 yrs</th>
<th>C - 30 yrs</th>
<th>D - 40 yrs</th>
<th>E - 32 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>T from delivery to diagnosis (day)</td>
<td>Postpartum hemorrhage</td>
<td>Intrauterine fetal death</td>
<td>Uterine atony</td>
<td>Preeclampsia</td>
<td>Abruptio placentae and miscarriage</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Period inbetween diagnosis and therapy beginning (h)</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>7</td>
<td>24</td>
</tr>
<tr>
<td>Dialysis need</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>T to return in range (day):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cre</td>
<td>20</td>
<td>13</td>
<td>27</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>PLT</td>
<td>15</td>
<td>3</td>
<td>4</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Hb</td>
<td>30</td>
<td>45</td>
<td>27</td>
<td>34</td>
<td>40</td>
</tr>
<tr>
<td>LDH</td>
<td>30</td>
<td>23</td>
<td>27</td>
<td>34</td>
<td>35</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>40</td>
<td>9</td>
<td>30</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Genetic test</td>
<td>-</td>
<td>-</td>
<td>IN PROGRESS</td>
<td>-</td>
<td>HETEROZYGOUS MISSENSE MUTATION CD46</td>
</tr>
</tbody>
</table>

Abstracts i1017
PREVALENE OF CHRONIC KIDNEY DISEASE IN PREGNANCY: A UK POPULATION STUDY

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Background and Aims: Women with chronic kidney disease (CKD) are at greater risk of adverse pregnancy outcomes. Historically CKD in has been proposed to affect 3% of all pregnancies (0.13% with moderate to severe CKD) but is based on expert opinion and numbers affected are propose to rise due to the rise of maternal obesity and age and could impact on service planning. However, there are no accurate estimates of CKD prevalence in pregnancy. This study aimed to investigate how many pregnancies may be affected by CKD, according to disease severity, in a UK population cohort.

Method: Routinely collected pregnancy data from three NHS Trust hospitals in Kent (UK) between 2010 and 2020 were extracted with Research Ethics Committee approval (19/LO/1242 and 18/SC/0158). Local laboratory and health care records were linked and used to identify women between 18 and 50 years of age with a confirmed eGFR measurement (Chronic Kidney Disease Epidemiology Collaboration 2009 without ethnicity correction) within two years prior to conception, and no current pregnancy recorded at the time of sampling. Baseline characteristics and prevalence of CKD at different stages were described.

Results: A total of 76, 755 pregnancies were recorded between 2010 and 2020, including 14,257/76,755 (18.6%) pregnancies with preconception eGFR (median eGFR 115 ml/min/1.73 m²) (IQR 21). There were 1,184/14,257 (8.3%) pregnancies with a preconception eGFR <90ml/min/1.73 m², including eGFR between 60-89 ml/min/1.73 m² (1170/14,257, 8.2%). Only 12/14,257 (0.08%) of pregnancies had an eGFR 30-59 ml/min/1.73 m² and two pregnancies (0.01%) had an eGFR between eGFR 15-29 ml/min/1.73 m². There were no pregnancies in the cohort with an eGFR <15 ml/min/1.73 m². The cohort was majority White ethnicity (1291/135790; 94%) with 6.4% (879/135790) from Black, Asian, Mixed and East Asian ethnicities. Women with pregnancies that were affected with CKD were significantly older at conception (27, SD 5.5, vs 30.8, SD 5.5, p < 0.001) and had greater prevalence of chronic hypertension (8.6% vs 11.3%, p = 0.013). Considering the whole cohort, including those without kidney function testing, the proportion of pregnancies affected by CKD was low (1,185/76,755; 1.5%).

Conclusion: This is the largest cohort reporting the prevalence of CKD including severity in pregnancies in the UK. Overall the total number of pregnancies affected by CKD was lower than previous estimates, especially for those with advanced disease. This finding may represent reduced fertility in women with CKD, individual decisions not to conceive, negative advice from clinicians or obstetric management at different centres not captured in this cohort. However, only 1 in 5 women prior to pregnancy had an eGFR and gestational changes in creatinine may mask identification of CKD in pregnancy. A further limitation includes only eGFR measurement prior to pregnancy was used thus women with temporary eGFR reduction may have been incorrectly included in the CKD cohort. Finally there were few women from ethnic minority groups who are disproportionately affected by CKD. Further information regarding kidney function in women of reproductive age and at conception is needed to enable true estimated of CKD prevalence in obstetric care.

#4764
NEPHROTIC SYNDROME IN PREGNANT DIABETIC WOMEN: MATERNAL AND PERINATAL OUTCOMES AT A TERTIARY CENTER

Estela Nogueira1, Rita Afonso2, Iolanda Godinho1, Mónica Centeno1, Luisa Pinto3 and José António Lopes4

1Centro Hospitalar Universitário Lisboa Norte, EPE, Nephrology and Renal Transplantation, Lisbon, Portugal, 2University Hospital Center of Algarve, Faro, Nephrology department, Faro, Portugal, 3Centro Hospitalar Universitário Lisboa Norte, EPE, Obstetric, Gynecology and Reproductive Medicine Department, Lisbon, Portugal and 4Centro Hospitalar Universitário Lisboa Norte, EPE, Nephrology department, Faro, Portugal

Equal contribution: Estela Nogueira and Rita Afonso

Background and Aims: Management of pregnant women with diabetic kidney disease and nephrotic range proteinuria or nephrotic syndrome constitute a challenge to clinicians. Maternal and perinatal outcomes, especially in patients with chronic kidney disease, remain poor. The authors describe the multidisciplinary approach and the outcomes of diabetic pregnant patients with nephrotic range proteinuria.

Method: Retrospective observational study in which the authors reviewed maternal, obstetric and perinatal outcomes in pregnant diabetic woman with nephrotic range proteinuria or nephrotic syndrome surveilled at our nephro-obstetric unit from 2011 until 2021.

Results: We evaluated 7 gestations in 6 patients. Mean age was 31.7±4.7 years (26-38), 5 were caucasian and 1 was black African, and 4 were nulliparas. They all had type 1 diabetes, with mean disease diagnosis at 9.9±5.9 years of age. All patients had chronic hypertension and 5/6 patients had poor glycaemic control before pregnancy (mean HbA1c of 11.9%). Mean baseline Scr was 1.1±0.5 mg/dl (0.5-2.8) and mean baseline proteinuria was 3697.2±2301.4 mg/day (73-6326), with 1/1/3/2 patients being on CKD stage 1/2/3/4, before pregnancy, respectively. Exposure to teratogenic therapy during the first trimester occurred in 5/7 gestations with a mean exposure of 7.4 ± 3.1 weeks. Proteinuria increased in all patients and renal function deteriorated in 5/7 gestations (mean Scr of 2.5±1.2; 0.67-4.07 mg/dl) in association with pre-eclampsia in 2 patients and with pregnancy hyperfiltration and nephrotic syndrome in all gestations. One patient started dialysis at week 28, due to urea levels >100mg/dL. Partial renal recovery occurred in 2 patients. To date, 3/6 patients initiated PD 15 months (6-29 months) after gestation, 1 of which received a kidney-pancreas transplant. Hypertension aggravated in 6 gestations. Aspirin and low molecular weight heparin were initiated in 6 gestations and they were all treated with furosemide to control volume overload. Regarding fetal outcomes, severe fetal growth restriction was responsible for 1 still birth and 1 medical termination of pregnancy, both at 24 weeks. Cesarean was performed in 4/5 gestations (one is still undergoing) due to pre-eclampsia, renal function deterioration and/or fetal growth restriction. Mean gestation age at delivery was 29.5±4.7 weeks, mean birth weight was 1389 ±203.3 mg (1190-1665) and mean apgar scores at 1/5/10 minutes were 9/10/10 respectively. Neonatal intensive care was needed in 4 newborns.

Conclusion: This study reinforces the idea that diabetic women with nephrotic range proteinuria have an increased risk of complications and worse outcomes during pregnancy, namely pre-eclampsia, fetal growth restriction, preterm delivery and renal function deterioration. As such, glycermic and proteinic control should be optimized and careful counseling regarding outcomes should be discussed before pregnancy. Management during gestation should involve an experienced multidisciplinary team including endocrinologist, nutritionist, nephrologist and obstetrician.
Figure 1: (A) Extracellular vesicles can effectively double dyeing by DID/DiI. (B) Define the optimal ratio of DID/DiI in extracellular vesicles. (C) The changes of MPO expression in AKI model were detected by WB and immunohistochemistry. (D) The changes of MPO expression in AKI model were detected by WB and immunohistochemistry.

**Conclusion:** In this study, we constructed in vivo imaging of extracellular vesicles in the kidney based on optical imaging. Chemiluminescence generated by inflammatory specific expression of MPO and detection of MPO enzyme activity and specific detection substance luminol in the kidney disease model formed fluorescence resonance energy transfer in extracellular vesicles of double-stained cells. Preliminary efficacy evaluation showed that the fluorescence intensity of the double-dyed extracellular vesicles system in this model is greater than that of the single-dyed extracellular vesicles. This method can be applied to the in vivo tracer of extracellular vesicles in the kidney, providing technical support for the treatment of extracellular vesicles in kidney disease and the study of drug delivery.

**Goal:**

**Abstracts** 1019

**AKI & CRITICAL CARE NEPHROLOGY**

**G1 - BASIC SCIENCE & EXPERIMENTAL**

#4838

**IN VIVO TRACING OF EXTRACELLULAR VESICLES IN ACUTE KIDNEY INJURY**

Wei Jiang, Bin Wang and Bicheng Liu

Zhong Da Hospital, Southeast University School of Medicine, Nephrology, Nanjing, P.R. China

**Background and Aims:** Extracellular vesicles, with their unique ability to migrate, target, and selectively internalize into specific cells, open up a new field of diagnosis, treatment, and drug delivery. However, a major disadvantage of translating exosome therapy into the clinic is that not enough is known about these endogenous nanovesicles, especially in vivo, and the tracing of extracellular vesicles in vivo can yield important information about their biological distribution, migration capacity, toxicity, biological role and mechanism of action. Therefore, to develop efficient, sensitive and biocompatible exosome markers. Recording and imaging techniques are much needed. Recent studies have developed different exosome labeling and imaging methods. However, due to the physiological location of the kidney and the distribution characteristics of extracellular vesicles in vivo, the specificity of live imaging of extracellular vesicles in the kidney is insufficient. Therefore, this study intended to construct a reliable and specific in vivo imaging method of extracellular vesicles in the kidney.

**Method:** Dual-mode imaging was used to trace extracellular vesicles in mice model of kidney disease, providing important technical support for tracing extracellular vesicles in vivo kidney and related drug delivery. Firstly, extracellular vesicles were separated for fluorescence staining, and the concentration variation rule of MPO, a disease-specific enzyme, was mastered in mouse kidney tissue. MPO, Luminol, DiI and DiD were used to construct a near-infrared imaging mode based on fluorescence resonance energy transfer to enhance fluorescence penetration, and targeted peptides were used to increase the aggregation of extracellular vesicles in vivo. This combines the sensitivity of fluorescence imaging with the specificity of kidney targeting peptides to reach deep tissues of extracellular vesicles.

**Results:** In the optical mode in vitro experiments, we found that exosomes could be co-stained by DiL and DiD. In addition, the dye ratio of 3:7 could make exosomes exhibit the strongest excitation light. In the presence of luminol sodium, the fluorescence intensity of exosomes co-stained by DiI and DiD lipophilic dyes was higher than that of exosomes with single dye. In the second mode of MRI, we found that our material can be efficiently adsorbed on exosomes by electron microscopy. Follow-up in vivo experiments are being further improved.

**Conclusion:** In this study, we constructed in vivo imaging of extracellular vesicles in the kidney based on optical imaging. Chemiluminescence generated by inflammatory specific expression of MPO and detection of MPO enzyme activity and specific detection substance luminol in the kidney disease model formed fluorescence resonance energy transfer in extracellular vesicles of double-stained cells. Preliminary efficacy evaluation showed that the fluorescence intensity of the double-dyed extracellular vesicles system in this model is greater than that of the single-dyed extracellular vesicles. This method can be applied to the in vivo tracer of extracellular vesicles in the kidney, providing technical support for the treatment of extracellular vesicles in kidney disease and the study of drug delivery.

#3768

**CDYL IS A THERAPEUTIC TARGET FOR ACUTE KIDNEY INJURY BY REGULATION PYROPTOSIS**

Ting Xiang, Lingzhi Li, Wu Yiting, Ping Fu and Liang MA

West China Hospital, Sichuan University, Kidney Research Institute, Division of Nephrology, chengdu, P.R. China

**Background and Aims:** Pyroptosis as a necrosis type related to inflammation, is involved in various diseases, including acute kidney injury (AKI). Here, we report that Chromodomain Y-like (CDYL) is critical for pyroptosis regulation in AKI.

**Method:** Cisplatin-induced mouse model and cisplatin-induced TCMK-1 cell model of AKI were established, serum creatinine (Cr) and blood urea nitrogen (BUN) were measured to evaluate kidney function, and renal tissue lesions were observed by HE staining. The expression of gene/protein in relation to inflammation and pyroptosis were measured by qPCR and western blot. The CDYL was overexpression in mice by rapid injection of a volume of naked plasmid DNA solution (30 ug) through the tail vein 2 hours before intraperitoneal injection of cisplatin.

**Results:** The results indicate that CDYL was increased in cisplatin-induced and sepsis-induced AKI, and overexpression of CDYL in mice would significantly increase the expressions of NGAL, NLRP3, Caspase-1, GSDMD, IL-1β, MCP-1, TNFα and IL-6 (Fig. 1). RNA-seq shown that the genes were mainly enriched in fatty acid metabolic process when CDYL overexpression, and FABP4 was finally identified as the key downstream factor (Fig. 2). Overexpression of CDYL in cisplatin-induced AKI further aggravated renal injury compared with the model mice, as indicated by the increased inflammation and pyroptosis protein expression, and worse tissue architecture, while the knockout of FABP4 will attenuate the injury (Fig. 3). In addition, treatment with CDYL inhibitors could attenuate inflammation and pyroptosis in cisplatin-induced renal injury (Fig. 4) and cisplatin-stimulated TCMK-1 cells (Fig. 5).

**Conclusion:** CDYL played a role in inflammation and pyroptosis regulation in AKI. Inhibition of CDYL could suppress renal inflammatory response and pyroptosis, and improve kidney function via modulation of FABP4 expression. The results highlighted that CDYL might represent a potential therapeutic target against AKI.
DIFFERENTIAL ROLES OF REGNASE3 IN RESIDENT MACROPHAGE VERSUS TUBULAR EPITHELIAL CELLS IN THE HEALTHY OR POSTISCHEMIC KIDNEY
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Background and Aims: Acute kidney injury (AKI) is a prevalent yet severe condition that occurs in clinical settings. The prognosis for AKI is poor, with many patients progressing to AKD, CKD, and even ESKD especially in those who were admitted to the ICU. RNA-binding proteins (RBPs) are a class of proteins that play a vital role in regulating gene expression and have been implicated in a wide range of diseases. Regnase3 is a member of the Regnase RBP family and has been shown to promote inflammation by increasing TNF in macrophages. Despite this knowledge, the full extent of the role played by Regnase3 in AKI remains unknown. Therefore, we hypothesized that Regnase3 plays a role in both macrophages and tubular epithelial cells, influencing inflammation and tubular repair in AKI.

Method: In order to investigate the role of Regnase3 in kidney injury, a series of genetically-modified mice were developed on the C57BL/6J genetic background. These mice included the paired box gene 8 (Pax8)-reverse tetracycline transactivator (tTA, Pax8rTtA), tetracycline resistance protein (TetO)-Cre (TetOCre), transgenic receptor activator of nuclear factor kappa-B (Rank)-Cre (RankCre), and Regnase3 floxed (Regnase-3fl/fl) mice. Using these genetically modified mice, we applied a range of experimental animal models to study the effects of Regnase3 on kidney injury, including unilateral kidney ischemia-reperfusion surgery with or without nephrectomy and nephrocalcinosis-related kidney injury. Additionally, we employed in vitro models utilizing primary cells to study Regnase3 on the cellular level. Furthermore, we utilized scRNA-seq and RNA-seq to investigate the underlying mechanisms of Regnase3's function.
Results: We conducted a thorough investigation and discovered that the Regnase3 is highly expressed in macrophages located within the kidney after AKI. The scRNA-seq showed the expression Regnase3 positively correlated with the phagocytosis, chemokines, and monocye maturation. Furthermore, Rank-Regnase3 mice suffered from more inflammation and kidney injury after AKI, characterized by an increase in CCR2 positive leukocyte infiltration. Additionally, in vitro experiments revealed that Regnase3 is involved in modulating macrophage behavior, acting as a regulator of macrophage polarization towards an M1 and M2 phenotype and influencing the capacity of cell migration. These findings indicate that Regnase3 is essential in the migration of macrophages after AKI, which contribute to both early phase inflammation and progression towards AKI-CKD. Next, we aimed to examine the role of Regnase3 in the context of renal tubule injury. We observed that Regnase3 is highly expressed in healthy renal tubules, but its expression is reduced following injury. Through in silico, in vivo and in vitro experiments, we found that Regnase3 controls early apoptosis, cell death, proliferation, and wound healing capacity of tubular epithelial cells. These effects contribute to kidney injury in postischemic kidneys. Additionally, we discovered that the deletion of Regnase3 provides protection against ischemic AKI (Figure 1). Mechanistically, Regnase3 targets pre-RNA and modulates alternative splicing. The deletion of Regnase3 provides protection against ischemic AKI (Figure 1). Mechanistically, Regnase3 targets pre-RNA and modulates alternative splicing. The deletion of Regnase3 provides protection against ischemic AKI (Figure 1). Mechanistically, Regnase3 targets pre-RNA and modulates alternative splicing. The deletion of Regnase3 provides protection against ischemic AKI (Figure 1). Mechanistically, Regnase3 targets pre-RNA and modulates alternative splicing. The deletion of Regnase3 provides protection against ischemic AKI (Figure 1).

Conclusion: In summary, our findings indicate that Regnase3 contributes to kidney injury in postischemic kidneys. However, the impact of Regnase3 is contingent upon the specific cell lineage in question. The Rank-Regnase3 leads to an exacerbation of kidney injury by increasing macrophage recruitment, whereas the Pax8-Regnase3 leads to an improvement in kidney injury through its effects on cell death and wound healing capacity of tubular epithelial cells. Therefore, the role of Regnase3 in kidney injury is dependent on the cell lineage, which ultimately determines the detrimental or beneficial impact on kidney injury.

#3665
DCR2 PROMOTES TUBULAR MALADAPTIVE REPAIR BY INHIBITING KETONE BODY–INDUCED FOXO3 SIGNALING AFTER ACUTE KIDNEY INJURY
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Background and Aims: The proximal tubule has a capacity for repair after acute kidney injury (AKI), but this capacity is limited, especially in severe AKI. Tubular maladaptive repair after AKI leads to chronic kidney disease (CKD), even to end-stage renal disease (ESRD). However, the mechanism of maladaptive repair is not fully clarified, and there is a lack of effective treatment for AKI in clinic. Our previous study found that decay receptor 2 (DCR2), a trans-membrane receptor of tumor necrosis factor-related apoptosis inducing ligand (TRAIL), was specifically expressed renal tubules and did not have the ability of proliferation in AKI, suggesting DCR2 may be associated with maladaptive repair of tubular cells. This study aims to investigate the role and mechanism of DCR2-positive tubular cells in the repair of AKI.

Method: The DCR2-GFP lineage trace mice, KSP-cre Dcr2f/f mice (Distal tubular Dcr2 Conditional Knockout CKO) mice and Ggt1-cre Dcr2f/f (proximal tubular Dcr2 Conditional Knockout CKO) mice were constructed, and three AKI mouse models (moderate and severe ischemia-reperfusion injury and cisplatin-induced AKI) were used. Light microscopic examination of paraffin-embedded sections stained with haematoxylin and eosin, periodic acid–Schiff stain and Masson stain. Confocal analysis the co-expression of Dcr2-GFP and proximal tubular markers(AQP1, Villin), distal markers (AQP2), failed repair markers (Vcam, Dcdc2), proliferative markers (Ki-67, Edu, PCNA), Ki61, differentiated markers (pax2, sox9, s1x2), senescent markers (P16, P21, SA-β-gal), senescent phenotype (IL-6, TGF-β1) and fibrotic markers (a-SMA, collagen I, Fibronectin). And wild type (WT) mice and Dcr2 CKO mice were used to compare the degree of kidney injury, renal function and tubular repair after AKI. Furthermore, quantitative proteomics and bioinformatics analyzed the downstream molecules of Dcr2 in renal tissues from WT-AKI and Cko-AKI, and validated studies were done.

Results: In this study, we found decay receptor Dcr2 was highly expressed in renal tubules and associated with kidney damage in AKI patients and mouse models. Dcr2-GFP transgenic mice verified that Dcr2 was specifically expressed in proximal tubular epithelial cells (PTECs) after AKI. The levels of Scr, BUN and urinary and renal acute and chronic injury scores were significantly lower in Ggt1-cre Dcr2f/f -AKI than that of WT-AKI. Meanwhile, the proliferative markers, senescent markers and area of renal fibrosis and fibrotic markers expression was decreased in Ggt1-cre Dcr2f/f mice compared with WT. However, the above effects were not obviously improved in Ksp-cre Dcr2f/f mice after AKI. These results suggested that proximal tubular Dcr2 knockout alleviated kidney injury and promote tubular repair after AKI. Consistent with findings in vivo, Dcr2 promoted cell senescence and inhibited cell proliferation in hypoxia-reoxygenation and cisplatin-treated primary PTECs. Further quantitative proteomics and validated studies showed Hmgcs2, a key enzyme for ketone-body, was increased in Ggt1-cre Dcr2f/f mice compared with WT. And the levels of urinary and renal β-hydroxybutyrate (β-OHB) were higher in Ggt1-cre Dcr2f/f mice, suggesting Dcr2 affects the synthesis of β-hydroxybutyrate through regulating the expression of Hmgcs2. Inhibition or deletion of Hmgcs2 aggravated kidney damage and repressed renal repair, but administration with β-OHB rescued these phenomena. Subsequently, PTEC-specific Dcr2/Hmgcs2 double deletion decreased β-OHB levels, which...
inhibited FOXO3 signaling by regulating histone acetylation, thereby boosting tubular maladaptive repair after AKI.

Conclusion: DcR2 promotes maladaptive repair of tubular cells by regulating Hmgs2-induced β-OHB production, and β-OHB affects FOXO3 signaling by regulating histone acetylation. The findings suggest that DcR2/Hmgs2/ketogenesis/FOXO3 signaling mediates tubular maladaptive repair, and DcR2 could serve as a promising target for improving renal repair and AKI prognosis.

#4145
ACLARA: AN ON-LINE CALCULATOR TO ESTIMATE CREATININE CLEARANCE IN RATS
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Background and Aims: Creatinine clearance (CICr) is a standard method for the measurement of glomerular filtration rate in rats. Recently, we developed ACLARA, an open and freely available neural network (NN)-based calculator of CICr in Wistar rats (http://idal.uv.es/aclara). By working solely on plasma creatinine concentration and body weight, ACLARA instantly and easily provides accurate CICr estimations with an identical concept to that underlying human glomerular filtration rate (GFR)-estimating formulae utility in the clinical setting. In addition to saving costs and time, ACLARA aligns with the 3Rs principles by providing a methodological refinement tool that reduces experimental animal stress derived from avoiding confinement in metabolic cages for individual, 24-hour urine collection. As a potential limitation, ACLARA was developed with data from Wistar rats. Accordingly, the aim of this study is to study ACLARA’s accuracy and utility in a different rat strain, namely the spontaneous hypertensive rat (SHR).

Method: In order to further validate the calculator, we used a dataset with 1,458 entries from unpublished experiments of AKI induced in Wistar and SHR male rats. Measured CICr (mCICr) was determined with a standard procedure, as we previously described [1], and estimated CICr (eCICr) was calculated using ACLARA. Calculator performance was assessed with the mean absolute error (MAE) and the Pearson product-moment correlation coefficient calculated as previously described [2]. Results of eCICr were compared with their corresponding mCICr values in the context of individual experiments.

Results: Our study reveals that ACLARA performs with reasonably high accuracy at CICr estimation in both Wistar and SHR rats as indicated by Pearson’s product-moment correlation coefficient (Crr) and MAE. The global Crr for the 1,458 measured versus estimated data values reaches 0.9, and a MAE of 0.18 mL/min. In general, estimated data provide identical results to measured data for individual experiments considered in the whole and, if anything, depict more congruent behavior. We interpret this improvement as the consequence of bypassing experimental errors introduced by the well-known discrepancies between the real and measured urinary flow in metabolic cages. Interestingly, ACLARA performs with accuracy through the range of ages and for all experimental conditions tested, including pharmacological treatments. Figure 1 shows a representative experiment in which measured and estimated data are compared holistically.

Conclusion: ACLARA is an easy-to-use and reliable tool to estimate creatinine clearance in SHR and Wistar rats from plasma creatinine concentration and body weight data. Validation for a second rat strain suggests a potential, wider application of ACLARA through laboratory rats, which needs to be further studied. In this sense, collaboration and use by independent investigators and recruitment of additional data sets from other laboratories is strongly sought to further adjust the calculator in order to enhance its accuracy, extend its applicability and improve its utility to the scientific community. This study was supported by Project PI21/01226, funded by Instituto de Salud Carlos III (ISCIII) and co-funded by the European Union, and a grant from the Consejería de Educación, Junta de Castilla y León (IES16020), Spain, co-funded by FEDER funds; and a grant from the Valencian Government with reference number CIAICO/2021/184. Noelia Diaz-Morales is recipient of a Juan de la Cierva-Formación postdoctoral contract (FJC2020-043205-I) funded by MCIN/AEI/10.13039/501100011033 and European Union “NextGenerationEU/PRTR”.

REFERENCES

#4668
CITRATE SYNTHASE LACTYLATION PROMOTES THE TRANSITION FROM ACUTE KIDNEY INJURY TO CHRONIC KIDNEY DISEASE BY ACTIVATING NLRP3 INFLAMMASOME
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Background and Aims: Renal interstitial inflammation has been postulated to play a critical role in the acute kidney injury (AKI) to chronic kidney disease (CKD) transition. Recent studies have shown that protein lactylation caused by lactate accumulation can regulate chronic organ injury. The purpose of this study was to investigated the role and mechanism of protein lactylation in AKI-CKD transition.

Method: Severe renal ischemia-reperfusion(I/R) injury (severe AKI) was constructed by bilateral renal ischemia for 35min. The lactylation enhancer rotenone and the lactylation inhibitor oxamate were used to verify the effect of protein lactylation. Lactylated proteomics was used to detect the changes of lactylated proteins in renal cortex at different time points (day 0, 3, and 7), and the lactylated proteins related to kidney injury were screened for verification.

Results: The pathological staining results showed that the severe AKI mice were most severely injured at day 3, partially recovered at day 7, and developed renal interstitial fibrosis at day 28. The Serum creatinine (Scr) levels did not return to baseline at day 28 after I/R injury. The levels of lactate and protein

Figure 1: Comparison of measured and estimated CICr for a whole representative experiment. B, basal. D, day. G, group.
lactylation modification detected by Elisa and western blot analysis showed the same tendency as the above pathological injury, indicating that protein lactylation might contribute to the chronic transition of severe AKI. The renal injury score was significantly increased at day 3 and the percentage of renal interstitial fibrosis was significantly increased at day 28 after treatment with protein lactylation enhancer. The renal injury score was significantly increased at day 3 and the percentage of renal interstitial fibrosis was significantly increased at day 28 after treatment with protein lactylation enhancer. IL-1β and IL-18 were found to be the most significantly enhanced inflammatory cytokines in the blood of mice, and the NLRP3 inflammasome activation was significantly enhanced in renal tissue at 3 days. The in vitro results further confirmed these findings. We found that protein lactylation might activate the NLRP3 inflammasome, therefore leading to AKI-CKD transition. Meanwhile, lactylation inhibitor had a protective effect on AKI-CKD transition. Lactylated proteins were detected by lactylated proteomics analysis at day 0, 3 and 7 after I/R, and the enrichment of differential lactylated proteins was analyzed. The results showed that the differential proteins with significant difference mainly existed in the tricarboxylic acid cycle. One of them is citrate synthase (CS), a key rate-limiting enzyme in the tricarboxylic acid cycle. Citrate synthase lactylation level increased significantly on day 3 after AKI. Among the three lactylation sites of CS, the further screening revealed that CS-K370 is the most significant. We constructed mutations of CS-K370 lactylation sites to verify its effects on the enzyme activity and function. Results showed in hypoxia/reoxygenation (H/R) model for mice renal tubular epithelial cells (mRTECs), compared with control group, the enzyme activity of CS in K370T group (modified status) decreased significantly, while in K370R group (unmodified status) did not decrease significantly. Moreover, the lactation modification of CS-K370 can lead to the activation of NLRP3 inflammasome. The above results indicated that the lactylation of CS-K370 site inhibited the enzyme activity of CS and activated NLRP3 inflammasome.

**Conclusion:** Renal protein lactylation promotes activation of NLRP3 inflammasome, leading to AKI-CKD transition. Citrate synthase may be the key lactylated protein.

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**Abstracts i1023**

**#6635**

**ARDT AND ALK3 MEDIATE RENO PROTECTION AFTER ISCHEMIC PRECONDITIONING**

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**Background and Aims:** Ischemia and following hypoxia are a common cause of acute kidney injury (AKI). Strategies for prevention and treatment of AKI are limited. In several animal models, ischemic preconditioning (IPC) has been established as an effective intervention to prevent ischemic organ injury. An IPC protocol of ischemia and reperfusion mediates organ protection for a few hours. This first phase of organ protection is followed by a second, protective phase occurring after 24–48 h. The second phase, named second window of protection (SWOP), persists for 3–4 d. Mechanisms and transcriptional mediators during SWOP are mostly unknown. The aim of the underlying study was to investigate effectors and target genes during SWOP and to identify a potential pharmacological therapeutic target.

**Method:** 6–8-week-old C57BL/6 mice were undergoing an IPC intervention; five minutes of renal sinistra artery ischemia was followed by five minutes of reperfusion. This cycle was performed five times. Mice were sacrificed 2, 4, 8, 12, 25, 48, 72 h after IPC. Two additional groups of mice were pharmacologically preconditioned for 48 h with low dose FK506 and small molecule GPI1046. Analysis of murine kidneys were performed by SDS-Page and Western blot.

**Results:** The first phase after IPC (2–4 h) was characterized by an increasing expression of hypoxia inducible factor-1α (HIF1α); 48 h after intervention a significant increase of expression of aryl hydrocarbon receptor nuclear translocator (ARNT) and consecutive activin receptor-like kinase 3 (ALK3) was observed. Comparable induction of ARNT and ALK3 expression was obtained by pharmacological preconditioning with FK506 or GPI1046.

**Conclusion:** Affected by hypoxia, HIF1α activates transcriptional upregulation of ARNT 48 h after IPC. The increasing expression of ARNT, follows an increased ARNT homodimerization. ARNT homodimer binds to the palindromic E-box 5′-CACGTG-3′ of the proximal ALK3 promoter. By this it induces the expression of the renoprotective ALK3 during SWOP. The organ-protective effects of constitutively expressed ARNT during SWOP can be mimicked pharmacologically by administration of FK506 or GPI1046 and may be used as a future therapeutic target.

**Figure 1:** Schematic illustration of the multiple role of ARNT. Under hypoxia or xenobiotic stress, ARNT is the functional heterodimeric binding partner of aryl hydrocarbon receptor (AHR) or HIF-1α. In tubular epithelium, ARNT homodimers induce transcription of ALK3 and consecutively mediate regenerative and antifibrotic effects via the canonical pSMAD1/5/8-signaling cascade. Created with BioRender.com.
Figure 2: Schematic illustration of IPC protocol. 
*Created with BioRender.com.*

Figure 3: Robust induction of ARNT and ALK3 expression 48 h after IPC intervention. (A) Schematic illustration of the effectors (HIF-1α, ARNT) during SWOP. (B) Representative Western blot showing protein levels of HIF-1α, ARNT, ALK3 and pSMAD1/5/8 in murine IPC kidneys at different post-intervention time points (2, 4, 8, 12, 25, 48 and 72 h). *Created with BioRender.com.*
#6839
MULTIDISCIPLINARY APPROACH TO STUDY THE BIOLOGICAL FUNCTION OF BBS10 IN THE PATHOGENESIS OF BARDET-BIEDEL SYNDROME (BBS)
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Background and Aims: Bardet-Biedl Syndrome (BBS) is a rare inherited ciliopathy resulting in multiple organ dysfunctions, including chronic kidney disease (CKD). Although BBS is highly heterogeneous at genetic level, BBS10 is one of the significant causative genes, accounting for almost 30% of cases of BBS cases in western countries. Despite the recent progress in the ciliopathy field, there is still little information on the mechanisms underlying renal disease. To elucidate the pathomechanisms, we have broadened the study’s criteria into a combination of the in silico-in vitro approach.

Method: This study integrates the molecular dynamics (MD) simulations with the results of nine distinct (SIFT, SNAP2, PROVEAN, Align-GVGD, ConSurf, I Mutant, MuPro, PremPS, and Dynamut) in silico pathogenicity prediction tools. For in vitro studies we have used the inner medulla renal epithelial cells lacking Bbs10 (IMCD3-Bbs10-/- cells). MTT assay, Colony formation assay, Real time PCR, Western Blot and other experiments were performed using the cultured wild-type and IMCD3-Bbs10-/-cells. BBS10 interactors have been studied using Mass Spec, after pulling down BBS10-FLAG in renal epithelial cells expressing the protein, after transfection.

Results: Our in-silico results showed that six BBS10 missense variants (Ser191Leu, Cys19Gly, Ile342Thr, Cys371Ser, Ala417Glu, and Tyr613Cys) could be potentially deleterious. IMCD3-BBS10-/- cells lacking Bbs10 showed hyperproliferation, increased aerobic glycolysis and signs of mitochondrial dysfunction. Additionally, among BBS10 interactors in vitro, we found several proteins involved in cellular metabolism and mitochondrial-related function. Interestingly, Bbs10 depletion affected PINK1/Parkin signalling, leading to the disruption of mitochondria quality control.

Conclusion: This multi-disciplinary approach could open new avenues to study the extra-ciliary biological function of BBS10 in renal epithelial cells and providing novel clues into our understanding of disease pathomechanisms.

#4392
TWEAK/FN14 SYSTEM IS INVOLVED IN RHABDOMYOLYSIS-INDUCED ACUTE KIDNEY INJURY
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Background and Aims: Rhabdomyolysis is a pathological syndrome associated with massive and severe skeletal muscle injury. A common complication of rhabdomyolysis is acute kidney injury (AKI), a process that increases mortality of these patients. In rhabdomyolysis, myoglobin (Mb) is released from muscle cells and subsequently absorbed by the renal tubular epithelium causing a series of deleterious effects. TWEAK/Fn14 axis regulates renal inflammation and tubular cell death, pathogenic mechanisms involved in AKI. However, the role of this pathway in rhabdomyolysis-AKI has not been previously analyzed. In this study we analyzed the role of TWEAK/Fn14 axis in AKI associated with rhabdomyolysis and the AKI to chronic kidney disease (CKD) transition.

Method: We performed an experimental model of AKI associated to rhabdomyolysis by the intramuscular injection of 50% glycerol (10mg/Kg of weight) in Wild Type C57BL/6 (WT), TWEAK deficient (TWEAK -/-) and Fn14 deficient (Fn14 -/-) mice (male, 12 weeks old). In another set of
Injury markers of kidney function characterized by elevated serum creatinine (CRE) levels and reduced long-term consequences, mainly fibrosis and inflammation.

Results: Fn14 renal expression was increased at earlier stages of rhabdomyolysis, correlating with decline of renal function. In MCTs cells, Mb induced Fn14 expression in a time- and dose-dependent manner, whereas TWEAK expression remained unchanged. The use of general antioxidants (N-Acetylcysteine) or Nrf2 inducers (curcumin or Sulforaphane) reduced Mb-mediated Fn14 upregulation in vivo and in cultured renal cells, whereas the opposite effect was observed with the HO-1 inhibitor tin protoporphyrin IX (SnPP). Furthermore, MAPK p38 and ERK1/2 inhibitors, such as SB203580 and PD98059 respectively, diminished Mb effects on Fn14 expression. Moreover, Mb enhanced pro-inflammatory effects of TWEAK in vitro. In the animal model, we observed that genetic TWEAK or Fn14 deficiency ameliorated rhabdomyolysis-related loss of renal function, reduced histological damage, tubular cell death, lipid peroxidation, and decreased the expression of inflammatory mediators (Ccl2, Tnf, Il6, Tlr4 and Ccl5), tubular injury markers (Haver1 and Lcn2) and endothelial dysfunction (Edh1 and Icam1). TWEAK or Fn14 knockout mice also showed decreased long-term renal fibrosis (Collagen content and Fn14 expression) and inflammation (F4/80 macrophage infiltration and Ccl2 expression) 30 days after rhabdomyolysis induction. Treatment with a blocking anti-TWEAK monoclonal antibody maybe a potential therapeutic target to decrease harmful effects of rhabdomyolysis.

Conclusion: Our data suggest that TWEAK/Fn14 axis is involved in AKI-rhabdomyolysis, as well as in the transition from AKI to CKD. TWEAK/Fn14 may be a potential therapeutic target to decrease harmful effects of rhabdomyolysis.

#5050
ANTIOXIDANT PORPHYRIN-BASED NANOZYME WITH SINGLE RUTHENIUM FOR TREATMENT OF ACUTE KIDNEY INJURY
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Background and Aims: Acute kidney injury (AKI) describes a sudden loss of kidney function characterized by elevated serum creatinine (CRE) levels and reduced urinary output. AKI patients have a high mortality rate, but limited treatment options are currently available. During the AKI progression, an excess of reactive oxygen species (ROS) leads to oxidative stress, which often results in cell damage and renal failure. Therefore, ROS scavenging has been considered a promising strategy for AKI treatment. Here we report a porphyrin-based nanozyme with single ruthenium (Por-Ru) as a ROS scavenger to cure AKI.

Method: The Por-Ru nanozyme was synthesised by one-pot synthesis. First, the 5,10,15,20-tetra(4-phenyl)-21H,23H-porphine (Por) was added to the solvent containing N, N-dimethylformamide. The RuCl3 was then introduced to form Ru-N coordinated porphyrin networks. We analysed the morphology and chemical structure using scanning electron microscopy (SEM) and X-ray photoelectron spectroscopy (XPS). We also tested its enzyme-mimicking abilities to scavenge ROS. The catalase-like (CAT) property was tested using a peroxide-titanium complex method, and the superoxide dismutase-like (SOD) property was tested using a •O2−- scavenging assay. In vitro, the protective effect of Por-Ru nanozyme against ROS damage was examined using the mouse tubular epithelial (TCMK-1) cell line. After biocompatibility evaluation, the therapeutic efficacy of Por-Ru nanozyme was investigated in glycerol-induced AKI mice.

Results: 1. Characterizations of Por-Ru nanozyme: The SEM image showed the Por-Ru nanozyme was spherical with an average diameter of 6-8 nm (Figure 1a). Meanwhile, the XPS revealed the presence of Ru and showed the detailed elemental components (Figure 1b). As shown in Figures 1c and d, the Por-Ru nanozyme had excellent CAT-like and SOD-like capabilities. Furthermore, the DPPH• assay confirmed the antioxidant property (Figure 1e). 2. Protective effect of Por-Ru nanozyme in vitro and in vivo: The results of cell counting kit-8 assay showed that Por-Ru nanozyme was not cytotoxic to TCMK-1 cells at concentrations ranging from 10 to 100 μg/mL. We further examined the cytoprotective effects of Por-Ru nanozyme against ROS damage. The flow cytometry results showed that the intracellular ROS level increased after treatment with H2O2, while the ROS level obviously decreased with the addition of Por-Ru nanozyme (Figure 2a, b). The protective effect of Por-Ru nanozyme against H2O2-induced apoptosis was also investigated. As shown in Figures 2c and d, the rate of cell apoptosis was significantly reduced with the addition of Por-Ru nanozyme. Before the in vivo experiments, the haemolysis assay (Figure 2c, d) showed that the Por-Ru nanozyme was synthesized to be less than 5% even at a dose of 200 μg/mL. Additionally, the in vivo toxicity assessment showed that Por-Ru nanozyme at test concentrations had no noticeable impacts on blood parameters, liver and kidney functions, and histopathology of major organs in normal mice. Then, we tested the therapeutic effect of Por-Ru nanozyme in AKI mice. As shown in Figures 2e and f, the CRE and blood urea nitrogen (BUN) levels of AKI mice treated with Por-Ru nanozyme were significantly lower than those of AKI mice group. Additionally, the results of haematoxylin and eosin (H&E) staining showed that many casts (marked as triangles) were observed in the kidney tissue of AKI mice, whereas no obvious damage area was found in AKI mice after the treatment of Por-Ru nanozyme.

Conclusion: Our findings demonstrate that the Por-Ru nanozyme has excellent anti-ROS enzyme-mimicking capabilities. In vitro experiments revealed that Por-Ru nanozyme alleviated ROS-induced cell apoptosis. In AKI mice, Por-Ru nanozyme effectively improved renal function and attenuated renal tissue damage. Taken together, Por-Ru nanozyme may become a novel agent for AKI treatment.
RIPK3 MEDIATES KIDNEY INJURY INDUCED BY A CYTOKINE STORM
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Background and Aims: Receptor-interacting protein kinase 3 (RIPK3) is traditionally involved in necroptosis, a regulated necrosis pathway which has been observed in diseases associated to cell death and inflammation. However, RIPK3 has been also associated to inflammatory responses independent of necroptosis. In previous studies we demonstrated that RIPK3 deficiency does not prevent renal injury but protects from inflammation in folic acid-induced AKI (FA-AKI), suggesting a proinflammatory role independently of cell death. In the present work, we aim to explore the role of RIPK3 in kidney injury and inflammation induced by a cytokine storm.

Method: Lipopolysaccharide (LPS) was used to induce cytokine storm-AKI in mice. For this, female 12- to 14-week-old wild type (WT), RIPK3-KO, MLKL-KO or NRLP3-KO C57BL/6J mice received a single intraperitoneal (i.p) injection of LPS 5 mg/kg or vehicle and were sacrificed 1h, 4h and 24 hours later. To generate chimera mice, WT and Ripk3-KO receptor mice were irradiated to deplete the autologous bone marrow (BM). BM was extracted from the femur and tibia of donor WT or Ripk3-KO mice, and 10^7 cells were transferred to irradiated receptor mice by intravenous injection. After 1 month, LPS-AKI was induced. Plasma was collected to assess kidney function. Kidneys were collected for RNA, protein studies, and histologic studies. Additionally, a WT group received 1.65 mg/kg of the necroptosis inhibitor Necrostatin-1 (Nec1) i.p. prior to LPS to evaluate the impact of necroptosis pathway. Liver, lungs and heart were also collected to assess the systemic inflammatory response. Additionally, cultured murine immortalized tubular MCT cells, and primary tubular cells, bone marrow dendritic cells (BMDC) and bone marrow derived macrophages (BMDM) isolated from WT and Ripk3-KO mice were studied. Cells were stimulated with 100 ng/ml LPS for 6h and RNA was studied. To analyze the impact of the inflammatory response on tubular cells, supernatants from LPS-stimulated BMDM and BMDC were collected and used to stimulate MCT cells. RNA expression was studied by RT-PCR and protein expression by Western Blotting.

Results: The kidney expression of RIPK3 mRNA and protein was upregulated in cytokine storm-AKI in mice, while Ripk3 deficiency improved survival and renal function, with less expression of proinflammatory cytokines and inflammatory infiltrate. Necroptosis did not seem to be implicated in cytokine storm-AKI, since neither Nec1 nor genetic MLKL ablation offered protection on renal function. Systemic inflammation in non-kidney organs was also milder with Ripk3 deficiency. In addition, inflammasome-related proteins were upregulated in cytokine storm-AKI, and this was reduced in Ripk3-KO mice. However, Nlrp3 deficient mice developed kidney injury and inflammation after LPS injection. Next, we explored the role of RIPK3 in BM-derived cells in cytokine storm-AKI by generating chimera mice. In this context, WT mice with Ripk3 deficient BM exhibited less inflammation and better renal function. This supports that RIPK3 from BM cells mediates kidney inflammation and injury during cytokine storm-AKI. In cultured cells, LPS induced RIPK3 expression in BMDMs but not in tubular cells, and RIPK3 mediated IL-6 expression in BMDMs but not in tubular cells. Moreover, IL-6 and conditioned media from LPS-exposed WT macrophages promoted proinflammatory responses in cultured tubular cells, that was partially ameliorated for RIPK3-KO LPS-macrophage conditioned medium.

Conclusion: In conclusion, RIPK3 mediates kidney injury and systemic inflammation induced by a cytokine storm independently of the necroptosis pathway. These results identify RIPK3 as a therapeutic target for renal inflammatory diseases.
Background and Aims: Direct tubular injury caused by several medications, especially chemotherapeutic drugs, is a common cause of AKI. Inhibition or loss of cyclin-dependent kinase 12 (CDK12) triggers a transcriptional elongation defect that results in deficiencies in DNA damage repair, producing genomic instability in a variety of cancers. Notably, 10-25% of individuals developed AKI after treatment with a CDK12 inhibitor, and the potential mechanism is not well understood.

Method: Here, we established a cisplatin-induced AKI mouse model with CDK12 knockdown mice and created stable in vitro models with CDK12 knockdown tubular epithelial cells. Cisplatin nephrotoxicity was induced by intraperitoneal injection of cisplatin (20 mg/kg). After 2 days following cisplatin treatment, blood and kidney tissues were harvested. Renal function and histology were evaluated. DDR, tubular apoptosis, cell proliferation were evaluated by immunofluorescence assays, real-time PCR, flow cytometer and western blot analysis. Notably, we performed single-molecule real-time sequencing (SMRT), a long-read sequencing platform, to identify the formation of novel transcripts involved in the above events.

Results: We found that CDK12 was downregulated in the renal tubular epithelial cells in both patients with AKI and murine AKI models. Moreover, tubular cell-specific knockdown of CDK12 in mice enhanced cisplatin-induced AKI through promotion of genome instability, apoptosis, and proliferative inhibition, whereas CDK12 overexpression protected against AKI. Using the single molecule real-time (SMRT) platform on the kidneys of CDK12\textsuperscript{RTEC−/−} mice, we found that CDK12 knockdown targeted Fgf1 and Cast through transcriptional elongation defects, thereby enhancing genome instability and apoptosis.

Conclusion: These data demonstrated that CDK12 knockdown could potentiate the development of AKI by altering the transcriptional elongation
Figure 2: Schematic illustration of the mechanism by which CDK12 knockdown aggravates cisplatin-induced AKI. In cisplatin-induced AKI, CDK12 knockdown could lead to DNA damage, apoptosis and abrogate cell proliferation via transcriptional elongation defects in Fgf1 and Cast.

defect of the Fgf1 and Cast genes, and more attention should be given to patients treated with CDK12 inhibitors to prevent AKI.

#6315
CHARACTERIZATION OF BRAIN DAMAGE AFTER ACUTE KIDNEY INJURY
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Background and Aims: Acute kidney injury (AKI) is a very common condition in inpatients. Severe AKI is frequently associated with by neurological disorders such as confusion, the mechanisms of which are poorly understood. We have shown in several animal models that chronic kidney disease is associated with impaired cognitive performance such as memory and increased permeability of the blood-brain barrier (BBB), related to the accumulation of uremic toxin indoxyl sulfate. The goal of these experiments was to highlight the influence of AKI on cerebral impairment in mice, particularly the BBB permeability, and to describe the mechanisms involved.

Method: We performed an AKI in C57/B6 WT mice, by unilateral nephrectomy and transient ischemia-reperfusion of the remaining kidney for 20 minutes (RIRI20 group) and compared them to two other groups: control mice and mice with unilateral ischemia-reperfusion without nephrectomy (IR20). Modified neurological severity score (mNSS) was performed daily. BBB permeability was assessed by quantification of the Evans Blue leakage in the brain and by cerebral 68Ga-DTPA TEP/CT imaging. Cerebral immunohistochemistry was performed to evaluate the neuro-inflammatory processes.

Results: Glomerular filtration rate at Day 1 was lower in AKI group compared to the control group 0.21 ± 0.26 vs. 0.94 ± 0.13 mL/min/100g b.w (p < 0.0001) and IR group: 0.75 ± 0.17 mL/min/100g b.w (p = 0.0007). Mice with AKI displayed a neurological impairment at day 1 and day 2 post-AKI, compared to control mice and IR20 mice, with mainly an impairment of the balance. Mean mNSS score at Day 1 was 2.6 ± 4.5 in AKI group, and 0.0 ± 0.0 in both the control and IR groups (p = 0.002). BBB permeability at Day 2 was higher in the AKI group than in the control group (p = 0.10) and the IR group (p = 0.0006) by Evans blue staining. Cerebral TEP imaging found similar results with increased BBB permeability in AKI mice to compared to control mice at D1 and D2 (p = 0.004 and p = 0.009, respectively). On immunohistochemistry, brains of mice after AKI displayed more astrocytosis and microglial activation compared to brains of control mice.

Conclusion: AKI in mice is specifically associated with early neurological damage, unlike renal ischemia-reperfusion alone, related to a BBB disruption in the first two days after AKI. AKI appears to induce astrocytosis and altered microglial phenotype, potentially due to increased neuroinflammatory processes following BBB disruption.
**Abstracts**

**#6693**

**INCREASED INFLTRATION OF LRG1+VCAN+LY6CHIGH MACROPHAGES ARE ESSENTIAL CONTRIBUTORS TO KIDNEY INJURY IN ADR MICE**

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**Background and Aims:** The ADR mouse model is a well-established rodent model for FSGS that can manifest with albuminuria. Resident macrophages are present in the tubulointerstitium of the kidney, and circulating macrophages can be recruited to the kidney in disease states. However, the presence of macrophages in glomeruli and the role of macrophages in podocyte injury in ADR mouse models remain unknown.

**Method:** Single-cell RNA sequencing comprehensively characterized the expression of macrophages in mice glomeruli. Eight-week-old male BALB/c mice were used to induce ADR model. Immunofluorescence was used to detect the changes of renal macrophages after injected with ADR at different time points. Transwell co-culture system were used to detect the effect of Lrg1+ Vcan+ Ly6Chigh macrophages on MPCS. HCH6-1, the FPR1 inhibitor were used to restrain ANXA1-FPR1 pathway.

**Results:** Totally 506 macrophages were sequenced and Lrg1Vcan Ly6Chigh macrophages were significantly increased in ADR induced nephrotic mice glomeruli (P < 0.01). The ligand receptor relationship between podocytes and macrophages were changed (P < 0.01, means±SD). Immunofluorescence demonstrated that macrophages are present in ADR glomeruli (P < 0.05). However, the temporal and spatial changes of macrophages in ADR glomeruli still need to be proved by further experiments. After co-culture of Lrg1Vcan Ly6Chigh macrophages and MPCS, the expression of nephrin in MPCS decreased (P < 0.05), which proved that macrophages can cause podocyte injury in ADR glomeruli. The ANXA1-FPR1 signaling pathway was activated and renal Lrg1 Vcan Ly6Chigh macrophage infiltration, albuminuria and renal injury were reduced in ADR+HCH6-1 group (all P < 0.05).

**Conclusion:** Lrg1 Vcan Ly6Chigh macrophages are recruited into glomeruli by activation of ANXA1-FPR1 signaling pathway and cause the damage of podocyte.

**#4662**

**MSC-DERIVED EXOSOMES PREVENT PERITONEAL FIBROBLAST TRANSDIFFERENTIATION IN PERITONEAL DIALYSIS-ASSOCIATED PERITONEAL FIBROSIS**

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**Background and Aims:** Peritoneal dialysis (PD) as a long-term renal replacement therapy is limited by peritoneal fibrosis. The purpose of our study was to identify the mechanism of mesenchymal stem cell-derived exosomes (MSC-Exos) in regulating the transdifferentiation of fibroblasts (FBs) to myofibroblasts (MFBS) in peritoneal dialysis-associated peritoneal fibrosis.

**Method:** The experimental mice were divided into 3 groups according to treatment: control group (Saline), peritoneal injury group (2.5% glucose peritoneal dialysate + LPS), and exosome group (2.5% glucose peritoneal dialysate + LPS + MSC-Exos). After six weeks of modeling, the parietal peritoneum was collected for histological analyses and transcriptomic analysis. We also verified the effects of MSC-Exos on fibroblasts in vitro and in vivo experiments referred to immunofluorescence, quantitative real-time RT–PCR assay, and western blotting analysis.

**Results:** First, tracing study of Dil-labeled exosome showed that exosomes can enter peritoneal tissue and peritoneal cells in vivo and in vitro. Our studies have found that MSC-Exos can alleviate peritoneal fibrosis in peritoneal injury mouse model. MSC-Exos treatment significantly decreased the expression of mouse peritoneal MFBS markers (α-SMA), while maintaining the phenotype of fibroblasts (Collagen I), indicating that MSC-Exos might inhibit the transdifferentiation of FBs to MFBS. The in vitro results further confirmed these findings. So we supported that MSC-Exos could alleviate peritoneal fibrosis by inhibiting the transdifferentiation of FBs into MFBS. Transcriptomic analysis results revealed that SPIC gene which is related to cell differentiation ranked first in the differential expression genes. The expression of Spi-C was significantly increased in peritoneal injury group, while were significantly down-regulated in MSC-Exos group. The results showed that Spi-C overexpression or knockdown had no significant impact in MSC-Exos group, while the transdifferentiation of FBs into MFBS greatly increased with Spi-C overexpression and significantly decreased with Spi-C knockdown in peritoneal injury group. The results indicated that Spi-C might be a critical molecule to promote peritoneal FBs to differentiate into MFBS in peritoneal injury models. Moreover, the mRNA sequencing results showed that miR-34b-3p is one of the main components of MSC-Exos, and it can specifically bind to SPIC gene sequence. The dual-luciferase reporter assay revealed that miR-34b-3p mimic significantly reduced the luciferase activity of Spi-C reporter. And miR-34b-3p mimics could down-regulate the expression of Spi-C, and the expression of Spi-C was not affected after miR-34b-3p inhibitor intervention. The above results suggested that MSC-Exos-derived miR-34b-3p could inhibit the transdifferentiation of FBs into MFBS by targeting Spi-C.

**Conclusion:** MSC-Exos-derived miR-34b-3p targeting Spi-C can alleviate peritoneal fibrosis by inhibiting the differentiation of subperitoneal mesothelial FBs in MFBS.

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**#3137**

**GASDERMIN D DRIVES THROMBOTIC ANGIOPATHY-RELATED AKI BY ACCELERATING IMMUNOTHROMBOSIS AS WELL AS NEUTROPHIL-MEDIATED NECROINFLAMMATION AND INFARCTION**

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**Background:** Thrombotic microangiopathy (TMA) is a life-threatening complication in glomerulonephritis and immune mediated glomerular diseases. It is characterized by the formation of complement-coated platelet-fibrin thrombi, which induce tissue damage and organ failure.

**Method:** We investigated the role of Gasdermin D (GSDMD) in thrombotic microangiopathy-induced AKI using a mouse model of DcR2 knockout mice, compared with the wild group, there was no significant difference in the level of histone lactylation, while peritoneal thickness and the expression of markers of fibrosis markers (α-SMA, Collagen I, and Fibronectin) were significantly reduced.

**Conclusion:** Histone lactylation leads to peritoneal fibrosis induced by high glucose peritoneal dialysate by promoting PMSCs senescence. Histone lactylation may be a vital mechanism of peritoneal dialysis-related peritoneal fibrosis.

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**#4645**

**HISTONE LACTYLATION ENHANCES PERITONEAL FIBROSIS BY INDUCING PERITONEAL MESOTHELIAL CELL SENESCENCE**

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**Background and Aims:** Peritoneal fibrosis (PF) is a serious complication limiting the application of peritoneal dialysis (PD). Histone lactylation has been recently found to increase with glycosylation and intracellular lactate levels, thereby mediating chronic organ damage. This study investigated the role and mechanism of histone lactylation in high glucose peritoneal dialysate-induced peritoneal fibrosis in mice.

**Method:** The PF mouse model induced by high glucose peritoneal dialysate was constructed by daily intraperitoneal injection of 4.25% glucose peritoneal dialysate combined with 40 mM Methylglyoxal for 2 weeks. We also used a lactylation enhancer (rotenone) and a lactylation inhibitor (oxamate) to limit the application of peritoneal dialysis (PD). Histone lactylation has been found to increase with glycosylation and intracellular lactate levels, thereby mediating chronic organ damage. This study investigated the role and mechanism of histone lactylation in high glucose peritoneal dialysate-induced peritoneal fibrosis in mice.

**Results:** In the PF group, the results of Masson staining and immunohistochemistry revealed increased peritoneal thickness and expression of fibrosis markers (α-SMA, Collagen I, and Fibronectin) and senescence markers (P16, P21, and DcR2) compared to the control group. We found that lactate and glycosylation levels were significantly higher in the PF group compared to the control group, and further immunoprecipitation results also showed enhanced levels of histone lactylation modifications in the PF group. We further found that the 101/1 of lactylation modification of H3K18a site increased significantly, suggesting that H3K18a site may play an important role in promoting PF. Similarly, in vitro, we verified that peritoneal mesothelial cells (PMCS) exhibited increased levels of lactate and lactylation in response to stimulation by high glucose, while we found an increasing expression of cell senescence phenotype (P16, P21, and DcR2) and senescence-associated cytokines secretion (IL-1β, IL-6, and TNF-α). By enhancing or inhibiting lactylation, we found that PMCS senescence was significantly enhanced in the lactylation-enhanced group, while the lactylation-inhibited group alleviated PF. Senescence induced by high glucose peritoneal dialysate. In the PF model of DcR2 knockout mice, compared with the wild group, there was no significant difference in the level of histone lactylation, while peritoneal thickness and the expression of markers of fibrosis markers (α-SMA, Collagen I, and Fibronectin) were significantly reduced.

**Conclusion:** Histone lactylation leads to peritoneal fibrosis induced by high glucose peritoneal dialysate by promoting PMSCs senescence. Histone lactylation may be a vital mechanism of peritoneal dialysis-related peritoneal fibrosis.
Background and Aims: Cholesterol crystal embolism (CCE) is a life-threatening complication of advanced atherosclerosis, in which CC can trigger clot formation, arterial occlusion, acute kidney injury (AKI), and ischemic infarction. Neutrophils play a role in this process by driving arterial crystalline immunothrombosis and undergoing regulated necrosis in necroinflammation surrounding ischemic kidney infarcts. In this study, we hypothesized that Gasdermin D (GSDMD) contributes to the pathogenesis of CCE by amplifying these processes.

Method: We injected CC (20 mg/kg) into the left kidney artery of wildtype (WT) or Gsdmd-knockout (KO) mice to induce CCE. The mice were sacrificed after 24 hours. Kidney injury was assessed through glomerular filtration rate (GFR), histological analysis using periodic acid-Schiff and TUNEL staining as well as assessment of infarct size and arterial obstruction via triphenyltetrazolium chloride and alpha-smooth muscle actin/fibrin staining, respectively. Neutrophils (Ly6G+) and mature neutrophils (Ly6G+ CD101+) were analyzed in several organs by flow cytometry. The presence of neutrophil extracellular traps (NETs) in kidney was evaluated by staining for citrullinated histone 3 (CitH3) and flow cytometry analysis of Ly6G+ CitH3+ neutrophils. Interventional studies using disulfiram, a GSDMD inhibitor, administered via intraperitoneal injection (50 mg/kg) to WT mice either 4 hours prior or 3 hours following CCE induction, followed by sacrifice and analysis after 24 hours. In vitro, healthy human neutrophils were stimulated with CC in the presence or absence of pretreatment with disulfiram, and the levels of IL-1 beta and lactate dehydrogenase (LDH) were evaluated in the culture supernatant.

Results: WT CCE kidneys showed increased expression of Gsdmd in peritubular cells as determined by immunohistochemical analysis, as well as an increased expression of cleaved Gsdmd by immunoblot analysis compared to WT control kidneys. Baseline levels of GFR and the number of both total and mature neutrophils were comparable in both groups under normal conditions. Compared to WT mice, Gsdmd-KO mice were partially protected from sudden GFR decline, tubular injury, kidney cell death, and kidney infarction following CCE. Arterial obstruction was significantly reduced in Gsdmd-KO mice following CCE. Gasdermin-deiciency reduced the number of mature neutrophils in bone marrow, spleen, and blood in comparison to WT mice. The amount of NETs in kidney exhibited a significant reduction in Gsdmd-KO mice. Consistently, preemptive and therapeutic treatment with disulfiram significantly reduced sudden GFR decline and kidney infarct size in WT mice compared to vehicle-treated controls. Blood and kidney neutrophils, as well as blood and kidney NETs were significantly reduced in WT CCE mice with disulfiram preemptive and therapeutic treatment in comparison to respective vehicle controls. In vitro, CC induced the release of IL-1beta and LDH from healthy human neutrophils, which disulfiram suppressed in a dose-dependent manner.

Conclusion: The deficiency and pharmacological inhibition of GSDMD alleviate crystal clot formation, AKI, and ischemic infarct growth following CCE via suppressing neutrophil recruitment, maturation, and NET formation. Thus, neutrophils significantly contribute to immunothrombosis and ischemic kidney infarction.

#3220
Z-DNA BINDING PROTEIN 1 AGGRAVATED THE SEPSIS-INDUCED ACUTE KIDNEY INJURY VIA PANOPTOSIS
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Background and Aims: Sepsis-induced acute kidney injury (SI-AKI) is a severe complication of critical patients with high morbidity and mortality. Apoptosis, pyroptosis, and necroptosis, regulated by a common pathway - PANoptosis, play essential roles in SI-AKI without the clarified mechanisms.

Method: We first established the SI-AKI model by intraperitoneal injection of the lipopolysaccharide (LPS) (O111:B4) in the C57B/L6J mice with increased Serum creatinine (Scr), blood urea nitrogen (BUN), and kidney injury biomarkers (NGAL, KIM-1) in renal tissue. The expression of crucial molecules in PANoptosis were examined by quantitative real-time PCR (qPCR) and Western blotting. RIPK1 inhibitor-necrostatin-1 (Nec-1) (1.65mg/kg) and pan-caspase inhibitor- Emricasan (10mg/kg) were further employed to mice with LPS. Potential interacting proteins of panoptosome were detected by co-immunoprecipitation. We also analyzed the methylation level of ZBP1 in cell-free DNA among sepsis-non-AKI and SI-AKI patients.

Results: The expression of crucial molecules in PANoptosis, including IL-1beta, mixed lineage kinase domain-like (MLKL) (0.67 vs. 0.41, P = 0.014), protein kinase 1 (RIPK1) (1.07 vs. 0.72, P = 0.002), cleaved-caspase 3 (1.13 vs. 0.59, P < 0.001), and FAS-associated death domain protein (FADD) (0.78 vs. 0.43 P < 0.001) elevated in the SI-AKI group. Z-DNA binding protein 1 (ZBP1), a typical sensor of PANoptosis, is dramatically activated in the SI-AKI mice. Co-immunoprecipitation showed that caspase 8, ZBP1, peptidoglycan recognition protein 1 (pglyrp1), and RIPK1 are potential components of PANoptosome. Nec-1 and Emricasan could attenuate the LPS-induced increases in the concentrations of BUN and inflammatory cytokine (TNF-a and IL-6), as well as the methylation level of ZBP1 in cell-free DNA decreased in SI-AKI patients versus sepsis-none-AKI (P = 1.60E-06).

Conclusion: ZBP1 exacerbated SI-AKI via activating PANoptosis with the potential PANoptosome of ZBP1, caspase 8, pglyrp1, and RIPK1.
PERICYTE AND CXCL12 PLAY CRUCIAL ROLE IN THE RECOVERY OF ACUTE KIDNEY INJURY
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Background and Aims: Pericytes are mesenchyme-derived perivascular cells attached to the abluminal surface of capillaries as well as the major origin of myofibroblasts in the animal model of unilateral ureteral obstruction (UOO) and ischemia-reperfusion injury (IRI). Although previous studies reported that myofibroblasts may be beneficial during acute kidney injury (AKI) via growth factor secretion, reconstitution and stabilization of the collagen framework for tubular cell regeneration, lack of solid evidence and definite mechanism make the role of pericyte/myofibroblast in AKI remain controversial.

Method: To clarify this, we used platelet-derived growth factor receptor β (PDGFRβ)-specific antibody following AKI in C57BL/6 mice to inhibit pericytes. In the meantime, We used Gli1-CreERT2;Cxcl12fl/fl genetically modified mice to conditionally knockout CXCL12 specifically in pericytes before IRI.

Results: The expression of PDGFRβ on pericytes increased after IRI. In group of administration of PDGFRβ antibody, proliferation and transition to myofibroblasts of pericytes were inhibited. Inflammation became worse and renal recovery was impeded after AKI. The chemokine stromal cell-derived factor-1 (SDF-1) which is also known as the C-X-C-type chemokine CXCL12 decreased as well. Furthermore, we demonstrated that CXCL12 was secreted mainly by pericytes and its receptor CXCR4 was expressed on tubular cell during IRI by in situ hybridization. When knockout of CXCL12 was performed before IRI, the renal microvascular rarefaction was noted after AKI and the recovery of renal function was impaired. Renal tubular cell proliferation decreased and apoptosis increased as well.

Conclusion: In summary, these findings demonstrated that pericytes contribute to renal repair after IRI through CXCL12 secretion.
Figure 1: Anti-PDGFβ Ab inhibited pericyte–myofibroblast transition and tubular regeneration after IRI. (A) Representative images showed αSMA+ cells of the kidneys at day 5 after IRI with or without anti-PDGFβ antibody administration. Bar chart showed the numbers of αSMA+ cells. (B) Representative images showed Ki67+ cells of the kidneys at day 5 after IRI with or without anti-PDGFβ antibody administration. Bar chart showed the numbers of Ki67+ cells. Scale bar, 50 μm. Original magnification ×200. n = 5 for each group. Data were expressed as the mean ± SEM. *P < 0.05, **P < 0.01, ***P < 0.001 by Student’s t-test.

#5715
IMMUNE LANDSCAPING IN RHABDOMYOLYSIS INDUCED ACUTE KIDNEY INJURY IDENTIFIES SENESCENCE AS A POTENTIAL TARGET
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Background and Aims: Worldwide, acute kidney injury (AKI) has an incidence of 13.3 million cases per year leading to 1.7 million deaths. Rhabdomyolysis (RM) accounts for 10% of the AKI cases, and frequently occurs due to falling (often in elderly), crush syndrome or exposure to drugs. By causing skeletal muscle damage, RM leads to a release of muscle contents such as myoglobin into the circulatory system and trigger renal sterile inflammation. The role of macrophages in driving inflammatory phase of RM-AKI lesions and fibrosis-related prognosis has been reported but both the role of other immune cells and the macrophage heterogeneity in RM-AKI still lack detail. The aim of this study was to describe renal immune cell recruitment and more specifically the mononuclear phagocytic cell (MPC) population (macrophages, monocytes and dendritic cells) during RM-AKI through single cell RNA sequencing (scRNA-seq) in mice.
Method: Two-month-old C57BL/6J male mice were administered intramuscularly saline (control) or 50% glycerol for induction of RM. Forty-eight hours later mice were sacrificed, kidneys were collected and dissociated and CD45 live cells were sorted. Single cell cDNA libraries were prepared, and sequencing was performed according to the 10X Genomics protocol. Creatinine phosphokinase and blood urea nitrogen were quantified to validate muscle injury and renal function respectively. A combination treatment of dasatinib and quercetin (DQ) protocol was performed according to the 10X Genomics protocol. Creatinine phosphokinase and blood urea nitrogen were quantified to validate muscle injury and renal function respectively. A combination treatment of dasatinib and quercetin (DQ) protocol was performed with and without RM-AKI.
Results: scRNA-seq of CD45+ renal cells revealed the existence of 7 immune cell clusters with macrophages and monocytes as the most highly recruited cells in RM-AKI condition, indicating a major change in the MPC population. Specific clustering of MPCs divulged 10 clusters (8 macrophages, 1 monocyte and 1 dendritic cell cluster) revealing a higher heterogeneity of this population compared to what was previously observed by flow cytometry. Trajectory, pseudotime and KEGG pathway enrichment analyses disclosed a unique cluster highly expressing Stat5b and present in both control and RM-AKI condition where 164 cells were observed in control condition which expanded to 333 cells in RM-AKI condition. This unique cluster was characterized by a bimodal expression of MHCIImarkers and a downregulation after RM-AKI suggesting a transcriptional reprogramming. Cellular senescence was observed to be a predominant pathway in this unique cluster. Senolytics were identified as a possible pharmacological target based on pathway analysis. DQ protocol accompanied with an improvement of kidney function as well as an attenuation of MPC phenotypic modifications.
Conclusion: This study revealed the MPC diversity in RM-AKI through immune landscaping, trajectory and pathways in RM-AKI in mice. A unique cluster associated with possible reprogramming of macrophages was identified. Senolytics were established as a potential nephroprotective strategy in RM-AKI.

#5330
CYCLIN D1 AMELIORATES ISCHEMIA/REPERFUSION-INDUCED ACUTE KIDNEY INJURY
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Background and Aims: Acute kidney injury (AKI) is a life-threatening condition. The absence of oxygen during the acute ischemic phase would disturb energy metabolism and cause kidney tubular epithelial cell damage. Fatty Acid Oxidation (FAO) is the main source of energy production of renal proximal tubular epithelial cells. Timely promoting FAO, increasing supplies of energy, and promoting cell proliferation are essential to improve kidney injury, but there is no clinically recognized effective treatment for this. Cyclin D1 (CCND1), a member of the cell cycle family, plays a vital role in cell proliferation. Our previous study found that CCND1 improved AKI accompanied with increased fatty acid oxidation. Therefore, we investigated the role and molecular basis for CCND1 involvement in fatty acid oxidation of AKI.
Method: CCND1 was evaluated in AKI in human kidney proximal tubular epithelial cells (HK-2 cells) and male C57BL/6j mice (wild type). The protective role of CCND1 in AKI was investigated in a mouse model of ischemia-reperfusion AKI treated by ultrasound-microbubble-mediated kidney-specifically transferring CCND1-expressing plasmids in male C57BL/6j mice (wild type). Eight-week-old male C57BL/6j mice (wild type) were subjected to bilateral renal artery occlusion for 30min followed by 24h of reperfusion. We evaluated FAO, proliferation, and autophagy in vitro
and in vivo. In addition, we evaluated the concentrations of blood urea nitrogen and creatinine, evaluated kidney ultrastructure and so on.

**Results:** In vivo studies had shown that activation of CCND1 can prevent AKI-induced lipid accumulation, kidney tubule injury and kidney function declined after ischemia-reperfusion injury. Compared to test control, the treatment significantly (p < 0.05) lowered the concentrations of blood urea nitrogen and creatinine. Kidney specific overexpression of CCND1 promoted FAO, promoted proliferation and reduced apoptosis. Mechanistically, CCND1 activated the AMPK pathway, which increased the expression of phosphorylation AMP activated protein kinase (p-AMPK) and upregulated FAO. On the contrary, inhibiting the expression of CCND1 exacerbated impairment of FAO and disturbed energy metabolism.

**Conclusion:** Thus, CCND1 improved FAO and reduced lipid accumulation via active AMPK pathway in kidney proximal tubular epithelial cells (PTECs). Hence, reconstruction of the expression of CCND1 may be a novel therapeutic strategy for treating AKI.

![Figure 1: Cyclin D1 ameliorates acute kidney injury by improving fatty acid oxidation.](image)

Eight-week-old male C57BL/6J mice (wild type) were subjected to bilateral renal artery occlusion for 30min followed by 24h of reperfusion to investigate the effect of Cyclin D1 in ischemia/reperfusion-induced acute kidney injury. (a) Western blot analysis of kidney injury molecule (KIM-1), proliferating cell nuclear antigen (PCNA), Cyclin D1 (CCND1), phosphorylation AMP activated protein kinase (p-AMPK), AMP-activated protein kinase (AMPK), peroxisome proliferator activated receptor-α (PPAR-α) in the kidneys (n = 3). β-Actin was used as the loading control. (b) Blood urea nitrogen (BUN) and creatinine (Cr) concentrations were measured in WT mice. (c) Representative images of periodic acid-schiff (PAS) staining. Representative images of immunohistochemistry staining of Cyclin D1 (CCND1) and kidney injury molecule (KIM-1). Representative images of immunofluorescent staining were used to evaluate the expression of proliferating cell nuclear antigen (PCNA; green) and 5′-bromo-2′-deoxyuridine (BrdU; green) in the kidneys. Representative images of Oil red O (ORO) staining.
MAGNESIUM DEFICIENCY ABROGATES THE RENOPROTECTIVE EFFECT OF DPP-4 INHIBITOR ON CISPLATIN-INDUCED KIDNEY INJURY

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Background and Aims: Cisplatin is an effective chemotherapeutic agent, but often induces acute kidney injury (AKI). Magnesium (Mg) deficiency is often found in cancer patients, and the nephrotoxicity of cisplatin is exacerbated under Mg deficiency [1]. We previously reported the potential of Dipeptidyl peptidase-4 (DPP-4) inhibitor to attenuate cisplatin nephrotoxicity in rats and diabetic cancer patients [2, 3]. However, it remains to be investigated whether DPP-4 inhibitor can preserve its renoprotective effect under Mg deficiency. The purpose of this study was to examine whether DPP-4 inhibitor can prevent cisplatin-induced AKI even under Mg deficiency.

Method: Sprague Dawley rats received Mg-deficient diet for 7 days to induce Mg deficiency. AKI was induced in rats by injecting cisplatin intravenously. Oral administration of a DPP-4 inhibitor, once a day, was started 1 day before injecting cisplatin. Mg sulfate was once injected intraperitoneally just before injecting cisplatin to correct Mg deficiency (Fig. 1A). By using our previous cohort data [3], we divided diabetic cancer patients treated with high-dose cisplatin (> 50 mg/m2)-containing regimens into 4 groups according to the use/unused of Mg sulfate or DPP-4 inhibitor. The change of estimated glomerular filtration rate (eGFR) within 2 weeks after cisplatin treatment was compared between the groups.

Results: At the peak of AKI (day 5), Mg sulfate supplementation significantly attenuated the increase of blood urea nitrogen (BUN), and combination of Mg sulfate and DPP-4 inhibitor further suppressed the increase of BUN as compared to rats received only cisplatin. However, DPP-4 inhibitor alone did not attenuate the increase of BUN under Mg deficiency (Fig. 1B). The result of serum creatinine (sCr) was consistent with that of BUN (Fig. 1C). This effect was associated with a reduced renal cell death as evaluated with the terminal uridine nick-end labeling (TUNEL)+ cells (Fig. 1D). The change of eGFR was significantly less in the patients treated with both of DPP-4 inhibitors/Mg supplementation, compared to those without DPP-4 inhibitors/Mg supplementation. The effect was not found in patients with either DPP-4 inhibitor alone or Mg supplementation alone as compared to those without DPP-4 inhibitor/Mg supplementation (Fig. 2).

Conclusion: Our results suggested that Mg deficiency must be corrected to exert the renoprotective effect of DPP-4 inhibitor on cisplatin nephrotoxicity. The molecular mechanisms underlying this phenomenon remain to be defined.

REFERENCES
Gasdermin D is required for control of necroptotic cell death in AKI
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Background and Aims: Contradicting previous reasoning, it is now established that necrotic rather than apoptotic cell death pathophysiologically drives acute tubular necrosis during AKI. Whereas involvement of necroptosis and ferroptosis has been demonstrated by various groups, the role of pyroptosis, a highly immunogenic form of cell death requiring proteolytic activation of gasdermin protein family members, remains uncertain upon AKI. Thus, we aimed to investigate the role of pyroptosis and its mechanism of action in AKI.

Method: We set to detect gasdermin D (GSDMD) expression in murine renal samples after ischemia/reperfusion injury (AKI) by immunohistochemistry. Furthermore, we investigated GSDMD-deficient mice in IRI and cisplatin-induced AKI. To conclude on mechanisms, we isolated fresh murine renal tubules and measured LDH release over time. We generated MLKL/GSDMDdko mice to investigate the interplay of these caspase-dependent forms of regulated necrosis in AKI.

Results: After IRI, we detected a specific GSDMD signal in areas surrounding necrotic tubules, whereas no such signal could be detected within necrotic areas. Whereas interference with other forms of regulated necrosis leads to reduced injury, GSDMD-deficient mice demonstrated higher levels of serum creatinine and urea as well as more severe tubular injury compared to wildtypes. In line with the findings of immunohistochemistry, we only found GSDMD protein expression in whole kidney lysates but not isolated renal tubules; and no difference in spontaneous cell death propagation was detectable. Co-deletion of MLKL (effector protein of necroptosis) reversed the sensitization to AKI by GSDMD-deficiency. These results could be reproduced in cisplatin-induced AKI.

Conclusion: Here, we found an unexpected protective role for GSDMD, the effector protein of pyroptosis, in two different models of AKI. Mechanistically, our studies indicate the effect of GSDMD to function outside the tubular compartment, specifically surrounding areas of tubular necrosis. These infiltrating innate immune cells appear to interfere with tubular necroptosis in a non-cell autonomous manner. Alongside with these mechanistic insights, our data urge caution when inhibition of pyroptosis is therapeutically considered.

Identification of an Antibiotic-Treated Mouse Model to Study the Gut-Kidney Axis
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Background and Aims: Microbiota and its modulation could influence several physiological functions, and there is growing interest in it as a cutting-edge research topic in the field of renal diseases. According to the literature, germ-free (GF) mice are the gold-standard animal model for studying the correlation between the changing microbiota and the effects in the host. Unfortunately, their generation and maintenance are often unfeasible and costly, and the lack of microbiota could influence the circulating levels of amino acids, thus affecting kidney growth. This study aims to identify a more advantageous mouse model, specifically an antibiotic-treated one, that exhibits a strong reduction of the gut microbiota without compromising the kidney functionality.

Method: Five-six weeks old C57/BL6 male mice were randomly divided into 5 groups: Group 1 (Tr1) received a cocktail containing ampicillin, gentamicin, metronidazole, neomycin (1mg/mL each) and vancomycin (0.5 mg/mL) by oral gavage for 10 days; Group 2 (Tr2) received drinking water (DW) supplemented with ampicillin (1 mg/mL) neomycin (1 mg/mL), metronidazole (1 mg/mL) and vancomycin (0.5 mg/mL) for 14 days; Group 3 (Comb3) was treated with amphotericin-B (0.2 mg/mL) by oral gavage for 3 days followed by an antibiotic cocktail composed by vancomycin (10 mg/mL), neomycin (20 mg/mL), metronidazole (20 mg/mL) and amphotericin-B (1 mg/mL) administrated by oral gavage and ampicillin (1 mg/mL) provided in DW for 7 days; Group 4 (Comb4) was treated with a combination of ampicillin, neomycin, metronidazole and vancomycin (40mg/mL each) both by oral gavage and DW. Control Group (Ctr) received milliQ water only. Fecal DNA was used to assess the reduction of the intestinal microbiota by the 16S gene rRNA sequencing, and intestinal permeability was determined both in vivo by FITC-dextran and by measuring the expression of Zonulin-1 (ZO-1) on intestine sections. To verify the kidney integrity after treatment, renal morphology and fibrosis were evaluated by multiphoton microscopy, while transdermal measurement of GFR occurred by using MediBeacon device.

Results: Apart from Tr1, with the less percentage of microbiota depletion, the rest of antibiotics cocktails exhibited a significant microbiota reduction. Data regarding intestinal permeability in vivo by FITC-dextran were consistent with hematolysin-esin staining and revealed a reduced expression of ZO-1 in all antibiotics-treated groups versus Ctr, confirming that microbiota has been depleted as expected. In all the experimental groups, particularly Tr2, urine/serum parameters reestablished at Ctr levels after recovery and only Comb4 showed signs of fibrosis. The low intragroup variability and the homogeneous decrease of the most abundant phyla, as well as renal physiology evaluation, point to Tr2 as the most promising antibiotics cocktail among the tested ones.

Conclusion: The potential of our study lies in the feasibility to have a manageable mouse model to perform studies on the gut-kidney axis. In particular, it will be specifically used for the evaluation of fecal microbiota transplant (FMT) with feces of patients affected by kidney diseases, enabling us to determine whether intestinal dysbiosis may impair the kidney functionality. However, the characterized mouse model might be employed to assess the effect of the FMT from patients with renal pathologies not only on kidneys but also at systemic level.

The Molecular Effect of SGLT2i on the Autophagy Pathway in Type II Diabetes Mellitus and Its Vascular Complications
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Background and Aims: Type II Diabetes mellitus (T2DM) is a severe metabolic disorder characterized by chronic hyperglycemia and its subsequent glucose toxicity that lead to irreversible damages in several organs such as Diabetic Nephropathy (DN) [1]. Autophagy is involved in catabolic processes and plays a key role in the degradation of damaged intracellular proteins in order to maintain intracellular homeostasis and cell integrity. Studies showed that autophagy-related protein 5 (ATG5) and Light chain 3-II (LC3-II) play a critical role in a variety of disease processes, like DN [3]. Empagliflozin (EMPA)
Figure 1: Physiology. A. Weight, B. water intake, C. urine, D. Urine protein, E. Urine creatinine, F. Urine glucose. Con group (black columns), DM mice (red columns), DM+EMPA (blue columns). * P<0.05 vs. Con, ** P<0.01 vs. Con, *** P<0.001 vs. Con, $ P<0.05$ vs. DM+EMPA, $$ P<0.01$ vs. DM+EMPA, $$$ P<0.001$ vs. DM+EMPA, £££ P<0.001 vs. one month, † P<0.05 vs. BL, †† P<0.01 vs. BL, ††† P<0.001 vs. BL.

Figure 2: Renal ATG5, LC3-II and fibronectin expression in Con, DM and DM+EMPA mice. A, E and I. Representative renal IHC staining of ATG5, LC3-II and fibronectin, respectively (Magnification x20). B, F and J Quantification of ATG5, LC3-II and fibronectin, respectively IHC staining. C and G. Representative Western blots of ATG5 and LC3-II protein levels in renal lysates. D, H Quantification of Western blots. (Unpaired student’s t-tests, *P<0.05, **P<0.01, *** P<0.001).
is sodium glucose transporter inhibitor (SGLT2i) which represents a new class of glucose lowering drugs and is recommended in T2DM [4]. We hypothesized that EMPA effects renal integrity and function via the autophagy mechanism. The proposed research aim to investigate the molecular effect of SGLT2i on the expression of ATG5 and its downstream collaborator LC3-II in diabetic mice model [5].

Methods: 8-week-old male mice: C57BL/6 Wild Type (Con), BTBR ob/ob (DM) and BTBR ob/ob treated with EMPA (1mg/kg/day P.O.) (DM+EMPA) were followed for 12 consecutive weeks for their weight, blood glucose and subsequent DN. EMPA preserves ATG5/LC3-II expression with SGLT2i treatment. Studies to address DM and vascular complications by selective modulation of autophagy may be translated into clinical practice approach and may lead to further studies to address DM and vascular complications by selective modulation of ATG5/LC3-II expression with SGLT2i treatment.

Results: Blood glucose level in DM mice was higher than Con, and lower in DM+EMPA. DM+EMPA mice drunk, urinated more and exerted more glucose than DM mice, yet had less protein in their urine. WB and IHC analyses revealed that renal ATG5 and LC3-II levels were reduced in DM mice compared with Con and DM+EMPA mice. Fibronectin expression was increased in DM compared to Con mice, and DM+EMPA mice.

Conclusions: EMPA treatment preserved DM mice renal dysfunction. Our data suggest that there is a link between DM and ATG5/LC3-II dysregulation and subsequent DN. EMPA preserves ATG5/LC3-II in DM mice. Our findings may be translated into clinical practice approach and may lead to further studies to address DM and vascular complications by selective modulation of ATG5/LC3-II expression with SGLT2i treatment.

REFERENCES

#3581
ACSS2-INDUCED FATTY ACID SYNTHESIS PROMOTES NLRP3 INFLAMMAMOSE AND PYROPTOSIS OF RENAL TUBULAR CELLS IN SEPSIS-INDUCED ACUTE KIDNEY INJURY
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Background and Aims: Cellular fatty acid metabolism was supposed to be tightly associated with immune responses. Pyroptosis is a form of programmed cell death dependent on the NLRP3 inflammasome activation. Previous studies have revealed that acyl-CoA synthetase 2 (ACSS2) promoted fatty acid synthesis under metabolic stress. However, whether ACSS2-mediated fatty acid metabolism can regulate pyroptosis and inflammatory responses of renal tubular cells in AKI remain unclear.

Method: lipopolysaccharide (LPS) was intraperitoneally injected to establish the sepsis mouse model, and in vitro HK-2 cell culture model was achieved by LPS stimulation. HE and PAS staining were carried out to evaluate pathological injury of kidneys in mice. The renal tissue immunostaining was conducted to detect IL-1β expression and macrophage distribution in kidney tissues of mice. Gene expression of inflammatory factors was evaluated by real-time PCR. Western Blot was conducted to the activation of the NLRP3 pathway and pyroptosis in vivo and in vitro.

Results: Here, we demonstrated that the expression of ACSS2 was significantly increased in the renal epithelial cells of mice with Lipopolysaccharide (LPS)-induced AKI when compared to wild-type mice. ACSS2 regulates NLRP3-mediated caspase-1 activation and IL-1β production through the stimulation of fatty acid synthase (FASN) in renal epithelial cells. The deletion of ACSS2 attenuated renal tubular pathological injury and inflammatory cell infiltration in an LPS-induced mouse model. Consistently, ACSS2-deficient mice displayed impaired FASN-mediated lipid synthesis and decreased IL-1β production in response to the LPS challenge. In HK-2 cells, ACSS2 deficiency suppressed NLRP3-mediated caspase-1 activation and decreased fatty acid synthesis through the downregulation of FASN. The treatment with the chemical inhibitor C75 suppressed NLRP3-mediated caspase-1 activation and pyroptosis of HK-2 cells under LPS treatment in renal tubular cells.

Conclusion: Our results suggested that ACSS2 regulated the NLRP3 inflammasome activation and pyroptosis by inducing the FASN-mediated fatty acid synthesis pathway in renal epithelial cells. These results identified ACSS2 as a potential therapeutic target in AKI.

#5322
RENALE BERIC GYCOLYSIS AND LOCAL LACTATE PRODUCTION IN AKI
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Background and Aims: Kidney is a high energy-consuming organ depending on fatty acid β-oxidation (FAO) to fulfill energy supply. During various biological stresses in AKI, FAO shuts down, and the aerobic glycolysis is enhanced. In this study, we aimed to investigate the effect of aerobic glycolysis and local lactate production in AKI.

Methods & Results: A maleic acid (MA) induced AKI model (MA-AKI) was established by MA intraperitoneally (i.p.) in C57BL/6 mice and sacrificed after 24h. The renal function in MA-AKI mice was damaged, accompanied by proximal tubular injury and mitochondrial dysfunction. RNA sequencing revealed a relative increase in glycolytic enzymes (HK1, PKM and PFKP) mRNA levels in the AKI phase. The protein level of glycolysis-related enzymes was also elevated with increased urinary lactate significantly (0.25±0.10 versus 8.60±0.74 mmol/L, P<0.0001) in MA-AKI. Furthermore, glycolysis inhibitor 2-DG was administrated after 2h of MA injection, which improved the renal function (indicated by decreased serum creatinine (Scr), 33.52±2.78 versus 57.15±4.81 μmol/L, P<0.001), proximal tubular histopathological injuries and mitochondrial dysfunction in MA-AKI. Mechanistically, we observed a significant positive correlation between the Scr and urinary lactate levels (R² = 0.78, P < 0.0001). In order to examine the role of lactate in AKI, the mice were pretreated with oxamate, an inhibitor of lactate dehydrogenase A (LDHA), and the level of Scr (59.18±5.83 versus 28.82±3.41 μmol/L, P<0.0001) was mitigated, with the reduction of urinary lactate (8.60±0.74 versus 4.90±0.98 mmol/L, P<0.01).

Conclusion: Our study demonstrated that inhibition of aerobic glycolysis to protect kidney function in MA-AKI might be via reducing lactate accumulation.

#5878
PROTECTIVE EFFECTS OF VITAMIN D ON HYPERANDROGENEMIA-INDUCED-ACUTE KIDNEY INJURY THROUGH THE INTERACTION WITH THE RAS/INOS PATHWAY
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Background and Aims: The onset and development of metabolic abnormalities are closely related to polycystic ovary syndrome (PCOS). It has not yet been determined whether PCOS contributes to kidney injury, and the mechanism underlying the condition is not fully understood. Treatment with vitamin D has been shown to have beneficial effects on women with PCOS and renal disease. This study investigated the hypothesis that vitamin D supplementation exerts renoprotective effects via regulating the renin-angiotensin system (RAS)/inducible nitric oxide synthase (iNOS) pathway.

Method: Female Sprague-Dawley rats were randomly divided into five groups (n = 10): (a) control, (b) sham, (c) dehydroepiandrosterone (DHEA, 6 mg/100 g day-1 S.Q), (d) DHEA + vitamin D (1000 IU/Kg; 3 days/week), and (e) vitamin D. Plasma, ovary, and kidney levels of angiotensin-converting enzyme (ACE) activity was determined using FAPGG-based colorimetric method. The amount of NO was measured by determining the concentrations of nitrite and nitrate end products in the plasma and tissue samples using the Griess method. Histopathological changes in the ovary and kidney were also evaluated.

Results: Plasma testosterone increased in DHEA-treated rats compared with controls, indicating a hyperandrogenic state. Further, hyperandrogenemia-induced-acute kidney injury increased the plasma, renal, and ovarian angiotensin-converting enzyme (ACE) activities in association with elevations in the plasma and urine nitrate and nitrite levels; these changes were reversed by vitamin D treatment.

Conclusion: Hyperandrogenemia causes systemic abnormalities through RAS imbalance and NO metabolism disturbances, followed by apparent destruction of renal and ovarian tissues. Vitamin D supplementation attenuated these
hyperandrogenemia-associated acute kidney injuries, likely via interaction with the RAS/iNOS pathway.

#4248

COMBINED EFFECT OF DEHYDRATION, HYPERTENSION, AND AGE ON RENAL FRAILTY

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¹Institute of Biomedical Research of Salamanca, Salamanca, Spain and ²University of Salamanca, Salamanca, Spain

Background and Aims: Renal frailty (RF) is a premorbid and, at least partly, modifiable condition arising from diminished renal functional reserve and defective adaptive response capacity predisposing to acute kidney injury (AKI). RF ensues from subclinical wear or distortion of the renal haemodynamic and tubular homeostatic responses that defend the renal excretory function from supervening circumstances (i.e., stressors such as drugs). In this work, we aimed to study the impact of RF generated by the combined effect of the hydration state, hypertension and ageing on the nephrotoxicity developed by a low dose of cisplatin in the rat.

Method: Young Wistar rats, young spontaneously hypertensive rats (SHR), and aged Wistar rats were used. Rats in each group were randomly subject to four experimental conditions:
- Control: rats with ad libitum water intake, receiving vehicle (0.9% NaCl, i.p).
- Cisplatin: rats with ad libitum water intake, treated with 2.5 mg/kg, i.p. cisplatin.
- Water deprivation: rats deprived of water for 48 h, receiving vehicle (0.9% NaCl, i.p.).
- Water deprivation + cisplatin: rats deprived of water for the 48 h prior to 2.5 mg/kg i.p. cisplatin administration.

Tail vein blood and 24-hour urine samples were collected at basal time (B), after water deprivation (D0), and 4 days after cisplatin/vehicle administration (D4, day of maximum kidney damage). Haematocrit was measured and plasma osmolality, plasma creatinine (Jaffé reaction) and urea (Jung method) concentrations were determined. Urine samples were analysed for volume (urinary flow), osmolality, and proteinuria (Bradford method). Body fluid composition was measured by bioimpedance spectroscopy with an ImpediVETTM VetBIS1 device.

Results: All rats showed clear signs of dehydration after 48 hours of water deprivation: weight loss, increases in plasma osmolality and haematocrit (more pronouncedly in young Wistar and SHR than in aged animals), and reduced flow of a highly concentrated urine (i.e., with elevated osmolality). Bioimpedance analysis revealed a parallel loss of intracellular and extracellular water and net loss of total body water (explaining most of weight loss), with no changes in the liquid distribution between the intracellular and extracellular compartments. Dehydration was reverted after 4 days of rehydration in vehicle-treated rats, and no alteration of renal function was observed due to water deprivation. Administration of cisplatin in young, normohydrated Wistar rats showed minimal loss of renal function that was not worsened by water deprivation. Hypertensive rats showed completely normal renal function when cisplatin was administered under normohydration. Interestingly, however, dehydrated SHR did suffer a cisplatin-induced AKI (significant increases in plasma creatinine, plasma urea and proteinuria). In aged Wistar rats, cisplatin compromised renal function (as supported by increases in plasma creatinine and urea concentration), and this effect was significantly amplified by water deprivation.

Conclusion: This study suggests that dehydration in fully competent young rats is not in itself a significant risk factor for AKI, while the combination of dehydration and hypertension in young rats significantly increases the risk of AKI. Furthermore, ageing poses animals in a state of frailty that renders their kidneys unable to respond to stressors (such as a low dose of cisplatin). Frailty is boldly worsened in dehydrated aged animals. In perspective, models reproducing conditions of increased vulnerability to AKI provide useful tools to search for biomarkers pre-emptively predicting undesired health outcomes before exposure to stressors, and for developing preventing strategies.

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Abstracts
ATP6V0A4 GENE MUTATION-ASSOCIATED NEPHROPATHY
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Background and Aims: The ATP6V0A4 gene is localized to chromosome 7q33-34 and encodes for vacuolar H+-ATPase (V-ATPase) α4 subunit. Decreased V-ATPase function due to mutations in the ATP6V0A4 genes could cause H+ excretion defect of α-intercalated cells in the renal collecting duct, resulting in hereditary distal renal tubular acidosis (dRTA). However, crucially, no gain-of-function mutations in the ATP6V0A4 gene have been reported previously. This study reports a gain-of-function mutation of ATP6V0A4 gene occurred in a 32-year-old male with metabolic alkalosis, hypokalemia and hearing loss, and further explore potential pathogenic mechanisms of this mutation.

Method: Clinical information was collected from the proband and his family members. Kidney tissue samples were collected for morphological observation and immunohistochemical staining. High-throughput sequencing analyses were done for the proband and his parents. ATP6V0A4 wild-type and mutant plasmids were constructed and used to transfect the 293T cells. After 48 hours of transfection, the expression of ATP6V0A4 was verified using WB analyses and V-ATPase activity was measured by ultraviolet spectrophotometry.

Results: The proband and his father both suffered from severe hypertension and hearing loss. Blood tests showed hypokalemia, metabolic alkalosis and renal insufficiency. Urinalysis indicated acidic urine. Laboratory tests on admission are shown in Table 1. Renal biopsy suggested malignant hypertensive kidney injury. Whole-exome sequencing demonstrated that the proband carried the heterozygous mutation c.1534G>T; p.V512L in exon 15 of the ATP6V0A4 gene. Sanger sequencing confirmed that the variant was inherited from his father. The immunohistochemical results implied the expression of V-ATPase α4 was significantly higher in renal tissues from proband than that of the control who was diagnosed with minimal change disease (Figure 1B). WB analysis showed 293T cells transfected with ATP6V0A4 mutant plasmids with darker protein bands, suggesting higher expression of V-ATPase α4 (Figure 1D). The cells transfected with mutant ATP6V0A4 plasmids showed significantly higher V-ATPase activity compared with wild-type ATP6V0A4 plasmids transfected cells (Figure 1E).

Conclusion: The ATP6V0A4 c.1534G>T; p.V512L mutation is a gain-of-function mutation and this result indicates the possibility that this mutation might enhance the normal physiological function of the V-ATPase, and likely contributes to the increased hydrogen ions excretion and thereby to the development of metabolic alkalosis (Figure 1F).

Table 1: Laboratory values.

<table>
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<th>Variable</th>
<th>Reference Range</th>
<th>Adults</th>
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<td>Serum hemoglobin (g/L)</td>
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Figure 1: (A) Family diagrams. (B) Immunohistochemical staining of kidney tissues for V-ATPase α4. (C) GFP fluorescence of the 293T cells transfected with plasmids. (D) WB analysis showed high expression of V-ATPase α4 in 293T cells transfected with ATP6V0A4 mutant plasmids (MT). (E) 293T cells transfected with mutant ATP6V0A4 plasmids (MT) showed significantly higher V-ATPase activity. (F) A possible mechanism diagram.
Method: Renal ischemia-reperfusion injury (IRI) in mice as a model of acute kidney injury (AKI) were set as a platform to investigate the role of LMO7 and its functional interacting proteins in the pathological progression of compromised tubular epithelial integrity. Additionally, renal epithelial cells cultured in hypoxia as the pathogenic condition equivalent to AKI were also employed to investigate the role of LMO7. We also search the STRING database with LMO7 as query to find out its functional interacting proteins. Pathological pattern associated with LMO7 and its functional interacting protein in mice suffering from AKI as well as loss of tubular epithelial integrity were examined by immunofluorescent visualization. The LMO7 in urine as well as conditioned medium determined from medium of hypoxia culture were quantified by Western blot analysis.

Results: Renal damage in IRI mice showed loss of epithelial integrity by histochemical staining, presence of LMO7 in urine, and high serum creatinine on the third day post IRI. Under the periodic acid-schiff (PAS) staining, loss of epithelial integrity is visible in proximal tubules, Henle's loops, and collecting ducts at the third day after reperfusion, and brush border impairment is observed in the outer stripe of the outer medulla. Most severe damages in renal tubules are present in Henle's loops where the epithelia express abundant LMO7. In the AKI mice, the LMO7 in renal tubules was apparently lower in Henle's loops. Additionally, the VANGL1, a LMO7 interacting protein participated in epithelial integrity and planar cell polarity in kidney, is also absent in Henle's loop of AKI mice. Hypoxia and glucose deprivation in cultured renal epithelial cells resulted in loss of epithelial integrity, and downregulation of LMO7 and VANGL1. LMO7 was also identified in conditioned medium in which cells exposed to hypoxia but not normoxia. Additionally, the LMO7 was detected in urine of some patients with chronic kidney disease. Conclusion: Presence of LMO7 in urine has been promising in experimental models holding compromised epithelial integrity. These approaches identified the role of LMO7 in maintaining epithelial integrity and that LMO7 being released into urine after renal epithelial damage as a novel marker for loss of REB.

CALYCOSIN ATTENUATES RENAL ISCHEMIA/REPERFUSION INJURY BY SUPPRESSING INFLAMMATION VIA PPARγ/EGR1 PATHWAY

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Background and Aims: Renal ischemia reperfusion injury (IRI) is a leading cause of AKI, and delayed recovery of IRI contributes to chronic kidney disease and even end-stage kidney disease. However, there is no effective prevention and treatment for IRI-AKI. Calycosin (CAL), an isoflavonoid phytoestrogen isolated from Radix astragali, has various pharmacological activities. However, whether CAL has a protective effect on renal IRI and its mechanism remains elusive. In this study, we aim to explore the effect and mechanism of CAL on IRI-AKI through bioinformatics and experiments in vitro and in vivo models, so as to provide potential candidate drugs for early intervention treatment of IRI-AKI.

Method: (1) In the first part, mice were intragastrically given CAL daily for 7 d, and subjected to bilateral renal artery occlusion for 35 min followed by reperfusion 24 h to establish the renal IRI model. HE staining was used to evaluate the renal pathological injury, and the renal function including serum creatinine (SCR) and blood urea nitrogen (BUN), was also examined. Meanwhile, inflammatory factors were detected. In cell experiments, HK-2 cells pretreated with 8.16 and 32 μM CAL were subjected with hypoxia/reoxygenation (H/R), and the effect of CAL on H/R induced cell injury were investigated by qRT-PCR and ELISA. (2) In the second part, the differentially expressed gene (DEGs) of IRI-AKI were obtained by bioinformatics analysis of GSE52004 dataset. Subsequently, the hub gene with the highest score was obtained by protein-protein interaction (PPI) analysis, and its upstream transcription factors were predicted by JASPAR database. In IRI-AKI mice, the predicted results of bioinformatics were verified by qRT-PCR, Western Blot and immunohistochemistry. In HK-2 cells, the regulatory relationship between the hub gene and its upstream transcription factor and the role of them in inflammatory process were verified by double luciferase reporter gene and siRNA. Furthermore, molecular docking was used to predict the interaction between CAL and the transcription factor, and the role of the target protein in the protection of H/R HK-2 cells by calycosin was verified by siRNA.

Results: (1) In the mice with renal IRI, CAL dose dependently alleviated SCR and BUN levels and renal tubular injury score. Meanwhile, the mRNA level of inflammatory cytokines were markedly inhibited by CAL pretreatment. (2) In the pre-experiment in vitro, the toxicity of CAL was negligible at concentrations of 32 μM or less for 24 h incubation. In H/R induced HK-2 cells, CAL incubation reduced the levels of hypoxia-inducible factor (HIF) and the inflammatory cytokines. (3) 58 DEGs were identified in the kidney of IRI mice. PPI analysis showed early growth response 1 (EGR1) is the hub gene the highest score. JASPAR database predicted that peroxisome proliferator-activated receptor γ (PPARγ) is the upstream transcription factor of EGR1. (4) In kidney after IRI, EGR1 was up-regulated and PPARγ was down-regulated, while the pretreatment of CAL decreased EGR1 and increased PPARγ in a dose-dependent manner. (5) In H/R induced HK-2 cells, after inhibited the expression of EGR1 by siRNA, the level of inflammatory factors decreased significantly, suggesting that EGR1 participated in and promoted the inflammatory process of tubular cells. In addition, dual luciferase reporter gene assay confirmed that PPARγ interact with EGR1 promoter, as EGR1 increased after EGR1 promoter plasmid transfection but decreased after PPARγ overexpression. (6) In mice after renal IRI, CAL promote PPARγ expression markedly. According to molecular docking, CAL, as a ligand, could be embedded into the orthosteric pocket of PPARγ with a binding energy of -6.46 kcal/mol. In CAL incubated cells, PPARγ increased and EGR1 decreased considerably. However, the protective effect of CAL on H/R induced inflammation was absent when PPARγ knockdown, indicated that CAL ameliorate renal IRI and inhibit inflammation via PPARγ/EGR1.

Conclusion: CAL could significantly modulate inflammation by targeting the PPARγ/EGR1 pathway, contributing to the alleviation of renal IRI.
RESOLVIN D1 ATTENUATES SEPSIS INDUCED ACUTE KIDNEY INJURY TARGETING MITOCHONDRIA AND NF-κB SIGNALING PATHWAY
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Background and Aims: Acute kidney injury is a highly common and multifactorial renal disease resulting in significant morbidity and mortality, especially sepsis-induced acute kidney injury. There is no effective therapy available to treat or prevent sepsis-induced acute kidney injury. One of the specialized pro-resolving mediators, Resolvin D1 exhibits special anti-inflammatory effects in several inflammatory disease models, but there is little evidence about the effect and mechanism of Resolvin D1 in sepsis-induced acute kidney injury. To explore the renal protective role of RvD1 in SI-AKI and to further explore the inherent pathophysiological mechanism, especially the role of mitochondrial function and NF-κB signaling pathway, invitro and invivo experiments were conducted.

Method: We conducted experiments to explore the effect and mechanism of Resolvin D1 in sepsis-induced acute kidney injury. In vitro, human proximal tubular epithelial cells were used to test the apoptosis ratio, cell viability and reactive oxygen species level. In vivo, C57BL/6 mice were injected with lipopolysaccharide to establish a sepsis-induced acute kidney injury model. Renal function and structure, apoptosis ratio of kidney cells, mitochondrial structure and function and related protein and gene levels were assessed.

Results: In vitro, the resolvin D1-treated group showed higher cell viability and lower reactive oxygen species levels and apoptosis ratios than the LPS group. In vivo, Resolvin D1 can not only improve renal function and mitochondrial function but also reduce the apoptosis ratio, while mediating mitochondrial dynamics and inhibiting NF-κB pathway.

Conclusion: Resolvin D1 has a good renoprotective effect by maintaining mitochondrial dynamics and inhibiting the NF-κB pathway. This provides an important basis for us to further develop the clinical therapeutic value of RvD1 in acute renal injury in sepsis.

LINACLOTIDE IS PROTECTIVE AGAINST RENAL ISCHEMIA-REPERFUSION INJURY
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Background and Aims: Renal ischemia-reperfusion injury is associated with delayed graft function and poor long-term graft survival following transplantation. Linaclotide is a guanylate cyclase C (GC-C) receptor agonist that increases intracellular cGMP concentrations and promotes intestinal transport capacity by activating the GC-C receptor. Since CKD is a deficiency of cGMP in the kidney, increasing cGMP in the kidney by linaclotide would suppress fibrosis, protecting the kidney.

Method: An AKI rat model of unilateral nephrectomy plus contralateral ischaemia (30 min) and impaired reperfusion (up to 14 days) was used. Linaclotide was administered before and after surgery for 2 weeks, and blood and renal tissue samples were collected to determine its effect on renal function and whether it was protective against the progression of CKD.

Results: In the I/R injury+ group, creatinine levels were lower in the linaclotide-treated group than in the non-treated group. Sirius red staining showed significant improvement in fibrosis. The hydroxyproline content of kidneys was determined by the basic hydroxyproline method. RNA seq showed that genes down-regulated in I/R injury+ were the oxidative stress markers SOD3 and Gpx1. The expression of genes down-regulated in I/R injury+ was up-regulated to a degree similar to that in I/R injury- by treatment with linaclotide. These data suggest that linaclotide may ameliorate renal fibrosis by suppressing renal dysfunction through its antioxidant effects.

Conclusion: The antioxidant effect of linaclotide was found to suppress the decrease in renal function caused by I/R. We would like to apply this finding to human renal transplantation in the future to prevent renal function deterioration due to I/R.
Figure 1: Results of creatinine values at varying linaclotide concentrations.

Figure 2: Sirius red staining.

Figure 3: Hydroxyproline content in kidney each group.
STING CONTRIBUTES TO LPS-INDUCED TUBULAR INFLAMMATION BY ACTIVATING IRE1/XBP1 PATHWAY IN ACUTE KIDNEY INJURY

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Background and Aims: Innate immunity and inflammation were recognized as the key factors for the progression of acute kidney injury (AKI) induced by lipopolysaccharide (LPS). Stimulator of interferon genes (STING) has emerged as a critical component of innate immune and inflammatory responses. This study aimed to explore the role of STING in LPS-induced tubular inflammation in AKI.

Method: 1. The AKI mice models were induced by intraperitoneal injection of LPS. Mice were randomly divided into CTL group, LPS 24 g group and LPS 48 g group: (1) STING protein expression in tubules was detected by IHC staining; (2) STING protein expression in kidney cortices was detected by WB.
2. The tubule-specific STING knockout (STING-cKO) mice were generated. Then WT mice and STING-cKO mice were randomly divided into WT group, WT+LPS group, STING-cKO group and STING-cKO+LPS group: (1) Blood samples and urine samples were collected for Scr, BUN and ACR measurement; (2) Tubular pathological changes were detected by PAS staining; (3) Inflammatory cell infiltration in kidney cortices was detected by IHC and IF staining; (4) Pro-inflammatory cytokines’ mRNA level in kidney cortices was detected by qPCR.

Results: 1. STING was activated in tubules from LPS-induced AKI mice. (2) STING protein expression in kidney cortices was detected by WB.
2. STING-cKO significantly suppressed LPS-induced renal dysfunction, tubular pathological changes, tubular inflammation and IRE1/XBP1 pathway activation.
3. The tubule-specific STING knockout (STING-cKO) mice were generated.

Conclusion: STING contributes to LPS-induced tubular inflammation by activating IRE1/XBP1 pathway. Targeting STING may be a promising therapeutic strategy for preventing septic AKI.

THE INTEREST OF THE COMBINATION OF AN ANTIOXIDANT AND ANGIOTENSIN II RECEPTOR ANTAGONISTS IN THE REDUCTION OF RENAL FIBROSIS

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Background and Aims: Chronic kidney disease represents one of the frequent pathologies of non-communicable diseases where the mortality rate is high. Oxidative stress is one of the main causes of the deterioration of renal function. The aim of this work is to develop a new therapeutic molecule with an anti-fibrotic effect associated with an antioxidant to increase renal clearance.

Method: This is an experimental study using the aminonucleoside model of puromycin (PAN) on Sprague-Dawley rats weighing between 100 and 150 g. Mice are resistant to the effect of PAN Administration of PAN can be subcutaneous (SC) intravenous (IV) and intraperitoneal (IP). The dosage for IV and IP administration of PAN is generally 150 mg/kg body weight and 120 mg/kg body weight for SC administration. Control rats receive an isotonic saline solution. The progression of glomerular lesions to glomerular fibrosis depends on the cumulative dose of PAN. The single injection of PAN induces reversible fibrosis lesions between the seventh and one month and after re-injection irreversible lesions. The mice benefited from PAN 2 injections on the 1st day and on the 40th day, the new molecular association was made on 15 days and 50 days.

Results: Two to four days after the injection of PAN, a disorganization of the ultrastructure of the pedicles is observed with a flattening of the podocyte feet, an effacement of the pedicles, a modification of the actin cytoskeleton and the disappearance of the diaphragm of cleft. The ultrastructural changes observed 10 days after PAN injection lead to podocyte detachment contemporary with proteinuria. If the aggression continues, podocyte apoptosis is associated with histological appearance of segmental and focal hyalnosis. After the injection of the molecular combination, a regression of the lesions was observed 15 days after the first injection and 30 days after the second injection.

Discussion: The anti-fibrotic-antioxidant drug combination has a significant anti-fibrotic effect, especially during the first injection, the effect is less important during the evolution of histological fibrosis. The antioxidant gave a synergistic effect to the anti-fibrotic effect.

Conclusion: The experimental study is very promising concerning the antioxidant ARII molecular association while waiting for the clinical trial that will hopefully be promising for this new association.

HIF-1α REGULATED LncRNA-ATP6V0E2-AS1 MEDIATES HYPOXIA-INDUCED MITOPHAGY IN RENAL TUBULAR CELLS

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Background and Aims: Mitophagy activation is crucial for hypoxia signaling in acute kidney injury (AKI). Selective removal of damaged mitochondria is mediated through a concerted function of coding and non-coding RNA expression. Insights on HIF-1α signaling in lncRNA-regulated mitophagy mechanism are not known. The study aims to investigate the role of hypoxia-inducible factor 1α (HIF-1α) regulated long non-coding RNA (lncRNA) ATP6V0E2-AS1 in acute kidney injury (AKI) by examining its effect on mitophagy.

Method: Mitophagy proteins (PINK1, p-PARKIN, LC3) were determined through western blot analysis. Immunofluorescence studies of PINK1 mitochondrial translocation and LC3/TOMM20 localization were determined using confocal analysis. HIF-1α interaction with lncRNA-ATP6V0E2-AS1 was analyzed by dual-luciferase reporter assay.

Results: Hyoxia upregulated PINK1, p-PARKIN, LC3 expressions, and mitophagosome in HK-2 cells. Overexpression and knockdown studies of hypoxia-regulated lncRNA-ATP6V0E2-AS1 significantly regulated PINK1/p-PARKIN expressions, subsequent PINK1 mitochondrial co-localization, and mitophagosome formation. shHIF-1α knockdown in HK-2 cells revealed that HIF-1α mediates PINK1/p-PARKIN mitophagy regulation under hypoxic conditions. In detail, HIF-1α binds to the promoter of lncRNA-ATP6V0E2-AS1 and down-regulates its expression under hypoxia. Deficiency of both HIF-1α and lncRNA-ATP6V0E2-AS1 reversed shHIF-1α mediated suppression of PINK1 expression and mitophagosome formation. Further, ATP6V0E2-AS1 post-transcriptionally regulates PINK1 expression by RNA-RNA interaction.

Conclusion: Altogether, our study shows novel findings on the HIF-1α mediated lncRNA-ATP6V0E2-AS1 in hypoxia-induced mitophagy regulation in the renal tubular cells. Thus, downregulated ATP6V0E2-AS1 expression with subsequent mitophagy activation is critical for hypoxia-induced mitophagy regulation through HIF-1α/ATP6V0E2-AS1/PINK1 axis.

Figure 1: Lésion histologique après histologique. L’injection unique du PAN.

Figure 2: Évolution des lésions après l’association thérapeutique anti-oxydant ARII.
PRO-INFLAMMATORY EFFECTS OF BISPHENOL A AND POLYETHYLENE MICROPLASTICS ON HUMAN RENAL TUBULAR CELLS

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Background: Growing evidence shows that microplastics (MP) and their chemical derivates contaminate the environment and accumulate in the gut, liver, lungs, and kidneys. Furthermore, MP can adsorb a wide range of toxic substances (heavy metals, polycyclic aromatic hydrocarbons, Bisphenol A [B]), causing the accumulation of multiple pollutants and so, enhancing their toxicity (the so-called “Trojan Horse” effect). An epidemic of chronic kidney disease (CKD) of uncertain etiology is emerging worldwide and understanding the involvement of environmental pollution may be critical for health policies and public health responses. Inflammation is intimately linked to renal disease, and proinflammatory cytokines and chemokines are important mediators of fibrosis in the tubulointerstitial compartments.

Aims: To evaluate the effects of B and Polyethylene (Pe)-MPs and their combination B+Pe-MP on human renal tubular cells (HK-2). To this end, the activation of the Aryl hydrocarbon Receptor (AHR), a transcription factor binding xenobiotics, and the expression of inflammatory molecules were explored.

Method: HK-2 were exposed to 0 (No Treated cells: NT), 100 nM B, 0.2 mg/ml Pe-MP (diameter 1-4 μm), and B+Pe-MP for 5-24 hrs. Cell uptake of (FL)uorescent Pe-MP was visualized by microscope; viability was assessed by
MTR; AHR, HSP90, CCL2, CCR2, CCL5, and CCR5 expression was studied by rt-PCR. Western blot, and immunofluorescence.

**Results:** After 5 hrs exposure, a FLPe-MP cytoplasmatic and perinuclear deposition was observed (Figure 1). After 24 hrs, Pe-MP and B+Pe-MP exposure reduced cell viability (~20% vs NT p < 0.001). The treatments increased AHR expression (1.5-3-fold vs NT, p < 0.05-0.001), which had a nuclear localization both at 5 and 24 hrs. Conversely, HSP90 expression, a chaperone that keeps AHR inactive, decreased (~20-40% vs NT, p < 0.05) (Figure 2). After 2 hrs, CCL2 levels rose (1.8-3.5 fold, p<0.05-0.001) vs NT) as well as its receptor CCR2 (2.3-6.7 fold, p<0.05-0.01). Similarly, CCL5 and CCR5 were, respectively, 1.6-2.7 and 3.8-4.8 fold overexpressed with respect to NT (p < 0.05-0.01). Interestingly, the co-exposure significantly enhanced the expression of these inflammatory molecules.

**Conclusion:** Our data suggest that B and Pe-MPs induce a pro-inflammatory response in renal tubular cells and that the combined effect of B and Pe-MPs induces a worse effect on HK2 than B or MPs alone, supporting the theory of the "trojan horse" effect mediated by MPs. Therefore, MPs could be a trigger of kidney damage, thus confirming the potential impact of the environment on the pathogenesis of the renal disease. Moreover, these data could address the importance of investigating any health implications associated with MPs.

#5666

**FATTY ACID BINDING PROTEINS (FABPS) INHIBITION IMPAIRS METABOLIC HOMEOSTASIS IN RENAL TUBULAR CELLS**

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**Background and Aims:** The fatty acid binding proteins family of lipid chaperones (FABPs) mediate lipid trafficking and lipid-mediated metabolic pathways. Despite inhibition of induced FABPs may be beneficial in kidney disease, their enrolment in renal metabolic homeostasis remains elusive. Therefore, we approached this issue in cultured renal tubular cells.

**Method:** FABP mRNA and protein expression were evaluated in C57/BLE mice subjected to folic-acid kidney injury. Mitochondrial redox status, proliferation, death rate, and fatty acid oxidation (FAO) were studied in renal tubular cells in conditions of overall FABP inhibition with BMS309403. In these conditions, lipid trafficking was addressed by oil red content and pulse-chase assays using the fluorescent lipid RedC12. Delivery of RedC12 within LD or mitochondria was followed with BODIPY493/503 and Mitotracker and assays using the fluorescent lipid RedC12. Delivery of RedC12 within LD or mitochondria was followed with BODIPY493/503 and Mitotracker and confocal microscopy. Free and esterified RedC12 species were assessed by thin-layer chromatography (TLC). The impact of ATGL lipase activity on cellular behaviour and bioenergetics were assessed by diethylumbelliferyl phosphate (DEUP)-mediated inhibition.

**Results:** Kidneys from mice with AKI exhibited early lowered FABPs tubular expression. In serum-depleted murine tubular cells, pharmaceutical FABPs inhibition with BM309403 (BMS) led to sudden necrosis, whereas, in non-depleted cells, BMS eventually leads to apoptosis, increased the mRNA expression of proinflammatory cytokines and oxidative stress-responsive genes, and response in proliferation. BMS also rapidly decreased ATP levels consistent with FAO inhibition and induced adaptive AMPK phosphorylation/activation and FAO gene program (but not glycolytic gene expression). BMS also mediates mitochondrial depolarization, mitochondrial oxidative stress and decrease of mitochondria number. Serum-depleted cells revealed lipid droplet (LD) voiding and RedC12 delivery to mitochondria. By contrast, in BMS-treated cells growing in serum, despite the lowered ATP content and transcriptional FAO upregulation, RedC12 neither localized with LDs nor with mitochondria, suggesting a low-energy state by impairment of both lipid transit and FAO. Accordingly, TLC assessment did not show lipid breakdown-derived products, which otherwise did appear in serum-depleted cells doing FAO. Mechanistically, ATGL inhibition protects from general ROS production, LD voiding and apoptosis.

**Conclusion:** In brief, FABP inhibition disrupts tubular energetical status and favours cell stress. Thus, protecting FABP activity could help to preserve tubular metabolic homeostasis during early kidney damage.

#4208

**CRP EXACERBATES SARS-COV-2-NUCLEOCAPSID PROTEIN-INDUCED ACUTE KIDNEY INJURY**

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**Background and Aims:** COVID-19, caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2), is a progressive viral pneumonia with a broad spectrum of clinical manifestations involving multiple organs. Acute kidney injury (AKI) is common in COVID-19, especially in critically ill patients. Our previous study proved that kidney-specifically overexpressing SARS-CoV-2 N protein induces AKI, which become worsen in mice under ischemic condition. Clinically, CRP is a risk factor for AKI in COVID-19 patients. Recent clinical study showed that CRP Apheresis is able to effectively remove the plasma CRP and thus improve the clinical outcome in critically ill COVID-19 patients. We thus hypothesize that CRP may not only be a biomarker or risk factor, but also a potential mediator or novel therapeutic target for COVID-19 AKI.

**Method:** The role of CRP in COVID-19 AKI was investigated in a mouse model of AKI induced by ultrasound-microbubble-mediated kidney-specifically transferring SARS-CoV-2 N-expressing plasmids in CRP-wide-type (WT) and Transgenic (Tg) mice. We also developed a novel therapy for SARS-CoV-2 N-induced by targeting CRP signaling with a neutralizing anti-CD32 antibody both in vivo and in vitro.

**Results:** In COVID-19 patients with AKI, serum levels of CRP were significantly elevated when compared with non-AKI group. In mice, kidney-specifically overexpressing SARS-CoV-2 N protein caused AKI including tubular necrosis and elevated levels of serum creatinine and BUN in CRP WT mice which became more severe in CRP Tg mice. Importantly, targeting CRP-CD32 signaling with a neutralizing antibody to CD32 significantly inhibited SARS-CoV-2 N-protein-induced AKI in CRP Tg mice. Mechanistically, we uncovered that CRP promoted SARS-CoV-2-N protein-induced AKI via the Sma3/p21-dependent G1 cell cycle arrest and NF-kB/p65-driven renal inflammation, which was blocked by anti-CD32 antibody in vivo and in vitro.

**Conclusion:** CRP is not only a biomarker or risk factor, but also a mediator in SARS-CoV-2 N-protein-induced AKI. CRP signals through CD32 mediate SARS-CoV-2-N-induced AKI via mechanisms associated with the Sma3-p21-dependent G1 cell cycle arrest and NF-kB/p65-driven renal inflammation. Targeting CRP-CD32 signaling may represent as a novel therapy for COVID-19-associated AKI.

#5458

**HISTOLOGICAL STUDY OF KIDNEY INJURY ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS COMBINED WITH CHEMOTHERAPY IN A MURINE MODEL**

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**Background and Aims:** The role of CRP in COVID-19 AKI was investigated in a murine model of AKI induced by ultrasound-microbubble-mediated kidney-specifically transferring SARS-CoV-2 N-expressing plasmids in CRP-wide-type (WT) and Transgenic (Tg) mice. We also developed a novel therapy for SARS-CoV-2 N-induced by targeting CRP signaling with a neutralizing anti-CD32 antibody both in vivo and in vitro.

**Method:** A murine model was designed in C57BL/6 mice treated with the combined therapy of cisplatin (10 mg/kg, single dose) and anti-CTLA-4 (10 or 15 mg/kg/day, for 6 days) administrated by intraperitoneal injection. In addition, groups treated with drug monotherapies and a control group were included. On the day of sacrifice (day 6) the kidneys were collected and histological sections were made and stained with hematoxylin-eosin. Histological quantification of kidney damage was performed blindly following a tissue damage quantification protocol. For this, 10 photos were taken per kidney (600X), 5 of the external cortex and 5 of the corticomedullary region. Each photo was segmented into 6 areas and a score was assigned to each area as follows: 0: no damage, 1: damage up to 1/3 of the area, 2: damage between 1/3 and 2/3, 3: damage above 2/3.
1/3 and 2/3 of the area, and 3: damage over 2/3 of the area. Subsequently, the mean scores of the kidneys from the same experimental group were calculated, as well as the standard error of the mean. Data was analyzed with the statistical software SPSS®.

Results: Our results showed tubular renal damage associated with cisplatin treatment. It was more pronounced in the external cortical area. However, no structural alterations associated with ICI treatment were found. Co-treatment with both drugs potentiated renal structural damage from cisplatin.

Conclusion: This potentiation was more evident in the corticomedullary region, so it seems that the drugs combination causes a deeper lesion in the kidney than cisplatin monotherapy. Our study suggests that the combined therapy of anti-CTLA-4 and cisplatin could induce generalized tubular lesions.

#6747
ACTIVATION OF GPR120 IMPROVES THE SENESCENCE OF TUBULAR EPITHELIAL CELLS IN SEPTIC ACUTE KIDNEY INJURY
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Background and Aims: Acute kidney injury (AKI) is a serious clinical complication that has high morbidity and mortality. Although there have been substantial advances in understanding AKI mechanisms, at present, there are no effective therapies to treat or prevent it.

Method: We had formerly found that TUG891, a GPR120 (a member of the G protein-coupled receptor (GPCR) family) agonist, alleviated tubular damage as well as renal dysfunction in mice with AKI. Nevertheless, the multifunctional effects of FFAR4 in the kidney have not been well described.

Results: In the current research, the GPR120 expression was abnormally reduced in tubular epithelial cells (TECs) of cecal ligation/perforation induced AKI mice, respectively. Systemic and conditional TEC-specific knockout of GPR120 aggravated renal function and pathological damage, whereas GPR120 activation by TUG-891 alleviated the severity of disease in AKI mice involved cisplatin. Notably, GPR120, as a key determinant, was firstly explored to regulate the cellular senescence in TECs and AKI mice injured kidneys, as represented through the activity of senescence associated β-galactosidase (SA-β-gal), marker protein p21, p53, Lamin B1, phospho-histone H2A.X, phospho-Rb expression, and secretory phenotype IL-6-6 level. Mechanistically, pharmacological activation and overexpression of FFAR4 reversed the decrease of aging-related SirT3 protein, where GPR120 regulated SirT3 expression to exhibit anti-senescence effect via Gq subunit-mediated CaMKKβ/AMPK signaling in cisplatin-induced mice and tubular epithelial cells.

Conclusion: These results underline the primordial role of renal tubular GPR120 in the cellular senescence through AMPK/SirT3 signaling and define GPR120 as a target for underlying drugs against septic AKI.

#4234
ADAM17 MODULATES IFN-MEDIATED INFLAMMATION IN RENAL TUBULAR CELLS
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Background and Aims: In diabetic patients, hyperglycemia has been associated with a hypoxic state that contributes to an increased rate of morbidity due to Acute Kidney Failure (AKI). For this reason, we are interested in studying the molecular mechanisms involved in the development of AKI to contribute to the search for effective therapies that can help prevent these episodes. We focused on ADAM17, a disintegrin and metalloproteinase that sheds the ectodomains of cell surface proteins, among which inflammatory cytokines stand out. In an animal model, we showed that the absence of ADAM17 in the renal tubule reduces protein expression related to fibrosis and inflammation induced by diabetes. In this context, we aimed to study the role of ADAM17 in modifying the expression of inflammatory molecules regulated by interferon (IFN) in renal proximal tubule cells subjected to hyperglycemic stress. In this study, we analyzed the effect of ADAM17 deletion in human renal tubular cells (HKC-8) incubated in high-glucose medium and subjected to hypoxia.

Method: ADAM17 was depleted using CRISPR/Cas9 (ADAM17-KO). Cells were incubated for 6 h or 24 h with high (35 mM HGl) or normal (5.5 mM NG) glucose concentrations and were subjected to hypoxia plus 2h re-oxygenation (HIXP). Gene expression of several IFN-regulated inflammatory markers (IL6, IL8, CXCL10, ISG15, IL1a, IL1b, IL12A, CCL5, and CCL2) was determined in wild-type (WT) and ADAM17-KO cells.

Results: The absence of ADAM17 in HKC-8 cells induced changes in the mRNA expression of genes controlled by IFN, which is accentuated by the hyperglycemic stimulus. Under hypoxic and re-oxygenation conditions, these changes were in the same line, with more discrete values compared to control cells. TNFa, CXCL10 and LNC2 were the most relevant genes reduced in injury conditions in the ADAM17-KO cell line.

Conclusion: ADAM17 deletion modulates the expression of most IFN-regulated genes that could undergo post-transcriptional changes and subsequently act as an acute mechanism of protection from injury. The results show that ADAM17 plays a major role in the underlying inflammatory response to acute kidney injury, indicating its potential as a therapeutic target. The analysis of circulating proteins will provide information about this process to better understand the mechanism of action of ADAM17 in the protection of renal tubular damage.

Figure 1: CXCR5+PD-1+ CD8 T cells analyze by flow cytometry and PD-1 mRNA expression in peripheral blood cells.
Table 1: Demographics and Characteristics of Kidney Transplant Study Population.

<table>
<thead>
<tr>
<th></th>
<th>KTX with DSA positive n=20</th>
<th>KTX with DSA negative n=22</th>
<th>Healthy control n=21</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>Group II</td>
<td>Group III</td>
</tr>
<tr>
<td>F/M</td>
<td>9/11</td>
<td>8/14</td>
<td>9/12</td>
</tr>
<tr>
<td>Age mean</td>
<td>35,7/28,6</td>
<td>32,1/37,1</td>
<td>32,1/34,3</td>
</tr>
<tr>
<td>PRA mean %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>68</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Class II</td>
<td>79</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Class I/Class II</td>
<td>69,6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HLA miss-match mean/median</td>
<td>2,09 ±6 (3)</td>
<td>2,18±6 (2)</td>
<td>-</td>
</tr>
<tr>
<td>HLA-DRB1* miss-match mean/median</td>
<td>1,05±2 (1)</td>
<td>0,95±2 (1)</td>
<td></td>
</tr>
<tr>
<td>Donor type D/L</td>
<td>4/16</td>
<td>5/17</td>
<td>-</td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATG</td>
<td>15</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>MMF/MFA</td>
<td>16</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>TAC</td>
<td>17</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>BAS</td>
<td>5</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>CSA</td>
<td>1</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>MYF</td>
<td>1</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Rejection (ABMR)</td>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* p<0.05, Group I vs Group II

PD1/PD-L1 genes in peripheral blood lymphocytes in recipients who de-novo DSA positive or negative after kidney transplantation (KTX).

Method: In this study, the expression levels of PD-1, PD-L1 genes were determined using the Real-Time Quantitative PCR method from peripheral blood samples of 22 KTX patients with de-novo DSA positive, 20 KTX patients with DSA negative and 21 healthy control (Table 1). Our patient groups were PRAnegative before transplantation. Expression (%) levels of target cells were evaluated by flow cytometry method. IBM SPSS Statistics for Windows Version 22 and R 3.3.2 software were used to evaluate the data.

Results: PD-1 expression level was higher in the KTX patients with de-novo DSA positive compared to the KTX patients with DSA negative group (p:0.006 CT: 0.84 ±0.23). According to the results of flow cytometry, CD8+CXCR5+PD1+ cell expression (%) levels were found to be significantly higher in patients (3.06 ±1.98) compared to the transplant control group (0,52±0,40) (p: 0.001) (Figure 1).

Conclusion: It shows that there may be a direct correlation between DSA and PD-1 / PDL-1 mRNA level and CXCR5+PD1+CD8+ follicular cytotoxic T cell in transplant patients after kidney transplantation.

G2 - EPIDEMIOLOGY & OUTCOME

#4162

COMPARISON OF EGFR CYSTATIN C AND EGFR CREATININE IN RECENTLY HOSPITALISED INDIVIDUALS

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1 University of Nottingham, Centre for Kidney Research and Innovation, Derby, United Kingdom, 2 University Hospitals of Derby and Burton NHS Foundation Trust, Renal Unit, Derby, United Kingdom, 3 University Hospitals of Derby and Burton NHS Foundation Trust, Department of Chemical Pathology, United Kingdom and 4 University Hospitals of Derby and Burton NHS Foundation Trust, Department of Informatics, United Kingdom

Background and Aims: Creatinine and cystatin C are endogenous biomarkers that can be used to estimate glomerular filtration rate (GFR). Cystatin C may be less dependent on age, gender and muscle mass. The comparative performance of these markers in recently hospitalised patients with acute kidney injury (AKI), who may have experienced changes in body composition, is unclear.

Method: Two matched cohorts of hospitalised individuals who had survived to 90 days after admission were recruited. The cohorts consisted of people who had sustained AKI during hospital admission and those who had not, and were matched 1:1 for age, baseline eGFR stage and diabetes. Serum creatine and serum cystatin C were measured at 3 months after hospitalisation and eGFR calculated using CKD EPI creatinine (eGFRcre) and CKD EPI cystatin C (eGFRcys) equations. Difference between the measures (eGFRdiff) was calculated as eGFRcys-eGFRcre and percentage difference (eGFR%diff) was relative to the mean of both eGFR measures. Primary outcome was mortality after 5 years of prospective follow up. Univariable survival analyses were conducted with the Kaplan Meier method and comparisons were performed with the log rank test, and a fully adjusted multivariable analysis performed with Cox proportional hazards model.

Results: 854 individuals were recruited, matched, and had paired creatinine and cystatin C measurements. 427 (50%) had sustained AKI. Median eGFRcys was lower than eGFRcre (53.5ml/min/1.73 m² [34.4-85.4] vs 68.4ml/min/1.73 m² [52.6-84.7], p<0.001). eGFRcys and eGFRcre were correlated (r =0.486, p<0.001) but Bland Altman analysis showed variable bias across the eGFR range. More individuals had an eGFR <60ml/min using eGFRcys (57%) compared with eGFRcre (35.6%). There was a graded relationship between eGFR%diff and outcome, with a shorter survival time (Figure 1) and higher proportion of deaths at 5 years (Q1 64 (30.0%), Q2 54 (25.4%), Q3 41 (19.2%), Q4 (31 (14.6%), p<0.001) in the first quartile. Cox proportional hazards analysis showed that eGFR%diff was an independent predictor of 5-year mortality after adjustment for age, Charlson index score and albuminuria (adjusted OR 0.995 [0.992-0.998], p = 0.002).

Conclusion: Cystatin C eGFR measures were lower than creatinine eGFR measures in recently hospitalised individuals. Lower eGFRcys relative to eGFRcre was independently associated with increased mortality. A larger difference between eGFRcys and eGFRcre may reflect loss of muscle mass (resulting in relatively lower serum creatinine) in somebody who has recently had an acute illness. Further, these results confirm how eGFRcre may overestimate kidney function and potentially miss patients with failed renal recovery at 3-months after AKI. The difference between eGFRcys and eGFRcre may be helpful in identifying people at greater risk of early mortality after an acute illness.
DETECTING NEONATAL AKI BY SERUM CYSTATIN-C

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Background and Aims: Serum creatinine is not a sensitive biomarker for acute kidney injury (AKI) in neonates. Unlike creatinine, cystatin-C (Cys-C) does not cross the blood placental barrier and the serum level in the neonates is not significantly impacted by the gestation age, birthweight, and the age during the first four weeks after birth. Therefore, serum Cys-C may be a better marker neonatal AKI than serum creatinine. We aimed to assess the performance of serum Cys-C as an alternative biomarker for detecting neonatal AKI.

Method: This is a large multicenter cohort study including 52,333 hospitalized neonates. First, we assessed the impacts of gestational age, birthweight, and days after birth on the level of Cys-C, and estimated the upper normal limit (UNL) and the reference change value (RCV) of serum Cys-C in neonates. Then, we proposed a Cys-C based criteria (CyNA) for detecting neonatal AKI based on both Cys-C level and the change in Cys-C using UNL and RCV as the cutoffs, respectively. Finally, we assessed the performance of CyNA in detecting neonatal AKI and the association of CyNA-detected AKI with the risk of in-hospital death, and compared the performance with that using the KDIGO creatinine criteria.

Results: Cys-C level in neonates did not vary with gestational age and birthweight, and remained relatively stable during the neonatal period (Figure 1). The UNL of Cys-C was 2.2 mg/L and the RCV (for Cys-C ratio) was 1.25. CyNA criteria defines AKI by a serum Cys-C of ≥ 2.2 mg/L (UNL) or an increase in Cys-C of ≥25% (RCV) during the neonatal period. Among 52,333 neonates 6,336 (12.1%) AKI cases were detected by CyNA criteria, of whom 96 (1.5%) died. In comparison, 202 (0.44%) death events occurred in 45,997 neonates who did not have AKI. After adjusting all comorbidities, CyNA-detected AKI was associated with a significantly increased risk of in-hospital mortality (adjusted HR 2.91, 95% confidence interval, 2.24 to 3.78). Among 45,839 neonates that had measurement of both Cys-C and SCr, 4,513 (9.8%) had AKI detected by CyNA only, 373 (0.8%) by KDIGO only, and 381 (0.8%) by both criteria (Table 1). After adjusting admission to ICU and comorbidities, AKI detected by CyNA only (C-/+K-) was associated with a significantly increased risk of in-hospital mortality compared with those without AKI by both criteria (C-/K-), with an adjusted hazard ratio of 2.86 (95% CI, 2.02 to 4.04). In comparison, the HR for those detected by KDIGO only (C-/K+) was lower at 2.15 (95% CI, 0.96 to 4.81). Neonates with AKI detected by both criteria (C+/+K+) had the highest risk of in-hospital mortality (HR 4.86, 95% confidence interval, 2.84 to 8.29).

Conclusion: Serum Cys-C is a robust and sensitive biomarker for detecting neonatal AKI. CyNA is 5.5 times more sensitive than the modified KDIGO in detecting neonates who are at an elevated risk of in-hospital mortality.

Table 1: In-hospital Mortality by AKI Status.

<table>
<thead>
<tr>
<th>AKI status</th>
<th>N</th>
<th>Death</th>
<th>1000 person days</th>
<th>Death per 100,000 person days</th>
<th>unadjusted HR (95% CI)</th>
<th>adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-/K-</td>
<td>40,572</td>
<td>137</td>
<td>626.7</td>
<td>21.9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C-/K+</td>
<td>373</td>
<td>7</td>
<td>8.0</td>
<td>87.8</td>
<td>5.64 (2.61, 12.2)</td>
<td>2.15 (0.96, 4.81)</td>
</tr>
<tr>
<td>C+/K-</td>
<td>4,513</td>
<td>51</td>
<td>83.5</td>
<td>61.1</td>
<td>4.25 (3.05, 5.92)</td>
<td>2.86 (2.02, 4.04)</td>
</tr>
<tr>
<td>C+/K+</td>
<td>381</td>
<td>22</td>
<td>8.9</td>
<td>247.0</td>
<td>11.8 (7.30 to 19.2)</td>
<td>4.86 (2.84, 8.29)</td>
</tr>
</tbody>
</table>

*AKI status was presented as a combination of absence (-) or presence (+) of AKI detected by CyNA (C) and KDIGO (K) criteria, respectively. Hazard ratios were estimated in the neonates with measurements of both Cys-C and SCr using a Cox proportional hazard model with adjustment for gender, admission to ICU, and common comorbidities. AKI status and admission to ICU were coded as time-dependent covariates in the model.
Background and Aims: The possibility that population demographic characteristics, changes in viral strain and therapeutic advances in management of COVID-19 might influence clinical outcomes is of great interest given potential regional variations. The aim of our study was to describe regional variation in COVID-19 hospitalisation rates in England and factors affecting in-hospital mortality as well as acute kidney injury (AKI).

Method: In this retrospective cohort study using hospital episode statistics, we collected data from all adult hospitalised patients with COVID-19 infection (diagnostic code U07.1 in any of the 20 diagnoses codes) between 1st March 2020 and 31st March 2021, to end of discharge period. We also extracted all available secondary diagnoses and procedure codes. Patients with codes for chronic dialysis were excluded. We divided the observation period as per the dominant SARS CoV-2 variant and further, in relation to publication of the RECOVERY trial. SARS CoV-2 "Other" strain was prevalent between 1st March 2020 and 21st December 2020 and "Alfa" between 22nd December 2020 to 17th May 2021. The end date of each phase was based on more than 50% decline in each variant.

Results: We extracted 3,24,748 finished consultant episodes (FCE) for all patients with U071 code in any of the 20 diagnoses codes and admitted during the study period. After exclusion of multiple FCEs within same spell, chronic RRT and patients not residing in England, there were 749,844 unique admission spells with ICD10 code of U071 in one of the diagnoses codes in 337,029 patients. London had the highest number of COVID-19 admissions at 131,338 (18%) followed by North-west region with 122,683 admissions (16%). Population incidence of COVID-19 hospital admissions was highest in North-west at 21.167 per million population (pmp) and lowest in South-west at 9.292 admissions pmp. Patients with COVID-19 were younger (67.0 ± 17.7 years) in London as compared to patients in East of England (72.2 ± 16.8 years). Length of stay was lowest in North-east (12.2 ± 14.9 days) and highest in North-west (15.2 ± 17.9 days). As compared to London, all eight regions had higher odds of death, ranging from OR of 1.04 (95% CI 1.00, 1.07) in South-west to OR 1.24 (95% CI 1.21, 1.28) in North-west. Odds of death were lower in patients with COVID-19 in post-RECOVERY period, both with "Other" (OR 0.72, 95% CI 0.71, 0.74) and Alfa strain of SARS CoV-2 (OR 0.75, 95% CI 0.74, 0.76). Overall, AKI incidence was 30.3%. All eight regions in England had lower odds of developing AKI as compared to London. Post-RECOVERY periods with the "Other" variant (OR 0.87, 95% CI 0.85, 0.88) and "Alfa" variant (OR 0.87, 95% CI 0.86, 0.88) both had lower odds of developing AKI.

Conclusion: This large national study of COVID-19 found a higher hospital admission rate and AKI incidence but lower odds of death in London compared with other regions in England. The incidence of AKI and mortality due to any cause were lower in the post-RECOVERY period irrespective of the prevalent SARS CoV-2 strain.

Figure 1: Distribution of serum Cys-C and creatinine stratified by day after birth in the neonates.
Figure 1a: Mortality predictors in patients with COVID-19.
Background and Aims: Acute kidney injury (AKI) is a major complication in cancer patients receiving immune checkpoint inhibitors (ICIs). Previous studies have not accurately distinguished the various potential underlying causes of AKI due to the limited use of renal biopsy. Here, we reviewed cases of biopsy-proven acute tubulointerstitial nephritis (ATIN) in patients treated with ICIs to describe the clinical and laboratory characteristics and outcomes of this condition.

Method: We conducted a pooled analysis of clinical cases published up to 1 May 2022. The search terms on PubMed were [(Pembrolizumab OR Nivolumab OR Ipilimumab OR Atezolizumab OR Avelumab OR Durvalumab) AND (Nephritis)]. Only cases with biopsy-proven ATIN were included. Among a total of 111 patients identified, 83 were eligible for this analysis. We added two patients from our Institution. We collected data on clinical characteristics, renal biopsy findings, and laboratory examinations. AKI was graded according to the KDIGO criteria. As outcomes, we considered: complete renal recovery if serum creatinine returned to baseline +0.3 mg/dL, no recovery if patients needed dialysis and partial recovery in other cases.

Results: Overall, 85 patients (56 male) with an age of 61.4±19 years were evaluated. 43 patients (51%) had melanoma, 25 (30%) non-small cell lung cancer, 8 renal carcinoma, and 9 other cancers. ICI treatment consisted of PD-1, PDL-1 (nivolumab, pembrolizumab, atezolizumab) and CTLA4 inhibitors (i) (ipilimumab) or combination PD-1i-CTLA4i (Table 1). Renal toxicity developed after a median of four cycles of therapy, but in most cases (n = 59) after at least three treatment cycles. Eleven patients (14%) presented with AKI stage 1, 16 patients (20.5%) with stage 2, and 51 patients (65.5%) with AKI stage 3, including five patients requiring dialysis. Among AKI3 patients there was a significantly higher prevalence of patients at the first therapy line (p = 0.04), while all the 19 patients treated with the dual ICI blockade developed AKI3, compared with 29 patients out of the 52 taking a single agent (Figure 1A). Seventy-seven patients received steroids, while 7 patients did not receive any therapy. ICI treatment was withdrawn in 65 out of 69 patients with available data. Following AKI resolution, in 15 patients ICI was restarted, but in six (40%) AKI recurred. Overall, 32 patients (40%) presented a complete renal recovery, 45 patients (56.2%) had a partial recovery, and 3 patients (3.8%) did not recover. Among patients who did not fully recover, there was a higher prevalence of those treated with dual ICI blockade and presenting with AKI stage 3 (Figure 1B). At logistic regression, complete renal recovery was inversely associated with dual ICI blockade (OR 0.1, 95CI 0.02-0.5, p = 0.006) and AKI 3 (OR 0.31, 95CI 0.1-0.9, p = 0.04), but only the association with dual ICI therapy remained significant at multivariate analysis.

Conclusion: ICI-related ATIN may develop late after the initiation of therapy. It may present as a severe form of AKI, particularly in patients with dual ICI blockade. Although this complication may be partially reversible, concerns

#2944
BIOPSY-PROVEN ACUTE TUBULOINTERSTITIAL NEPHRITIS IN PATIENTS ON IMMUNE CHECKPOINT INHIBITORS: A POOLED ANALYSIS OF CASE REPORTS
Annarita Bottini1, Elvina Lecini1, Francesca Cappadona2, Michela Piaggio1, Lucia Macciò1, Carlo Genova1, Francesca Viazzi1,2 and Pasquale Esposito1,2
1DIMI, Internal Medicine, Genova, Italy and 2IRCCS Policlinico San Martino, Nephrology, Genova, Italy

Table 1: Clinical and laboratory characteristics of patients evaluated in the pooled analysis.

<table>
<thead>
<tr>
<th>N patients</th>
<th>85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61.4±19</td>
</tr>
<tr>
<td>Gender-m (%)</td>
<td>56 (65.9)</td>
</tr>
<tr>
<td>Comorbidities, n</td>
<td>N (%)</td>
</tr>
<tr>
<td>- Hypertension</td>
<td>41 (48.2)</td>
</tr>
<tr>
<td>- Heart disease</td>
<td>12 (14.1)</td>
</tr>
<tr>
<td>- Diabetes</td>
<td>8 (9.4)</td>
</tr>
<tr>
<td>Cancer, n</td>
<td>85</td>
</tr>
<tr>
<td>- Melanoma</td>
<td>43 (50.6)</td>
</tr>
<tr>
<td>- NSCLC</td>
<td>25 (29.4)</td>
</tr>
<tr>
<td>- CRCC</td>
<td>8 (9.4)</td>
</tr>
<tr>
<td>- Other</td>
<td>9 (10.6)</td>
</tr>
<tr>
<td>ICI drug, n</td>
<td>79</td>
</tr>
<tr>
<td>- Nivolumab single agent</td>
<td>28 (35)</td>
</tr>
<tr>
<td>- Pembrolizumab</td>
<td>21 (26.5)</td>
</tr>
<tr>
<td>- Atezolizumab</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>- Ipilimumab single agent</td>
<td>9 (11.4)</td>
</tr>
<tr>
<td>- Nivolumab+Ipilimumab</td>
<td>19 (24)</td>
</tr>
<tr>
<td>First line therapy, (n = 49)</td>
<td>27 (55)</td>
</tr>
<tr>
<td>Therapy cycles at AKI, median (IQR)</td>
<td>4 (2.2-6.7)</td>
</tr>
</tbody>
</table>

Percentages were expressed considering the data available for each parameter. Immune checkpoint inhibitors (ICI), non-small cell lung cancer (NSCLC), Clear cell renal cell carcinoma (CRCC).
remain about the renal function sequelae and the possibility of restarting treatment after AKI resolution due to the risk of recurrence.

Figure 1: Prevalence of AKI stage 3 (A) and renal recovery (complete vs partial/no recovery) in patients on single or dual ICI blockade. Fisher’s test.

Abstracts 

#6039
EPIDEMIOLOGY AND OUTCOMES OF ACUTE KIDNEY INJURY: DON’T FORGET THE CHILDREN
Flavia Chisavu, Ramona Stroescu, Lazar Chisavu, Mihai Gafencu and Adalbert Schiller
University of Medicine and Pharmacy ‘Victor Babes’ from Timisoara, Romania, Timisoara, Romania

Background and Aims: Acute kidney disease (AKI) has evolved from a primary single renal disease to a syndrome secondary to other systemic illness. The aim of this study is to assess AKI epidemiology in a large East European country database comprising a mixt paediatric population (critically ill and non-critically ill) and the impact on mortality and hospitalization length.

Method: We conducted a retrospective observational study on all the admitted paediatric patients from 1 day to 18 years old between first of January 2014 until the 31 December 2021. Out of 137760 admissions, 2194 patients were included in the study. We classified the different age groups as: premature (all the babies born before 37 weeks of gestation), full-term new-borns, infants (between 28 days and 12 months of life), toddlers (over 12 months up to 3 years), preschoolers (between 3 and 5 years), scholars (6 years to 11 years) and adolescents (12 to 18 years).

Results: The overall incidence of AKI was 15.92/1000 hospital admissions with a 4.77 times fold increased incidence over the 8 year period, from 6.72 in 2014 to 32.12/1000 admissions in 2021. The most prevalent age group, accounting for almost half the AKI cohort (49.49%), was represented by the neonatal setting with 527 (24.02%) preterm and 539 (25.47%) full-term neonates. The paediatric age groups were represented by 10.84% infants, 8.29% toddlers, 6.65% pre-schoolers, 10.57% school aged children and 14.17% adolescents. Staging AKI according to AKIN, stage 1 was identified by us in 24.24% of the AKI cases, stage 2 in 31.03% and stage 3 in 44.71%. Only 25 patients (1.1%) required RRT. Dividing the cases by AKI causes, the most common was represented by prerenal AKI in 85.64% of the cases, followed by 12.16% renal causes respectively 2.18% postrenal causes. Over the 8-years period, from the 137 760 admitted children, 0.32% (449 patients) died of whom 255 (56.79%) presented AKI diagnosis. The risk of death in the presence of AKI was 109 times higher than in the no-AKI group (p < 0.0001, 95% CI: 90-132), mortality in the AKI group being 11.62%. Stage 3 AKI group had a higher risk of death than stage 1 with an OR of 3.31 (CI = 2.516-4.355, p < 0.001). The average hospitalization period for all admitted patients (137 760) was 5.76 days. In the presence of AKI the average hospitalization period increased to 20.9 days ± 19.3 days.

Conclusion: The neonatal setting portends poor outcomes with the highest incidence of AKI. We can state that in the 21st century patients do no die of AKI but with AKI. Hospitalization increased significantly in the presence of AKI.

#3004
INCIDENCE, RISK FACTORS, AND OUTCOMES OF ACUTE LIVER INJURY IN HOSPITALIZED ADULTS WITH ACUTE KIDNEY INJURY: A LARGE MULTICENTER STUDY
Lin Yuxin, Jiao Liu, Sheng Nie and Xu Xin
P.R. China

Background and Aims: Acute kidney injury (AKI) and acute liver injury (ALI) were associated with poor outcomes during hospitalization, respectively. However, the clinical outcome of AKI combined with ALI (AKI-ALI) was still remains unknown. The current study was aimed to describe the incidences, risk factors, and outcomes of AKI-ALI.

Method: The study population included AKI patients aged 18–99 years with enough serum creatinine testing and liver function testing (LFT) hospitalized at 19 medical centers throughout China between 2000 and 2021. AKI was defined by Kidney Disease Improving Global Outcomes and ALI was defined by the change of liver enzymes based on Asia Pacific Association of Study of Liver consensus guidelines. The Cox proportional hazards model was used to identify risk factors for AKI-ALI, and a time-dependent Cox proportional hazards regression model was used to estimate the association between AKI-ALI and in-hospital mortality.

Results: Among the 18461 patients with AKI (median [Interquartile Range, IQR] age, 65.71 [52.78, 76.36] years, 9725 (52.7%) males), ALI occurred in 1689 (9.1%) patients. Patients with AKI who were male, have used drugs including antibiotics, diabetes agents, diuretics, glucocorticoids, immunosuppressants, nonsteroidal anti-inflammatory drugs or vasopressors, with heart failure, respiratory failure, malignant tumor or shock, have lower platelets levels, higher aspartate aminotransferase levels or higher glutamyl transpeptidase levels at baseline, have received general surgery or thoracic surgery were associated with higher risk of AKI-ALI. Patients with AKI-ALI had longer length of hospital stay and were associated with a higher risk of in-hospitalized mortality (Hazard ratio [95% Confidence Interval] 1.51, [1.33, 1.72]) compared with patients with AKI but without ALI. In addition, a stronger association between AKI-ALI and in-hospital mortality was found in those with lower AKI grades (P for interaction = 0.036).

Conclusion: ALI was common among patients with AKI and AKI-ALI was associated with an increased risk of in-hospital mortality. This study suggests interventions for liver function early to improve in-hospital prognosis of patients with AKI.
Figure 1: Stratified analyses of the association between AKI-ALI and in-hospital mortality.

Table 1: Risk of in-hospital mortality in patients with AKI-ALI.

<table>
<thead>
<tr>
<th>Group</th>
<th>Total, No</th>
<th>Death, No (%)</th>
<th>Model</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI-nonALI</td>
<td>16772</td>
<td>1116(6.7)</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>AKI-ALI</td>
<td>1689</td>
<td>348(20.6)</td>
<td>3.49</td>
<td>&lt;0.001</td>
<td>3.72</td>
<td>&lt;0.001</td>
<td>3.62</td>
</tr>
</tbody>
</table>

Abbreviation: AKI-nonALI: acute kidney injury without acute liver injury; AKI-ALI: acute kidney injury combined with acute liver injury; HR: hazard ratio; CI: confidence interval; aHR: adjusted hazard ratio.

Model 1: adjusted for age group, sex, Charlson Comorbidity Index.
Model 2: adjusted for the variables in Model 1, along with time-dependent operations.
Model 3: adjusted for the variables in Model 2, along with comorbidities, need for intensive care, mechanical ventilation.
Model 4: adjusted for the variables in Model 3, along with time-dependent medications, aspartate aminotransferase, blood urea nitrogen, glucose, potassium, sodium, total cholesterol, uric acid, D-Dimer, time-dependent albumin, estimated glomerular filtration rate, percentage of neutrophils, international normalized ratio, platelets, urine protein, and white blood cell value.
ACUTE KIDNEY INJURY AS A RISK FACTOR FOR THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE AND MORTALITY IN HOSPITALIZED PATIENTS

Julio Francisco Colina García, Lucía Cordero García-Galán, Marta Rivero Martínez, Paúl Hernández, Celia González-García, Sergio Huerga Lozano, Justo César Sandino Pérez, Pilar Auñón, Eduardo Gutiérrez and Enrique Morales

University Hospital October 12, Nephrology, Madrid, Spain

Background and Aims: Acute kidney injury (AKI) is a complication that affects more than 5% of all hospital admissions and up to one third of patients admitted to critical care units. This entity, whose incidence is on the rise, remains a major cause of morbidity and mortality. In addition, AKI has been linked as an independent risk factor for mortality, especially in severe forms, and of those patients who survive, a percentage will develop chronic kidney disease (CKD) during follow-up. We conducted this study to analyse the incidence of CKD at 6 and 12 months follow-up in hospitalized patients with AKI, to identify possible risk factors leading to its development and to determine mortality in this group of patients.

Method: This is a retrospective study of a cohort of cases with AKI (baseline eGFR > 60 mL/min/1.73 m² without previous structural damage) from our hospital, taking place from June 2020 to February 2021. Regarding the evolution of the AKI, four possibilities were considered: recovery of normal kidney function, development of CKD at 6 months, development of CKD at 12 months or death during follow-up.

Results: We studied 148 patients (55% male), with a median age of 83 years (74-87). Thirty-six patients (24.3%) developed CKD at 6 months follow-up and 30 patients (20.3%) at 12 months. Forty-one patients (27.7%) died within the first 12 months following an episode of AKI. The risk factors identified for development of CKD at 12 months were older age (85 vs 77; p = 0.03), higher serum lactate dehydrogenase levels at admission (246 U/L vs 201 U/L; p = 0.04) and at 3 months (252 U/L vs 192 U/L; p = 0.039), and eGFR < 60 mL/min/1.73 m² at 1 week (74.5 vs 57; p = 0.004) and at 3 months (79 vs 50; p < 0.001) of follow-up. Identified risk factors and predictors of AKI-associated mortality were older age (84 vs 80.5; p = 0.018), concomitant oncological pathology (10.8% vs 7.4%; p = 0.018), higher Charlson index (6 vs 5; p < 0.001), higher AKI stage (p = 0.042), lower serum albumin levels at first (3.35 g/dL vs 3.90 g/dL; p = 0.014) and at third month (3.2 g/dL vs 4 g/dL; p < 0.001) of follow-up.

Conclusion: Our study showed a high incidence of CKD in patients who have had an episode of AKI. Several risk factors for development of CKD were identified, being the older age and the greater length of recovery period from AKI the most useful predictors in the clinical practice. AKI-associated mortality was very high in those older patients with higher comorbidity and persistence of AKI. Despite advances, we need non-classical biomarkers for early diagnosis and more effective therapeutic measures to avoid this high prevalence of CKD and mortality.

ASSOCIATION BETWEEN TRANSIENT AKI AND ALL-CAUSE MORTALITY IN PATIENTS WITH CRITICAL ILLNESS: AN INTERNATIONAL MULTICENTRE RETROSPECTIVE COHORT STUDY

Pang Mingzhen1, Sheng Nie1,2 and Fan Fan Hou1

1Guangzhou, P.R. China and 2P.R. China

Background and Aims: Transient acute kidney injury (AKI) is common in critically ill patients. However, the effect of transient AKI on prognosis of patients remains controversial. We aimed to investigate the association of transient AKI with all-cause mortality and kidney outcomes in critically ill patients.

Method: We conducted a multicentre retrospective cohort study involving 40168 critically ill patients from CRDS and 8657 patients from MIMIC-IV databases. Among them, 10147 patients were diagnosed as AKI according to KDIGO criteria and classified into transient (duration ≤ 48 h) and persistent (duration > 48 h). The study outcomes included mortality in hospital, by day 30 and up to 1 year, and risk of progression to CKD. We determined the effect of transient AKI on mortality by Cox regression model adjusting for confounding variables and analyzed CKD incidence by Fine-Gray model adjusted for difference in biologically plausible confounders.

Results: AKI occurred in 20.8% of 48825 critically ill patients, of which 36.4% was classified into transient and 63.6% persistent. Compared with those without AKI, Patients with transient AKI were older, more often received diuretic therapy and sedative therapy, and higher Charlson comorbidity index. After adjusting confounders including AKI severity, transient AKI was independently associated with increased risk of hospital death (HR 1.97, 95% CI 1.68 to 2.31), 30-day mortality (HR 1.73, 95% CI 1.51 to 1.98) and 1-year mortality (HR 1.31, 95% CI 1.19 to 1.44). Meanwhile, the risk of all-cause mortality increased with the duration of AKI in those with persistent patients (P < 0.05). Among survivors without history of CKD, compared with patients without AKI, transient AKI was also associated with increased risk of incident CKD after discharge (HR 1.61, 95% CI 1.33 to 1.96).

Figure 1: The hazard ratios of clinical outcomes among patients at different stages and durations of AKI. Hazard ratio were estimated using a Cox proportional hazard model with adjustment for gender, age, ethnicity, RASS, diabetes drugs, diuretics, NSAID, pressor, Scr, cardiac surgery, neurology, cerebral bleeding, cerebral infarction, CHD, CKD, congestive heart failure, diabetes, hypertension, sepsis, Charlson comorbidity index.
Table 1: The effect of AKI subtype on CKD incidence.

<table>
<thead>
<tr>
<th>Incident CKD</th>
<th>Events</th>
<th>Subhazard Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AKI</td>
<td>796/4191</td>
<td>1 (reference)</td>
<td></td>
</tr>
<tr>
<td>Transient AKI</td>
<td>144/457</td>
<td>1.61 (1.33, 1.96)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Persistent AKI</td>
<td>323/699</td>
<td>2.54 (2.12, 3.04)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*All-cause mortality was competing risk in Fine-Gray model adjusted for difference in biologically plausible confounders, including gender, age, ethnicity, RASS, diabetes drugs, diuretics, NSAID, pressor, Scr, cardiac surgery, neurology, cerebral bleeding, cerebral infarction, CHF, congestive heart failure, diabetes, hypertension, sepsis, Charlson comorbidity index and Kidney Disease: Improving Global Outcomes stage of AKI at AKI diagnosis.

**Conclusion:** Transient AKI was associated with increased risk of all-cause mortality and incident CKD in critically ill patients. Raising of awareness about transient AKI was required to urge clinician monitor such patients closer.

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**#4606**

**INNOVATIVE METHOD TO EVALUATE MATURATION OF NEWLY CREATED ARTERIO-VENOUS FISTULAS: INSIGHTS FROM A QUALITY IMPROVEMENT PROJECT**

Laura Rosales Merlo¹, Xiaoling (Janice) Ye¹, Hanjie Zhang¹, Brenda Chan¹, Marilou Mateo¹, Frank Van Der Sande¹², Jeroen Kooman¹³ and Peter Kotanko¹

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**Background and Aims:** Recently, we introduced central-venous oxygen saturation (ScvO2) and estimated upper-body blood flow (eUBBF) to monitor the maturation of newly created arterio-venous fistulas (AVF) in hemodialysis (HD) patients [1]. The approach was implemented in a clinical quality improvement project (QIP).

**Method:** The QIP involved two Renal Research Institute dialysis centers in New York City that use the Crit-Line monitor (CLM, Fresenius Medical Care, Waltham, MA, USA) as part of the standard of care. CLM measures automatically and non-invasively hematocrit and oxygen saturation (i.e., ScvO2 in patients with central venous catheter as vascular access). eUBBF was computed as described previously [1]. Patients with a with a newly created AVF were included, irrespective of their HD vintage. The QIP team comprised a registered nurse per clinic, two research physicians, and two data analysts. The team met weekly to assess the AVF maturation progress based on eUBBF and ScvO2 data that were displayed on a specific dashboard. Successful AVF maturation is typically accompanied by a rise in cardiac output and eUBBF that starts immediately after AVF creation. However, it is unknown what degree of eUBBF increase indicates a subsequently successful AVF maturation. To identify predictive eUBBF thresholds, we correlated eUBBF changes with the progress of AVF maturation in the six weeks following AVF creation. We defined maturation as unsuccessful when the newly created AVF required an intervention (e.g., angioplasty) or was abandoned.

**Results:** We studied 39 patients (age 56 ± 18 years; 25 males). Twenty-eight of them were incident patients. Two patients had a second AVF created. In 15 patients AVF maturation was unsuccessful. In these patients, eUBBF increased to an average of 119.2% (SD 35.2) compared to pre-AVF creation. In patients with successful AVF maturation (N = 24), eUBBF increased to an average of 153.7% (SD 31.6) (Figure 1). The difference between the groups is 34.4 percentage points (95% CI: 12.4 to 56.4; p = 0.003). Using eUBBF as a diagnostic measure to discriminate successful vs. failed AVF maturation, an area under the receiver operating characteristics curve of 0.824 (95% CI: 0.673 to 0.973; p = 0.001) was obtained. An eUBBF increase of 25% had a sensitivity of 59% and a specificity of 92% to predict AVF maturation outcomes.

**Conclusion:** Computation of eUBBF provides a simple and non-invasive means to track AVF maturation and predict its outcomes.

**REFERENCE**


**Figure 1:** Estimated upper body blood flow (eUBBF) in the six weeks after AVF-creation, expressed as % of pre-AVF creation eUBBF. The left box and whisker plot shows failed AVF maturations (N = 17; median 125.6%, IQR 92.9 – 134.3), the right successful ones (N = 24; median 146.7%, IQR 132.8 – 170.1). *Two patients had a second AVF created.*
ASSOCIATION BETWEEN NEPROLITHIASIS AND KIDNEY DISEASE PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE PATIENTS: A PROSPECTIVE COHORT STUDY
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1Seoul National University College of Medicine, Department of Internal Medicine, Seoul, Rep. of South Korea, 2Seoul National University Hospital, Department of Internal Medicine, Seoul, Rep. of South Korea, 3Hallym University Kangnam Sacred Heart Hospital, Department of Internal Medicine, Seoul, Rep. of South Korea and 4Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Borame Medical Center, Seoul, Rep. of South Korea

Background and Aims: Nephrolithiasis is a common complication in Autosomal dominant polycystic kidney disease (ADPKD) patients and is known to occur in up to 8% to 36% of the patients. A few in vitro and in vivo studies showed that kidney and ureter stone formation could accelerate renal disease progression in ADPKD. However, its association between nephrolithiasis and renal function deterioration remains unknown in ADPKD patients.

Methods: This is a study from single center prospective cohort called HOPE-PKD. A total of 410 study subjects with abdominal computed tomography (CT) scan within 1 year before the enrollment were analyzed. Study subjects were divided into two groups according to the CT results as follows: Patients with papillary calcification, calyceal stone, ureter stone, or renal stone were classified as a stone group and those without any stones were classified as no-stone group. Each was manually inspected. Patients were excluded who were not suitable for inclusion (e.g. paediatric data, incomplete records, patients without relevant diagnoses). Non-parametric Kruskal Wallis testing was used via R statistical software.

Results: There was no difference in the baseline characteristics between the stone group and the no-stone group. During a median 5.18 (interquartile range 3.41 - 8.03) year of follow-up, the primary and secondary outcomes occurred in 51 (12.4%) and 96 (23.4%) patients, respectively. In the unadjusted Cox regression analysis, there was no significant difference in the survival analysis between the two groups. However, after adjusting possible confounding factors (age, sex, body mass index, eGFR, comorbidity of hypertension and diabetes, serum uric acid, phosphorous and calcium level, results of PKD1 and PKD2 gene analysis, and Mayo classification), the stone group showed an increased risk of the primary and secondary outcome of HR 2.84 (95% CI 1.26 - 6.38; p-value 0.012) and HR 1.83 (95% CI 1.03 - 3.27; p-value 0.041), respectively compared to the no-stone group (Figure 1).

Conclusion: This is the first prospective cohort study showing that nephrolithiasis is associated with poor renal outcomes in patients with ADPKD. Further clinical studies of nephrolithiasis in ADPKD patients are warranted to improve renal outcomes.

Figure 1: The survival graph of composite renal outcome from multivariate Cox regression analysis. After adjusting with baseline age, sex, body mass index, estimated glomerular filtration rate, comorbidity of hypertension and diabetes, serum uric acid, phosphorous, calcium level, results of PKD1 and PKD2 gene analysis, and Mayo classification, there was significant risk increased in the stone group compared to the no-stone group with hazard ratio of and HR 1.83 (95% CI 1.03 - 3.27; p-value 0.041).

THE WEST OF SCOTLAND AND THROMBOTIC MICROANGIOPATHY
Ciaran Groome and Neal Padmanabhan
Queen Elizabeth University Hospital, Nephrology, Glasgow, United Kingdom

Background and Aims: Thrombotic microangiopathy (TMA) is a diagnosis made on tissue biopsy manifesting as acute organ dysfunction. It has a variety of causes broadly categorised as: primary hereditary/genetic, primary acquired, secondary, and infection-related [1]. On blood testing there is evidence of microangiopathic haemolytic anaemia (MAHA) –, thrombocytopenia, raised lactate dehydrogenase (LDH), reduced haptoglobin and fragments on blood film. Renal involvement with acute injury is evidenced by an elevation in creatinine; together with MAHA this is haemolytic uraemic syndrome (HUS). We sought to examine the TMA/MAHA population as it presented to nephrology in the West of Scotland and evaluate if there was differences in presentation between TMA with and without MAHA.

Method: This is a retrospective case series of adult nephrology patients. We extracted health data from the west of Scotland renal electronic patient records database Strathclyde Electronic Renal Patient Record (“SERPR”) provided by VitalDataClient. We ran a query to identify patients in whom TMA and/or MAHA and/or HUS was inputted as a diagnosis. 363 patients were identified. Each was manually inspected. Patients were excluded who were not suitable for inclusion (e.g. paediatric data, incomplete records, patients without relevant diagnoses). Non-parametric Kruskal Wallis testing was used via R statistical software.

Results: 134 patients were identified. The underlying diagnoses were: hypertension (n = 34), the atypical HUS (aHUS, n = 22), drug-induced (n = 17), autoimmune (n = 12), thrombotic thrombocytopenic purpura (n = 12), malignancy (n = 10), inflammatory (n = 10), peri-partum (n = 9). Others included: transplant-related, unknown, Ecoli 0157, diarrhoea-related, IgA, AAV, MPGN, and essential thrombocthyemia. Note: many patients had
multiple possible contributors to their diagnosis. The average biochemical levels at presentation were: creatinine 591umol/L; haemoglobin 82; platelet count 98.7; LDH 1674.2; bilirubin 34.5. Renal recovery was observed in n = 27 (19%); CKD3 n = 32 (24%); CKD4 n = 10(7%); CKD5 n = 7(5%); those who have progressed to ESRF (requiring renal replacement therapy) n = 40(31%); persisting transplant function n = 5(4%). 15 patients died (10%). We categorised patients into 3 groups. 1 – presence of TMA on biopsy without MAHA (n = 28). 2 – TMA on biopsy plus evidence of MAHA (n = 41). And 3 – MAHA in those not biopsied (n = 62). 3 patients with MAHA did not have TMA on biopsy. Those in group 1 had on average a lower serum creatinine at 331umol/L compared with group 2 (634 umol/L) and group 3 (666 umol/L). This result was significant p <0.05. Hypertension was a leading cause in groups 1 and 2. aHUS was not present in group 1 - all patients presented with MAHA. All peri-partum patients were in group 3 i.e. not biopsied.

Conclusion: It is evident from the dataset that hypertension is a major contributor to acute and chronic renal impairment. With aHUS contributing to a significant number of cases, given the advances in testing and therapeutics, early liaison with national services in complement disorders is paramount to protecting the kidneys. With 19% of patients regaining an eGFR >60ml/min prompt investigation is crucial to reducing the burden of disease. Long term renal follow-up should be offered. 21% of patients had no evidence of MAHA –we should be wary of excluding a TMA process in the absence of MAHA.

Method: Retrospective cohort study, analyzing data of 413 hospitalized adult patients. Immunosuppressed patients have been excluded. Descriptive analysis was done with t-test, Mann-Whitney and Fisher test. Mediation analysis was done modelling time-to-HAI through a Cox regression, including AKI as the exposure of interest, the use of medical devices as mediator, and age, diabetes and multimorbidity as confounders.

Results: Clinical characteristics of patients are shown in Table 1. AKI patients resulted more fragile and with a higher frequency of HAI (10.8% vs 5.9%, p = 0.07). Univariate logistic regression showed that the presence of urinary catheter (OR 5.053, 95% CI 2.040-12.520) and a longer hospital stay (OR 1.115, 95% CI 1.075-1.157) were risk factors for the development of HAI. Compared to other AKI etiologies, intrinsic AKI had a significantly higher frequency of HAI (38.5%, p<0.01) (Fig. 1). HAI frequency also increased progressively with increasing AKI stage (15.2% in stage I-II and 6.4% patients without AKI or stage I, p = 0.01) (Fig. 1). From the Cox regression model, none of the variables showed an independent association with HAI (Table 2). The total effect of AKI on HAI development was estimated in a HR of 0.970 (95% CI 0.438-3.016). Part of this effect was found to be mediated by the medical devices (HR 1.155, 95% CI 0.982-1.393), while the direct effect of AKI was a HR of 0.840 (95% CI 0.352-2.411).

Conclusion: AKI patients are more fragile and have a higher frequency of HAI, especially in intrinsic and stage II-III AKI. However, we didn’t observe an independent effect of AKI on the development of HAI. Further research is needed.

REFERENCE


#5895
HOSPITAL-ACQUIRED INFECTIONS IN HOSPITALIZED PATIENTS WITH ACUTE KIDNEY INJURY: A RETROSPECTIVE COHORT STUDY

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Background and Aims: Acute kidney injury (AKI) is recognized as a systemic disease that leads to several complications, including infections. However, only few studies have investigated the relationship between AKI and subsequent development of hospital-acquired infections (HAI). The aim of this study was to evaluate this relationship.
Figure 1: HAI incidence in patients with AKI, according to stage and cause of AKI. Intrinsic AKI has significantly higher frequency of HAI (38.5%, p<0.01). HAI frequency also increased progressively with increasing AKI stage.
Background and Aims: Multiple myeloma (MM) is the 2nd most common haematological neoplasm and a largely heterogeneous malignancy in what regards cytogenetics, clinical presentation, therapy response and overall survival. Renal impairment related to MM is known to be diagnosed in at least 50% of patients during the course of this disease. Recent studies have shown an association between high-risk cytogenetic abnormalities (CA) with lower disease-free survival and lower overall survival. However, there is still scarce knowledge in what regards the kidney implications of MM CA. The purpose of this study is to identify an association between MM cytogenetic profile and acute kidney injury (AKI) at presentation.

Method: This was a single-centre retrospective cohort study of all adult patients diagnosed with MM between Jan./2018-Dec./2021 in a tertiary care university hospital in Lisbon. Diagnosis of MM was made according to the International Myeloma Working Group criteria. Patient variables were collected from individual clinical records. Categorical variables were described as the total number and % and continuous variables as median (P25-P75). Normally distributed continuous variables were compared with the Student-t-test, non-normally distributed continuous variables with the Mann-Whitney U-test and categorical variables with the chi-squared test. A multivariable backward stepwise regression model was performed to investigate predictors for AKI. Statistical significance was defined as p < 0.05. Analyses were performed with the statistical software package STATA 16.0.

Results: 114 patients were included (median age 69.8±11.4 years, 48.1% male, 90.4% caucasian). 61.5% had hypertension, 21.2% diabetes and 33.9% CKD. 50% of patients during the course of this disease. Recent studies have shown an association between high-risk cytogenetic abnormalities (CA) with lower disease-free survival and lower overall survival. However, there is still scarce knowledge in what regards the kidney implications of MM CA. The purpose of this study is to identify an association between MM cytogenetic profile and acute kidney injury (AKI) at presentation.

Conclusion: Our study suggests there is an association between CA and AKI at presentation, which may implicate a worse overall survival, have treatment implications and highlights the need for prevention and early diagnosis. MM cytogenetics is being studied since the 2000s and research is still on going in the attempt of creating a MM profile that can guide prevention, treatment and predict outcomes. It is known that renal impairment in MM particularly at diagnosis is associated with lower overall survival. However, to the best of our knowledge, the potential association between cytogenetic profile and AKI has not been thoroughly studied.

#6719
ACUTE KIDNEY INJURY AND MULTIPLE MYELOMA-THE ROLE CYTOGENETICS: A COHORT STUDY
Natacha Rodrigues1, Carolina Branco1, Guilherme Sapinho3, Joana Vieira2, Hugo Silva1, Carlos Martins2, Graça Esteves2, João Raposo3 and José António Lopes4
1 Centro Hospitalar Universitário Lisboa Norte, EPE, Nephrology and Renal Transplantation, Lisbon, Portugal and 2 Centro Hospitalar Universitário Lisboa Norte, EPE, Hematology, Lisbon, Portugal

Background and Aims: Multiple myeloma (MM) is the 2nd most common haematological neoplasm and a largely heterogeneous malignancy in what regards cytogenetics, clinical presentation, therapy response and overall survival. Renal impairment related to MM is known to be diagnosed in at least 50% of patients during the course of this disease. Recent studies have shown an association between high-risk cytogenetic abnormalities (CA) with lower disease-free survival and lower overall survival. However, there is still scarce knowledge in what regards the kidney implications of MM CA. The purpose of this study is to identify an association between MM cytogenetic profile and acute kidney injury (AKI) at presentation.

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Results: 114 patients were included (median age 69.8±11.4 years, 48.1% male, 90.4% caucasian). 61.5% had hypertension, 21.2% diabetes and 33.9% CKD. 50% of patients during the course of this disease. Recent studies have shown an association between high-risk cytogenetic abnormalities (CA) with lower disease-free survival and lower overall survival. However, there is still scarce knowledge in what regards the kidney implications of MM CA. The purpose of this study is to identify an association between MM cytogenetic profile and acute kidney injury (AKI) at presentation.

Conclusion: Our study suggests there is an association between CA and AKI at presentation, which may implicate a worse overall survival, have treatment implications and highlights the need for prevention and early diagnosis. MM cytogenetics is being studied since the 2000s and research is still on going in the attempt of creating a MM profile that can guide prevention, treatment and predict outcomes. It is known that renal impairment in MM particularly at diagnosis is associated with lower overall survival. However, to the best of our knowledge, the potential association between cytogenetic profile and AKI has not been thoroughly studied.

#6962
INCIDENCE AND PROGNOSIS OF HYponATREMIA IN HOSPITALIZED PATients WITH ALCOHOLIC LIVER DISEASE
Tae Won Lee1,2,3, Seoje Lee1,2, Jun Ha Ryu1, Eunjin Bae1,2,3 and Dong Jun Park1,2,3
1 Gyeongsang National University College of Medicine, Jinju, Department of Internal Medicine, Jinju-si, Rep. of South Korea, 2 Gyeongsang National University, Institute of Health Science, Jinju-si79, Rep. of South Korea and 3 Gyeongsang National University Changwon Hospital, Division of Nephrology, Department of Internal Medicine, Changwon-si, Rep. of South Korea

Background and Aims: Hyponatremia is a common electrolyte disorder in hospitalized patients and has a poor prognosis leading to an increased risk of poor quality of life, morbidity, and mortality. Although the prevalence and prognosis of hyponatremia in early liver disease or alcoholic liver disease (ALD). Therefore, the purpose of this study was to investigate the prevalence and prognosis of hyponatremia in ALD group.

Method: We performed a retrospective, single centre study of patients admitted to the hepatology department from March 2016 to December 2022. Adults aged 18 years or older were included, and patients with liver cirrhosis, one of the common causes of hyponatremia, were excluded from the study. Based on the electronic medical records, the study was conducted by dividing the ALD group including alcoholic hepatitis and heavy alcohols into a control group.
Table 1:

<table>
<thead>
<tr>
<th></th>
<th>Non-ALD (n=711)</th>
<th>ALD (n=119)</th>
<th><em>p</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>59.3±16.6</td>
<td>53.3±11.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>283 (39.8%)</td>
<td>25 (21.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>128.6±19.7</td>
<td>123.8±19.1</td>
<td>0.014</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>76.6±11.3</td>
<td>77.6±12.6</td>
<td>0.387</td>
</tr>
<tr>
<td>BMI</td>
<td>23.7±3.6</td>
<td>22.8±3.8</td>
<td>0.011</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>176 (24.8%)</td>
<td>22 (18.5%)</td>
<td>0.138</td>
</tr>
<tr>
<td>HTN, n (%)</td>
<td>256 (36.0%)</td>
<td>28 (23.5%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>12.2±2.4</td>
<td>10.3±3.1</td>
<td>&lt;0.001</td>
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<tr>
<td>Platelet, 10^9/L</td>
<td>194.6±100.2</td>
<td>140.9±81.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>19.4±13.9</td>
<td>18.6±13.4</td>
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</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>0.97±0.70</td>
<td>1.12±0.90</td>
<td>0.080</td>
</tr>
<tr>
<td>Protein, g/l</td>
<td>6.7±0.9</td>
<td>6.1±1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, g/l</td>
<td>3.6±0.7</td>
<td>2.8±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR(EPI), ml/min/1.73m²</td>
<td>86.5±28.0</td>
<td>85.8±32.2</td>
<td>0.809</td>
</tr>
<tr>
<td>All-cause mortality, n (%)</td>
<td>86 (12.1%)</td>
<td>27 (22.7%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Death at admission, n (%)</td>
<td>28 (3.9%)</td>
<td>10 (8.4%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Serum Na &lt; 135 mmol/l</td>
<td>203 (28.6%)</td>
<td>64 (53.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum Na &lt; 120 mmol/l</td>
<td>29 (4.1%)</td>
<td>13 (10.9%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Readmission, n (%)</td>
<td>160 (22.5%)</td>
<td>47 (39.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of Stay (day)</td>
<td>10.5±9.1</td>
<td>13.5±10.9</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Results: A total of 830 patients were included, hyponatremia (under 135 mmol/L) occurred in 32.2%, and the ALD group showed a significantly higher prevalence than the control group (53.8% vs. 28.6, p<0.001). In addition, the ALD group was statistically significantly higher than the control group in mortality at hospitalization (8.4% vs. 3.9%, p = 0.031) and all-cause mortality (22.7% vs. 12.1%, p = 0.002). The length of hospital stay was significantly longer (13.5±10.9 vs. 10.5±9.1, p = 0.006), and the readmission rate was also higher in the ALD group (39.5% vs. 22.5%, p < 0.001). Kaplan-Meier analysis revealed significantly higher overall survival in the control group than the ALD group (87.9% vs. 77.3% p = 0.002).

Conclusion: Our study shows that ALD has a higher incidence rate of hyponatremia, which is followed by a poor prognosis, such as an increase in readmission rates, length of hospitalization, and mortality. Therefore, clinicians should realize the importance of electrolyte imbalance in ALD patients and strive to improve prognosis through early and appropriate treatment.

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National Clinical Research Center for Kidney Disease, State Key Laboratory of Organ Failure Research, Nanfang Hospital, Southern Medical University, Guangzhou, China, Division of Nephrology, Guangzhou, P.R. China

Background and Aims: Acute kidney injury (AKI) has been associated with increased risks of new-onset and worsening proteinuria. However, the epidemiologic data of post-AKI proteinuria was still lacking. This study aimed to determine the incidence, risk factors and clinical correlations of post-AKI proteinuria among hospitalized patients.

Method: This study conducted a multicenter cohort from Chinese Renal disease Data System (CRDS), including patients aged 18–100 years with hospital-acquired AKI (HA-AKI) hospitalized at 19 medical centers throughout China. AKI was defined according to the Kidney Disease Improving Global Outcomes (K/DOQI) creatine criteria. The results of both quantitative and qualitative urinary protein tests were used to determine post-AKI proteinuria. The primary outcome was the incidence of post-AKI proteinuria. Secondary outcomes included AKI recovery and kidney disease progression. Cox proportional hazard model with stepwise regression was used to determine the risk factors for post-AKI proteinuria. The associations of post-AKI proteinuria with kidney disease progression were analyzed by logistic regression models.

#3610
EPIDEMIOLOGY AND CLINICAL CORRELATES OF POST-AKI PROTEINURIA IN CHINESE HOSPITALIZED ADULTS
Table 1: Baseline characteristics of the HA-AKI patients stratified by post-AKI proteinuria.

<table>
<thead>
<tr>
<th>Variables</th>
<th>New-onset proteinuria dataset (N=6,206)</th>
<th>Worsening proteinuria dataset (N=5,137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Without N=4,104</td>
<td>Without N=4,243</td>
</tr>
<tr>
<td></td>
<td>With N=2,102</td>
<td>With N=894</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>Male (%)</td>
<td>63.5 (51.1, 73.8)</td>
<td>63.2 (50.5, 74.2)</td>
</tr>
<tr>
<td></td>
<td>2377 (57.9)</td>
<td>2665 (62.8)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.001</td>
<td>539 (60.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>Baseline eGFR, ml/min/1.73 m²</td>
<td>88.8 (66.2, 105.2)</td>
<td>71.2 (44.8, 95.4)</td>
</tr>
<tr>
<td></td>
<td>1085 (26.4)</td>
<td>1343 (31.7)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU</td>
<td>673 (16.4)</td>
<td>915 (21.6)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage AKI (%)</td>
<td>673 (16.4)</td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>3083 (75.1)</td>
<td>3051 (71.9)</td>
</tr>
<tr>
<td></td>
<td>1270 (60.4)</td>
<td>549 (61.4)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>631 (15.4)</td>
<td>682 (16.1)</td>
</tr>
<tr>
<td></td>
<td>418 (19.9)</td>
<td>159 (17.8)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>390 (9.5)</td>
<td>510 (12)</td>
</tr>
<tr>
<td></td>
<td>414 (19.7)</td>
<td>186 (20.8)</td>
</tr>
<tr>
<td>CCI</td>
<td>4 (3, 6)</td>
<td>4 (3, 6)</td>
</tr>
<tr>
<td></td>
<td>5 (3, 6)</td>
<td>5 (3, 6)</td>
</tr>
<tr>
<td>LOS, days</td>
<td>22 (15, 33)</td>
<td>21 (14, 33)</td>
</tr>
<tr>
<td></td>
<td>24 (16, 39)</td>
<td>24.5 (15, 39)</td>
</tr>
</tbody>
</table>

Abbreviations: SCR, Serum Creatinine; eGFR, estimated Glomerular Filtration Rate; ICU, Intensive Care Unit; HA-AKI, Hospital Acquired-Acute Kidney Injury; CCI, Charlson Comorbidity Index; LOS, Length of stay.

Table 2: The association of post-AKI new-onset and worsening proteinuria with the risk of kidney disease progression.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total N</th>
<th>Events N (%)</th>
<th>Crude model</th>
<th>Adjusted modela</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Events (%)</td>
<td>OR (95% CI)</td>
<td>aOR (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>Post-AKI new-onset proteinuria</td>
<td>No 1,137</td>
<td>256 (22.5%)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td></td>
<td>Yes 521</td>
<td>109 (20.9%)</td>
<td>0.91 (0.71, 1.17)</td>
<td>0.93 (0.70, 1.23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.47</td>
<td>0.60</td>
</tr>
<tr>
<td>Post-AKI worsening proteinuria</td>
<td>No 1,081</td>
<td>342 (31.6%)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td></td>
<td>Yes 212</td>
<td>85 (40.1%)</td>
<td>1.45 (1.07, 1.96)</td>
<td>1.64 (1.15, 2.32)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.02</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Abbreviations: HA-AKI, Hospital Acquired-Acute Kidney Injury; hospital-acquired acute kidney injury; CKD, Chronic Kidney Disease; OR, Odds ratio; CI, Confidence Interval; Ref., Reference.
aAdjusted for age, sex, status of drinking and smoking, baseline eGFR, ICU admission, CCI, stage AKI, hospital, division, hypertension, and diabetes.

Results: Of 6,206 HA-AKI patients without proteinuria at baseline, 2,102 (33.9%) had new-onset proteinuria, whereas, of 5,137 HA-AKI with baseline proteinuria, 894 (17.4%) had worsening proteinuria after AKI (Table 1). Higher AKI stage and preexisting CKD diagnosis were risk factors for new-onset proteinuria and worsening proteinuria, whereas treatment with RAS inhibitors was associated with an 11% lower risk of incident proteinuria. About 60% and 75% of patients with post-AKI new-onset and worsening proteinuria, respectively, recovered within 3 months. Worsening proteinuria was associated with a lower incidence of AKI recovery and a higher risk of kidney disease progression (Table 2).

Conclusion: Post-AKI proteinuria is common and usually transient among hospitalized patients. The risk profiles for new-onset and worsening post-AKI proteinuria differed markedly. Worsening proteinuria after AKI was associated with adverse kidney outcomes, which emphasized the need for close monitoring of proteinuria after AKI.

4124

SEX AND CARDIOVASCULAR DISEASE IN STAGE G2-5 CKD PATIENTS

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1Nephrology, Dialysis and Transplantation Unit, GOM BMM, Reggio Calabria, Italy; 2IHC-CNR, Section of Reggio Calabria, Reggio Calabria, Italy; 3Renal Research Institute, New York, United States of America; 4BIOGEM, Ariano Irpino, Italy and 5IPNET, Reggio Calabria, Italy

Background and Aims: Male sex is considered a major risk factor for cardiovascular (CV) disease in the general population, but the role of this factor in the high risk for CV disease in the pre-dialysis CKD population is still debated.

Methods: We tested the relationship between sex and fatal and non-fatal major CV events (myocardial infarction, heart failure, arrhythmia, angina, stroke, transient ischemic attack, peripheral vascular disease, major arterial or venous thrombotic episodes and sudden death) in a cohort including 759 stage 2-5 CKD consecutively recruited from 22 Nephrology units in southern Italy between October 2005 and September 2008. After the initial assessment, patients were followed up for a median time of 36 months (range 0.3–48 months).

Results: Four hundred fifty-five patients were males (60%). The proportion of smokers was about 4 times higher in males (71.4%) than in females (17.4%). Males and females differed in the prevalence of diabetes (38.5% versus 29.6%) and the frequency of background CV comorbidities (35.6% versus 19.7%, P<0.001). Waist circumference (100.9±12.4 versus 96±14.1 cm), eGFR (37.5±13.4 versus 33±12.7 ml/min/1.73 m²), 24-hour urinary protein excretion (median: 0.7 g/24h, IQR: 0.2-1.6 g/24h versus 0.5, IQR: 0.2-1.2 g/24h), and haemoglobin (13.4±1.9 versus 12±1.4 g/dL) were higher in males than in females. Serum phosphate (3.6±0.75 versus 3.9±0.75 mg/dL), hs-CRP (median: 2.2 mg/dL, IQR: 1.4-7.4 mg/dL versus 2.8 mg/dL, IQR: 1.2-6.4 mg/dL) and total cholesterol (178±3±42.1 versus 198±8±45.6 mg/dL) were lower in males than in females. During follow-up, 42 patients died, and 118 had fatal and non-fatal CV events. On univariate Cox regression analyses, male gender failed to be associated with all-cause mortality but was strongly related to the incidence rate of fatal and non-fatal major CV events [HR 1.75, 95% CI: 1.18-2.60, P=0.006]. Data adjustment for a series of major potential confounders did not materially affect the strength of this relationship [HR 1.78, 95% CI: 1.18-2.60].

Figure 1:
1.03-3.09). Further analysis testing the effect of age on major CV outcomes by gender showed an effect modification by this risk factor on the same outcome (P=0.037) because the hazard ratio of male versus female CV events increased progressively with ageing (Figure 1).

Conclusion: The excess risk for CV mortality by the male gender in the general population holds in stage G2-5 CKD patients. Age is a modifier for the excess risk for CV events in CKD patients because the risk excess of the male gender increases linearly across a wide age spectrum in CKD patients.

#3424
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Background and Aims: Antineutrophil cytoplasmic autoantibody-associated vasculitis (AAV) is a type of necrotizing small vessel inflammatory disease, including alveolar hemorrhage and rapidly progressive glomerulonephritis. Elderly patients with antineutrophil cytoplasmic autoantibody-associated vasculitis (AAV) commonly experience renal impairment and poor prognosis. Based on the cohort of inpatients with AAV in Peking Union Medical College Hospital, this study aimed to analyze the clinical manifestations, diagnosis and treatment characteristics of elderly patients compared with non-elderly patients, and establish a risk scoring system for predicting composite renal outcomes in patients with AAV in elderly patients.

Method: This retrospective observational study included all AAV patients hospitalized in a single-center tertiary hospital in China between January 2013 and April 2022. Patients aged ≥ 65 years were defined as elderly and randomly divided into development and validation cohorts (2:1). Logistic regression analysis was performed in the development cohort to analyze risk factors. The scoring system was established accordingly and further validated in the validation cohort.

Results: A total of 1203 patients were enrolled in the study, among whom the elderly group accounted for 36% with a mean age of 71.4 ± 0.3 years. The elderly group had a worse prognosis, a higher mortality rate (8.9% vs. 3.5%, P < 0.001), a higher rate of end-stage renal disease (17.6% vs. 10.2%, P < 0.001), and worsening renal function (7.4% vs. 4.5%, P = 0.04). Logistic regression showed that age > 75 years, chronic heart disease, elevated serum creatine, and D-dimer values were risk factors for poor prognosis in patients with AAV. The development and validation cohorts in AAV patients produced area under the curve values of 0.823 (0.794–0.862) and 0.833 (0.777–0.888), respectively (Figure 1). When the risk score was ≥ 2 points, the risk of acquiring composite renal outcomes increased significantly with a sensitivity and specificity of 75.0% and 79.9%, respectively.

Conclusion: We established risk-scoring systems based on baseline clinical characteristics to predict composite renal outcomes in patients with AAV. Our results suggest that more attention should be paid to elderly patients who have severe renal impairment and active inflammation.

Figure 1: The scoring system for predicting composite renal outcomes and the receiver operating characteristic curve (ROC) in AAV patients.

#3958
PROTON PUMP INHIBITORS AND THE RISK OF ACUTE KIDNEY INJURY IN PATIENTS RECEIVING IMMUNE CHECKPOINT INHIBITORS: A POPULATION-BASED COHORT STUDY
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1Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus N, Denmark, 2Aarhus University, Department of Clinical Medicine, Aarhus, Denmark, 3Aarhus University Hospital, Department of Renal Medicine, Aarhus N, Denmark and 4Aarhus University, Department of Clinical Medicine and Biomedicine, Aarhus, Denmark

Background and Aims: Proton pump inhibitors (PPI) are commonly used in cancer patients. Multiple studies have found that PPI use is associated with a more than 2-fold increased risk of acute kidney injury (AKI) in patients treated with immune checkpoint inhibitors (ICI). However, this association could possibly be explained by confounding by indication for PPI use.

Method: In a population-based cohort study, we compared the risk of AKI in users and non-users of PPI among cancer patients treated with ICI in Denmark during 2011-2021. We assessed exposure to PPI by filled prescriptions for PPI within 90 days before ICI initiation and identified AKI events within the first year after ICI initiation using plasma creatinine measurements from laboratory databases. We included information on potential confounders including important comorbidities and comedication. We estimated the propensity score for PPI use using logistic regression and calculated unweighted and standardized mortality ratio (SMR)-weighted absolute risks and hazard ratios (HRs) of AKI. To address any switch in PPI exposure during follow-up, we did an additional per-protocol analysis censoring patients upon switch in PPI exposure. We furthermore applied inverse probability of censoring (IPC) weights to mitigate informative censoring.

Results: We included 9,955 cancer patients treated with ICI. Among these, 2,668 (26.8%) were users of PPI. During the first year of follow-up, AKI occurred in 1,932 of the included patients, yielding an overall unweighted incidence rate of 30.1 per 100 person-years and a 1-year AKI risk of 21.3%. PPI users had an increased risk of AKI compared with non-users (1-year risk, 24.4% versus 20.2%; HR, 1.17 [95% CI, 1.04-1.31]); however, this association attenuated when accounting for confounders by SMR weighting (SMR-weighted 1-year risk, 24.0% versus 23.3%; SMR-weighted HR, 1.05 [95% CI, 0.93-1.18]). In the per-protocol analysis, the unweighted HR was 1.82 (95% CI, 1.60-2.07), while the SMR- and IPC-weighted HR was 1.22 (95% CI, 1.03-1.45).

Conclusion: PPI use at the time of ICI initiation was not associated with an increased risk of AKI after SMR weighting. When considering switching of PPI exposure during follow-up, we observed that PPI use was associated with an increased risk of AKI; however, the association was much weaker than previously reported.

#4489
EFFECT OF RENAL ARTERY CALCIFICATION ON THE OCCURRENCE OF ACUTE KIDNEY INJURY AND MORTALITY
Hae Eun Jeon1, Soie Kwon2 and Jin Ho Hwang1
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Background and Aims: Renal artery stenosis not only causes secondary hypertension and drug-resistant hypertension by enhancing renin-angiotensin-aldosterone system (RAAS), but also causes ischemic acute/chronic kidney injury by impeding blood flow to the kidneys. Renal artery calcification (RAC) suggests chronic severe ath erosclerotic changes, but the relationship between its severity and clinical prognosis has not been established.

Method: This study was conducted on subjects aged 60 years or older who had serum creatinine measured more than 3 times among patients prescribed and performed abdominal CT at Chung-Ang University Hospital from January 1, 2005 to February 28, 2020. The renal artery calcification score (RACS) was obtained by Agatston score measurement, and the incidence of AKI and mortality were compared between the groups.

Results: Of a total of 29,410 patients, 17,478 had no RAC and 11,932 was RAC (+). The median value of the group in which RACS was measured was 117.8. The prevalence and history of diabetes mellitus (DM), hypertension, dyslipidemia, and history of cardiovascular disease were significantly higher in the RAC (+) group, lower eGFR and higher proteinuria, and higher prescribing rates of ARB or ACEi, spironolactone, and statin. In the group of RAC (+), the incidence of AKI (HR 1.231, CI 1.174-1.292, P < 0.001, Figure 1) and all-cause mortality (HR 1.265, CI 1.182-1.355, P < 0.001) was high. Regardless of DM or RACS, the risk of AKI was higher in those who were prescribed ACEi or ARB
Figure 1: AKI-free survival by renal artery calcification.

(HR 1.786, CI 1.7-1.875, P < 0.001). In patients with DM, mortality risk was reduced in those taking ACEi or ARB regardless of the presence of RACS (HR 0.759, CI 0.645-0.892, P < 0.001).

**Conclusion:** RAC(+) was associated with higher AKI and mortality risk than RAC(-). The use of RAAS blockades increased the risk of AKI regardless of the presence of RAC, but reduced mortality in patients with DM regardless of the presence or absence of RACS.

**#5525**

**NEPHROTOXICITY OF CHIMERIC ANTIGEN RECEPTOR T CELL (CAR-T) THERAPY: ACUTE KIDNEY INJURY AND ELECTROLYTE DISORDERS**

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**Background and Aims:** Chimeric antigen receptor T cell therapy (CAR-T) has improved the prognosis of patients with refractory hematologic malignancies. The most important toxicities are the cytokine release syndrome (CRS), where interleukin 6 (IL-6) plays a major role, and the immune effector cell-associated neurotoxicity syndrome (ICANS). A low incidence of acute kidney injury (AKI) with a high frequency of electrolyte imbalance has been described with CAR-T therapy. The aim of our study is to describe the nephrotoxicity of CAR-T therapy and to focus on AKI and the physiopathology of hypophosphatemia.

**Method:** A prospective single-center case series was performed which included all patients undergoing CAR-T therapy between 2020 and 2022. Clinical data included medical history, previous chemotherapy treatments, concomitant treatments, and clinical evolution. Daily monitoring of renal function, electrolytes and IL-6 was obtained after infusion of CAR-T. A urine sample was obtained on days 0, +7 and +14 with parathyroid hormone (PTH) and 25-OH vitamin D. AKI was classified according to the KDIGO criteria.

**Results:** 40 patients received CAR-T therapy during the follow-up period. The median age was 62 years. The same number of men as women were included. The most frequent comorbidities were hypertension (27.5%), followed by diabetes (12.5%) and chronic kidney disease (12.5%). 12 patients presented AKI. Baseline serum creatinine (SCr) in patients with AKI was 0.9 mg/dL (0.68-1.04) with a SCr peak of 1.27 mg/dL (1.1-1.7). The time from CAR-T therapy infusion to SCr peak was 6.5 days (4-10). Of these 12 patients, 8 presented stage 1, 3 stage 2, and 1 stage 3 AKI. There were no differences between the AKI and non-AKI group in baseline characteristics, inflammatory markers, CRS, ICANS or hospital length stay. Hypophosphatemia was the most frequent electrolyte imbalance, occurring in 36 patients (90 %), 22 (61 %) patients experienced moderate hypophosphatemia (phosphorus < 2 mg/dL) while 14 (39 %) patients experienced mild hypophosphatemia. 29 patients (72 %) presented hypokalemia and 25 patients (62.5 %) hyponatremia. Patients with moderate hypophosphatemia had a significantly higher elevation of IL-6 but there were no differences in PTH or vitamin D (Table 1). Although there were no significant differences in fractional excretion of filtered phosphate (FEPO4), patients with moderate hypophosphatemia trend to have higher FEPO4 values.

**Conclusion:** Electrolyte disturbances are common in CAR-T therapy, with hypophosphatemia being the most frequent. There is probably a mechanism for renal phosphorus loss related to systemic inflammation. AKI is less frequent and has mild characteristics in these patients.
Table 1: Grade of hypophosphatemia with inflammatory markers and phosphorus homeostasis parameters.

<table>
<thead>
<tr>
<th></th>
<th>All patients (N=40)</th>
<th>Moderate hypophosphatemia (n=22)</th>
<th>Mild-no hypophosphatemia (n=18)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Scr (mg/dL)</strong></td>
<td>0.71 (0.48-0.9)</td>
<td>0.56 (0.44-0.75)</td>
<td>0.77 (0.70-1.01)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>AKI (pg/mL)</strong></td>
<td>12 (30 %)</td>
<td>6 (27 %)</td>
<td>6 (33 %)</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>PTM +0 (pg/mL)</strong></td>
<td>53 (39-84)</td>
<td>56 (40-92)</td>
<td>52 (38-60)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>PTM +7 (pg/mL)</strong></td>
<td>59 (39-108)</td>
<td>77 (41-166)</td>
<td>50 (39-79)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Vit D +0 (ng/mL)</strong></td>
<td>11 (6-87)</td>
<td>9 (7-15)</td>
<td>13 (10-17)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Vit D +7 (mg/mL)</strong></td>
<td>11 (6-15)</td>
<td>10 (6-14)</td>
<td>12 (10-15)</td>
<td>0.26</td>
</tr>
<tr>
<td><strong>FEPO4 +7 (mg/mL)</strong></td>
<td>18 (13-63)</td>
<td>22 (17-44)</td>
<td>13 (7-24)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>IL 6 peak (ng/mL)</strong></td>
<td>408.5 (28-2815)</td>
<td>1958 (283-5700)</td>
<td>80 (50-452)</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>A1M u +7 (mg/dL)</strong></td>
<td>3.2 (1.6-2.5)</td>
<td>2.8 (1.5-2.1)</td>
<td>2.6 (1.3-3.0)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>CRS</strong></td>
<td>21 (87 %)</td>
<td>20 (87 %)</td>
<td>19 (83 %)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>ICANS</strong></td>
<td>21 (87 %)</td>
<td>20 (87 %)</td>
<td>19 (83 %)</td>
<td>0.15</td>
</tr>
</tbody>
</table>


**#6825**

**ECOLOGICAL APPROACH FOR KIDNEY REPLACEMENT THERAPY IN CRITICAL CARE: SLED MAY BE A STRATEGY**

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**Background and Aims:** Dialysis has an enormous environmental impact, not only for disposable consumables, but also for the water and energy consumption. Despite increasingly evidence regarding comparable outcomes between continuous kidney replacement therapy (CKRT) and slow low efficiency dialysis (SLED), ecological-based endpoints are not frequently evaluated. Literature in critical care concerning the environmental impact of these techniques is scarce. We aimed to determine the waste production, water and energy consumption in SLED and CKRT and identify the technique with higher environmental impact.

**Method:** We conducted a cross-sectional, observational, single-center study in patients with acute kidney injury requiring kidney replacement therapy admitted to an intensive care unit (ICU). We analyzed the waste weight of each dialysis technique (Fresenius Medical Care 5008 for SLED and Baxter Prismaflex for CKRT) before and after the treatment. We estimated the unpurified water consume of 8-hours and 12-hours SLED treatment was 237 L and 345 L, respectively. For CKRT, we estimated a consume of 43.2 L a day and 129.6 L for a 72-hour treatment. SLED had an energy consumption of 5.71 kW and 8.43 kW, for 8-hours and 12 hours treatment, respectively. The CKRT consumed about 12 to 14.4 kW per day.

**Results:** A SLED session produced 1600 g of waste (1200 g was hazardous and 400 g was non-hazardous waste). A CKRT session produced 2700 g of waste, not considering the substitution solution volume, which can vary up to a maximum of 15000 g/treatment. Waste consumables for each technique are discriminated in Table 1. The unpurified water consume of 8-hours and 12-hours SLED treatment was 237 L and 345 L, respectively. For CKRT, we estimated a consume of 43.2 L a day and 129.6 L for a 72-hour treatment. SLED had an energy consumption of 5.71 kW and 8.43 kW, for 8-hours and 12 hours treatment, respectively. The CKRT consumed about 12 to 14.4 kW per day.

**Conclusion:** Our study highlights the quantity of waste produced, water and power consumption of dialysis techniques in the critical patient. CKRT produces more hazardous waste, that generates a larger carbon footprint. Hazardous waste cannot be recyclable and implies specific management and disposal, which is more expensive and laborious than non-hazardous. CKRT has also a higher power consumption due to treatment duration and technology used to generate electricity. SLED has higher water consumption, nevertheless, current strategies used in hemodialysis units could also be implemented in ICU to minimize this effect. For example, the rejected water can be reused to agriculture and toilet flushing; more efficient water purification system with a lower proportion of rejected water can also reduce water consumption. SLED has unequivocal clinical benefits in the critical patient and, from an ecological perspective, seems to be a more sustainable option.
Background and Aims: Haemolytic uraemic syndrome (HUS) is a disease which affects the kidneys presenting with acute kidney injury (AKI), microangiopathic haemolytic anaemia (MAHA) and thrombocytopenia. In 90% of cases it is precipitated by shiga-toxin producing E coli [1]. The remaining 10% of cases have been termed atypical haemolytic uraemic syndrome (aHUS) and complement system overactivation is the underlying mechanism [2]. This can take the form of autoantibody production or complement gene mutations [2]. Eculizumab has been proven to significantly ameliorate disease progression [3]. In this series, we sought to explore the West of Scotland’s experience with this ultra-rare population evaluating outcomes and access to therapies.

Method: This is a retrospective case series. We extracted data from the west of Scotland renal electronic patient records database Strathclyde Electronic Renal Patient Record (“SERPR”) provided by VitalDataClient. We ran a query to identify patients in whom TMA and/or MAHA and/or HUS was inputted as a diagnosis. 363 patients were identified. Filtering for aHUS in the adult population, 22 patients were identified spanning 19 years.

Results: The incidence rate is 0.43/million of the population. 14 patients had either genetic mutations (n=13) or acquired antibodies. Genetic mutations: C3, n=5; Complement Factor H (CFH) n=5; Complement Factor I (CFI) + CD46 n=1; CFI alone n=1, variants of uncertain significance n=1. One patient with CFH mutation was positive for the nephritic factor; another with CFH mutation had detectable Factor H autoantibodies. The only acquired patient without a genetic mutation had Factor H autoantibodies. The mean levels of biochemical markers at presentation are: Haemoglobin (g/L) 72; Creatinine, (μmol/L) 603; Platelet count, (×10⁹/L) 89; Lactate dehydrogenase (IU/L) 1853; and Total Bilirubin, (μmol/L) 90. Eculizumab is an available treatment for aHUS utilised in coordination with The National Renal Complement Therapeutics Centre. The outcomes of patients with and without genetic defects and/or antibodies, with the number in parenthesis denoting those who received Eculizumab, are listed below, stratified by CKD staging. Those with identifiable genetic/acquired defects: Recovered 2(2); CKD3 3(3); CKD4 1(0); Renal replacement therapy dependent 7(6)*. Total 14(11). Those with no identifiable defect: Recovered 2(2); CKD3 2(0); CKD4 0; Renal replacement therapy dependent 4(3)**. Total 8(5). *4 of the 6 have successfully functioning transplants. **Of the 3 patients who received Eculizumab, 2 had a brief trial. The third received it after transplantation but the transplant failed.

Conclusion: It is clear from the above data that long term renal outcomes are poor for these patients with the majority being left with residual impairment to some degree. Furthermore, in those for whom transplantation is being considering, it is imperative that Eculizumab is introduced, if already withdrawn, to cover transplantation and is maintained to prevent recurrence in the new organ. Even in those without RRT requirements, use of the C5 inhibitor is necessary to stabilise and allow for recovery of at least some native function. Therefore, clinicians in encountering MAHA and TMA in their practice should always consider aHUS and liaise with the Newcastle centre promptly to ensure diagnostics are sent and treatment can be commenced, otherwise the outcomes can be catastrophic.

REFERENCES
Results: Of the 29,635 patients administered iodine-based contrast media, 6.3% were included. There were 139 patients who mix-administered iodine-based contrast media and GBCA. Mixed group showed significant higher rate of development of PC-AKI compared with iodine-based contrast media alone group in total cohort (adjusted OR, 3.09 [95% CI, 2.09 – 4.58]) and PSM cohort (adjusted OR, 2.38 [95% CI, 1.25 – 4.55]). On multivariate analysis to investigate risk factors in Mixed group, osmolality (adjusted aOR, 1.05 [95% CI, 1.01–1.10]) and eGFR (adjusted OR, 0.931; 95% CI, 0.883–0.983) were associated with PC-AKI.

Conclusion: Mixed administration of iodine-based contrast media and GBCA on same day at ED visit may be a risk factor for PC-AKI compared with single administration of iodine-based contrast media alone. Osmolality and eGFR may be independently associated with PC-AKI after mixed administration of iodine-based contrast media and GBCA.

#5044
FLUID BALANCE AND GLOMERULAR FILTRATION RATE AS PREDICTORS OF OUTCOME AMONG COVID-19 PATIENTS IN THE ICU

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Background and Aims: Acute kidney injury (AKI) is associated with an increased risk of progression to a severe form in every disease and, moreover, is associated with an increased mortality, and so it is also with coronavirus disease 2019 (COVID-19). AKI is a frequent complication in COVID-19 patients admitted to ICU for severe respiratory failure. ICU treatment itself indirectly could cause or exacerbate renal damage, through suboptimal fluid management, drug toxicity, or low human resources. The aims of this study were to assess AKI prevalence, fluid balance and glomerular filtration rate as a predictor of outcome in COVID-19 patients treated in the intensive care unit.

Method: We retrospectively analysed all adult patients admitted to the ICU at a regional hospital in northern Bavaria, from 1st March to 31st December 2020. Clinical data and laboratory results were retrospectively retrieved from the hospital information system and electronic case files. According to the severity of AKI based on the KDIGO criteria, and laboratory values were followed on the first 7 days on the ICU. In total 320 patients patients were included in the study. Level of significance was set to p<0.05.

Results: The mean age was 65±19 years, 135 (42%) patients were females, 185 (58%) were males. Median length of ICU stay was 7 (2–13 days) in females, and 8 days (4–21 days) in males. At the ICU, 177 patients needed some form of ventilation, from which 109 needed Invasive mechanical ventilation). During ICU stay, 81 patients have died, with mortality rate of 25%. Patients with AKI (n=48, 15%) at the admission to the ICU, had 2.1 times higher risk of death at the ICU than patients without AKI. There was a statistically significant difference in ICU survival based on a glomerular filtration rate, fluid balance, CRP and leukocyte values, F=1.957, p=0.026; Wilk’s Λ=0.724, partial η2 = 0.276

Conclusion: Acute kidney injury is common in coronavirus disease 2019, and it is associated with poor clinical outcomes. Even first couple of days at the ICU could point to the outcome, with markers of inflammation, glomerular filtration rate, and fluid balance being most valuable variables.
among children. Such information is important for AKI prevention, resource allocation, and future research. In this study, we aimed to examine overall temporal changes in the rate of hospital- and community-acquired pediatric AKI and to describe associated changes in potential underlying risk markers.

**Method:** In this population-based cohort study, we included children aged 0-17 years from 1 January 2007 to 31 December 2021 in Denmark. In 2021, the Danish population consisted of 1,168,222 children. We obtained clinical plasma creatinine measurements from the Danish laboratory databases to identify all KDIGO-defined AKI episodes within the study period. For each child, only the first AKI episode per year was included and we defined an AKI episode as a period of 30 days. AKI was defined as community-acquired if the plasma creatinine at time of AKI was taken in the outpatient clinic or the first day of admission/acute setting. We estimated the annual AKI rate for first AKI episodes in a year among children residing in an area covered by the laboratory databases divided by the number of children residing in this area in the same year. Unadjusted rates as well as sex- and age-standardized rates was reported. Using Danish medical databases, we identified potential risk markers for AKI, such as use of nephrotoxic medication, surgery, sepsis, and perinatal factors including low birth weight and preterm birth.

**Results:** In total, 14,262 children contributed with 16,492 AKI episodes. The average annual rate of AKI was 149 per 100,000 children and was stable throughout the study period (figure). Of the AKI episodes, 10,921 (66.2%) were community-acquired and 12,714 (77.1%) were stage 1 AKI. No major changes were seen in the prevalence of risk makers among AKI episodes.

**Conclusion:** The rate of AKI among Danish children was stable from year 2007 to 2021 and potential risk markers were largely similar over time.

**#4356**

**DYNAMIC EFFECT OF PROTEINURIA ON ADVERSE KIDNEY OUTCOMES WITH TARGETED MAXIMUM LIKELIHOOD ESTIMATION METHOD: RESULT FROM THE KNOW-CKD STUDY**

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**Background and Aims:** Proteinuria is a risk factor for the progression of chronic kidney disease (CKD), but its causal inference may be challenging due to time varying exposure and confounding, the changing its degree, and loss to follow up.

**Method:** A total of 1,223 patients enrolled as part of The Korean Cohort Study for Outcome in Patients With Chronic Kidney Disease (KNOW-CKD) were analyzed at 3 observational points (baseline, 3-year, early, and 7-year, late) at which spot urine protein creatinine ratio (UPCR) was measured. We used longitudinal targeted minimum loss-based estimation (TMLE) and marginal structural models (MSM) to estimate the cumulative incidence of adverse kidney outcomes (eGFR halving and kidney failure requiring replacement therapy) of dynamic exposure to high proteinuria (UPCR ≥1g/g) comparing counterfactuals (UPCR <1g/g) adjusted for time varying confounding (systolic blood pressure, estimated glomerular filtration rate, and renin-angiotensin-aldosterone blockers) and baseline covariates (age, sex, diabetes, cardiovascular disease, and smoking).

**Results:** Patients with sustained high proteinuria throughout 7-year follow-up had significant higher risk of renal events than those with counterfactuals (relative risk [RR], 3.120; 95% confidence interval, 2.150-4.528; P < 0.001). The RR were 0.168 (0.055-0.517; P = 0.002) and 0.613 (0.337-1.114; P = 0.108) for early and late proteinuria reduction comparing sustained high proteinuria, respectively. In MSM, hazard ratio (HR) of accumulative high proteinuria frequency were 1.612 (1.463-1.844; P < 0.001) up to 3 years and 1.102 (0.877-1.387; P = 0.404) up to 7 years, respectively.

**Conclusion:** In CKD patients, sustained higher proteinuria is the main risk factor during the entire observation period. However, considering dynamic exposure, proteinuria reduction from the beginning has a protective effect on renal progression, but the effect weakens as the observation period becomes longer.
BP, background CV comorbidities, anti-hypertensive drugs, haemoglobin, albumin, phosphate, hs-CRP, 24h proteinuria, and eGFR, the hazard rate (HR) of renal events decreased in a dose-dependent fashion from the lowest bicarbonate trajectory (reference category, HR 1) to the moderate (HR:0.70, 95%CI 0.43-1.14), high moderate (HR:0.54, 95%CI 0.31-0.93), and high bicarbonate category (HR:0.31, 95%CI 0.12-0.80) (P for trend=0.005). Thus, for patients in the high bicarbonate category (27.9± 2.8 mEq/L), there is an 69% risk reduction for renal composite endpoint.

Conclusion: In a longitudinal analysis of a cohort of CKD patients, high bicarbonate levels are associated with a substantially reduced risk of renal events. These findings represent a strong call for well-designed, adequately powered randomised trials testing the effect of bicarbonate supplements or pharmacologic interventions that increase serum bicarbonate on renal outcomes. Given the substantial risk reduction in patients in the highest bicarbonate trajectory, these trials are an absolute clinical research priority.

THE EFFECT OF COVID-19 WITH OR WITHOUT ACUTE KIDNEY INJURY ON INPATIENT MORTALITY IN ENGLAND

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Background and Aims: COVID-19 and acute kidney injury (AKI) are each associated with increased mortality but the interaction between these two conditions has not been adequately investigated with appropriate control groups. The aim of this national study was to assess patient characteristics and mortality and well as associations with higher mortality in patients with or without COVID and with or without AKI.

Method: We extracted 3,324,748 finished consultant episodes (FCE) of all adult patients admitted patients between March 20 and March 21 from England’s national database of all hospitals. We excluded patients on chronic dialysis, acute dialysis in CKD, acute dialysis with no AKI codes or not residing in England. We also excluded multiple FCEs within same spell and duplicate FCEs. We divided the study period in two phases of SARS CoV-2 strains. "Other" strain of SAR CoV-2 was dominant between 1st March 2020 and 21st December 2020 and "Alfa" strain was dominant between 22nd December 2020 to 17th May 2021. The end date of each phase was based on more than 50% decline in each variant. We further categorised phases based on publication of the RECOVERY trial.

Results: There were 663,628 patients with 2,385,337 admissions out which 856,544 had AKI as identified by N17 codes while 1,528,793 had no AKI. There were 1,008,774 admissions in 133,988 patients who did not have AKI or COVID (group 1) and 520,019 admissions in 256,037 patients who had COVID (group 2). Amongst admission with AKI, there were 630,342 admissions in 218,270 patients who did not have COVID-19 (group 3) and 226,202 admissions with COVID in 55,333 patients (group 4). Patients in group 4 were older (75.4 ± 13.8 years) and had greater length of stay (17.1 ± 17 days) than all other groups. Acute dialysis was performed in 1.4% of patients in group 3 and 3.6% of patients in group 4. Crude in-hospital mortality was highest in group 4 at 28.7% and lowest in group 1 (1.1%). Critical care requirement was lowest in group 1 (1.2%) compared to group 4 (10.9%) as was ITU mortality (4.8% versus 47.8%). In multivariable analysis, when compared with group 1, patients in group 4 had highest odds of death (OR 22.28, 95%CI 21.79, 22.78) followed...
by patients with group 2 (OR 9.67, 95%CI 9.46-9.88) (Figure 1). Patients in group 3 had OR of 6.44, 95%CI 6.30-6.58. Odds of death were lower during post-RECOVERY phase with "Other" (OR 0.80, 95%CI 0.79, 0.81) and "Alfa" (OR 0.86, 95%CI 0.85, 0.87) SARS-CoV-2 strains (Figure 2).

**Conclusion:** This national study shows that the COVID pandemic had great impact on mortality in England and the odds of death increased substantially when complicated by AKI. Moreover, AKI associated with COVID was associated with a substantially higher odds of death than AKI due to other causes. The change in practice after publication of the RECOVERY trial was associated with a lower odds of death.

#3372

**HOST RESPONSE CHANGES ASSOCIATED WITH PERSISTENT ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS WITH COVID-19**

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**Background and Aims:** In sepsis, the dysregulated host response has been, at least in part, linked to development of acute kidney injury (AKI) and its duration. Data on the host response to COVID-19 and development of persistent-AKI (duration > 48 h) in critically ill patients are scarce. We hypothesized that COVID-19 infected patients who develop persistent-AKI have different host response aberrations. To address this hypothesis, we sequentially measured host immune response biomarkers in critically ill patients admitted to the intensive care unit (ICU).

**Method:** We included patients admitted to the ICU from two tertiary hospitals and one primary care hospital between March and July 2020 (first wave). All patients had PCR-confirmed COVID-19. Excluded were readmitted patients, transfers from another ICU, and patients with chronic kidney disease (CKD stage 3 or higher). The presence of AKI was assessed by using hourly urine output and daily serum creatinine levels, and classified into 3 stages according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria. In a subset of patients admitted to the two tertiary hospitals (n=113), 41 plasma protein biomarkers were sequentially measured using a Luminex platform or ELISA, and categorized into five pathophysiological domains: systemic inflammation, endothelial cell activation and dysfunction, coagulation activation, kidney dysfunction, and lung dysfunction. Mixed effects models were used to analyse longitudinal data.

**Results:** Of 185 ICU admissions enrolled, 8 were excluded because of existing CKD. Of the remaining 177 patients, 106 patients (59.9%) had AKI within the first 48 h of admission; of these, 76 patients (71.7%) had persistent AKI and 30 patients (28.3%) transient AKI. Patients with persistent AKI more often were obese and had a history of hypertension. A higher disease severity – as determined by the sequential organ failure assessment (SOFA) score - was observed in the persistent AKI group, which was driven by the renal component as the non-renal SOFA score was similar between no-AKI, transient- and persistent AKI. Sequential protein biomarker analyses revealed that five biomarkers were significantly elevated in persistent-AKI compared to transient-AKI in the first four days, mainly related to inflammation (triggering receptor expressed on myeloid cells-1 [TREM-1], p=0.003; tumour necrosis factor receptor 1 [TNF-R1], p < 0.001; lung dysfunction (clara cell secretory protein [CC16], p < 0.001), and kidney dysfunction (Cystatin C [p < 0.001]; neutrophil gelatinase-associated lipocalin [NGAL], p < 0.001). Plasma protein biomarkers reflective of endothelial cell- and coagulation activation were not different in patients with persistent-AKI as compared to patients with transient-AKI. No differences in plasma biomarkers were observed between transient AKI and no-AKI.

**Conclusion:** Transient AKI and no-AKI revealed little to no differences, while the persistent AKI group demonstrated stronger host response anomalies across the pathophysiological domains of inflammation and lung dysfunction. In contrast to what has been observed in non-COVID-19-related sepsis, endothelial injury and coagulation activation markers were not associated with AKI trajectories. These findings suggest that COVID-19 can induce a robust immune response that contributes to persistence of AKI, largely mediated through inflammatory responses.

#3534

**ASSOCIATION OF STOPPING RENIN-ANGIOTENSIN SYSTEM INHIBITORS DURING AN ACUTE KIDNEY INJURY EPISODE WITH CARDIOVASCULAR AND ALL-CAUSE MORTALITY**

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**Background and Aims:** The management of angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB) in patients with ongoing acute kidney injury (AKI) during hospitalization is debated. This study is aimed to explore whether the use of ACEI or ARB (ACEI/ARB) during an AKI episode is associated with adverse clinical outcomes.

**Method:** This nationwide, retrospective cohort study included 10,559 patients aged 18–100 years who had a hospital-acquired AKI (HA-AKI) episode and who were using ACEI/ARB at the time of AKI detection during the hospitalization between January 1, 2000 and May 26, 2021 from 19 medical centers across China. The primary exposure was stopping or continuing the use of ACEI/ARB after HA-AKI detection during hospitalization. The primary outcome was all-cause mortality (30-day, 180-day, and in-hospital mortality) after HA-AKI. Secondary outcomes included cardiovascular death and new-onset chronic kidney disease (CKD). Propensity scores were used to construct a matched-pairs cohort of patients who stopped or continued the use of ACEI/ARB during the HA-AKI episode.

**Results:** This study included 10,559 adults (mean [standard deviation] age, 67.4 [14.4] years; 6,606 [62.6%] male). A total of 2,015 (19.1%) participants stopped the usage of ACEI/ARB within 1 day after AKI detection. Among 1,915 matched-pairs, compared with those continued the use of ACEI/ARB, stopping the use of ACEI/ARB was associated with lower risks of 30-day all-cause mortality (adjusted hazard ratio (aHR), 0.67; 95% confidence interval [CI], 0.51-0.87), 180 day all-cause mortality (aHR, 0.77; 95%CI, 0.63-0.94) and in-hospital all-cause mortality (aHR, 0.64; 95%CI, 0.46-0.87). Similar results were found between stopping the use of ACEI/ARB and the risks of 30-day cardiovascular death (aHR, 0.58; 95%CI, 0.49-0.69), 180-day cardiovascular death (aHR, 0.57; 95%CI, 0.36-0.80), in-hospital cardiovascular death (aHR, 0.41; 95%CI, 0.19-0.86), and new-onset CKD after discharge (aHR, 0.76; 95%CI, 0.61-0.96). These protective effects were consistent in multiple sensitivity analyses.

**Conclusion:** Our study for the first time demonstrates that stopping the use of ACEI/ARB during an AKI episode is associated with lower risks of mortality and new-onset CKD. These findings provide strong evidence for the recommendation of avoiding renin-angiotensin system inhibitors during AKI from clinical guidelines.
**INCIDENCE, OUTCOMES AND RISK FACTORS OF ACUTE KIDNEY INJURY IN PATIENTS THAT UNDERWENT TRANSCATHETER AORTIC VALVE REPLACEMENT**

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**Background and Aims:** The incidence of acute kidney injury (AKI) in transcatheter aortic valve replacement (TAVR) varied among different centers and populations. The studies about the AKI in TAVR in Asian population were relatively scarce. Here, we reported the first descriptive study of AKI in patients underwent TAVR in Thailand. We also analyzed the risk factors of AKI in patients underwent TAVR.

**Method:** We reviewed the medical records of patients underwent TAVR in Chulabhorn hospital from August 2019 to September 2022. Baseline characteristics, serum creatinine and estimated glomerular filtration rate (eGFR) at baseline, day 2, day 7 and at discharge were recorded. Patients who did not have serum creatinine measured at day 2 or day 7 were excluded from our study. Patients who already underwent hemodialysis or peritoneal dialysis before TAVR also excluded from our study. We used the definition of AKI by KDIGO guideline. Outcome of AKI including 30-day mortality, 1-year mortality and renal replacement therapy were also recorded.

**Results:** We included 113 patients who underwent TAVR, all of which had the diagnosis of severe symptomatic aortic stenosis. 56 patients (49.6%) were male patients. The mean age was 80.2 +/- 5.6 years. The average length of stay was 9.9 days. 54 patients (47.8%) had pre-existing chronic kidney disease (CKD) before underwent TAVR. Other co-morbidities were hypertension (81/113 = 71.7%), dyslipidemia (71/113 = 62.8%), prior myocardial infarction (53/113 = 46.9%), diabetes (36/113 = 31.9%), and prior stroke or transient ischemic attack (5/113 = 4.4%). AKI occurred in seven patients (6.2%). Four patients (4/7 = 57.1%) underwent acute dialysis after TAVR. 30-day mortality rate was 0% and 1-year mortality rate was 1.8%. The 1-year mortality rate in patient with AKI was 14.3% compared with 0% in patient without AKI. The univariate analysis revealed that age, prior myocardial infarction, pre-existing CKD and pre-TAVR serum creatine were risk factors for developing AKI after TAVR.

**Conclusion:** This is the first study exploring incidence, outcomes and risk factors of AKI in patients underwent TAVR in Thailand. The incidence of AKI was 6.2%, relatively low compared with previous study.

**USEFULNESS OF CYSTATIN C IN MEASURING RENAL FUNCTION AND PREDICTING METHOTREXATE ASSOCIATED TOXICITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background and Aims:** Rheumatoid arthritis (RA) is a representative chronic disease accompanied by muscle loss, and cystatin C may be more useful than traditional creatinine (Cr) when measuring renal function. RA is affected not only by drug dose but also by side effects of treatment according to renal function. Therefore, we tried to compare the estimated glomerular filtrate rate (eGFR) using cystatin C and Cr and analyze the methotrexate (MTX) associated toxicities after treatment.

**Method:** A total of 436 RA patients was enrolled in this study. The eGFR was calculated using the Chronic kidney Disease Epidemiology Collaboration (CKD-EPI) equation based on cystatin C and serum Cr. According to eGFR, CKD stages and drug dosing stages were classified and MTX associated toxicities were evaluated.

**Results:** Mean eGFR using the CKD-EPI Cr and CKD-EPI cystatin C equations were 95.36 and 89.44 mL/min. In the CKD-EPI Cr group, there were 11 patients with eGFR less than 50 mL/min that required dosing reduction, and 38 patients in the CKD-EPI cystatin C group. According to eGFR, CKD stages and drug dosing stages were classified and MTX associated toxicities were evaluated.

**Conclusion:** Mean eGFR using the CKD-EPI Cr and CKD-EPI cystatin C equations were 95.36 and 89.44 mL/min. In the CKD-EPI Cr group, there were 11 patients with eGFR less than 50 mL/min that required dosing reduction, and 38 patients in the CKD-EPI cystatin C group, showing a statistically significant difference (Table 1A). In addition, CKD stage 3B and 4 patients were also higher in the CKD-EPI cystatin C group compared to those in CKD-EPI Cr group (Table 1B), and anemia and nephrotoxicity were high in the MTX related toxicity stage upgraded group.
Conclusion Our study showed that eGFR by CKD-EPI C2 can be overestimated than that by CKD-EPI Cystatin C, and also demonstrated higher MTX associated toxicities in the group, which the stage was changed upward. Therefore, this study suggests that cystatin C is a useful predictor in measuring renal function and predicting MTX associated toxicities in RA patients

#6405
PROGRESSION TO END-STAGE RENAL DISEASE AND ONE-YEAR MORTALITY IN ACUTE CARDIORENAL SYNDROME
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Background and Aims: Approximately 25% of patients with chronic congestive heart failure (CHF) present a reduction in glomerular filtration rate (GFR) independent of the left ventricular ejection fraction (LVEF). A meta-analysis of 80,000 patients revealed that patients with lower GFR (<53 mL/min) had a higher one-year mortality rate (51% versus 38%). Therefore, this reduction in GFR seems to have an important impact on both morbidity and mortality. The aim of this study was to analyze the factors associated with progression to advanced chronic kidney disease (CKD) and one-year mortality in a retrospective cohort of patients hospitalized due to acute decompensation of cardiorenal syndrome (CRS).

Method: Patients hospitalized for CRS between September 2013 and June 2020 who presented acute kidney injury (AKI) associated with CHF. Clinical, meta-analysis of 80,000 patients revealed that patients with lower GFR (<53 mL/min) had a higher one-year mortality rate (51% versus 38%). Therefore, this reduction in GFR seems to have an important impact on both morbidity and mortality. The aim of this study was to analyze the factors associated with progression to advanced chronic kidney disease (CKD) and one-year mortality in a retrospective cohort of patients hospitalized due to acute decompensation of cardiorenal syndrome (CRS).

Results: The study included 100 patients with a majority of males (64%) and a median age of 79.5 years (72.3–85.0). Around 38% of the patients were dependent, 49% had ischemic heart disease, 51% were diabetic, 27% had left ventricular hypertrophy, 56% had moderate to severe pulmonary hypertension, and 59% had moderate to severe valve disease. In terms of LVEF, 27% showed severe dysfunction while 42% had preserved function. The median baseline creatinine was 1.6 mg/dl (1.3–2.0) with an estimated glomerular filtration rate (eGFR) of 36 mL/min (29.0–46.5). At the time of acute renal failure (ARF), creatinine was 3.3 mg/dl (2.8–4.0) and at hospital discharge the eGFR (CKD-EPI) was 29.5 mL/min (20.1–40.0). After one year of follow-up, 49 patients had died, 7 were admitted for chronic hemodialysis, and 6 showed a drop in eGFR greater than 40%. A logistic regression analysis was conducted for the outcome variable of "death or severe progression of CKD (considering entry into CKD grade V or loss of more than 40% of GFR)". Hyperphosphatemia (76% death/progression vs 48%, p=0.004), discharge eGFR less than 30 mL/min (74% vs 50%, p=0.013), and renin-angiotensin system (RAS) blockade (48.1% vs 77.1%) were significantly associated with the outcome. Systolic dysfunction was associated with 70.4% of death/progression (52.2% p=0.06).

In the multivariate analysis, variables with a trend in the univariate analysis (p<0.2), such as prolonged hospital stay, non-revascularized coronary disease, hyponatremia, and proteinuria, were included. The analysis showed that five variables were significantly associated with the risk of death/CKD progression: proteinuria (OR 2.8, 95% CI 1.03-7.37, p=0.04), discharge eGFR (OR 2.7, 95% CI 1.05-6.82, p=0.04), LVEF (OR 0.97, 95% CI 0.94-1.00, p=0.06), hyponatremia (OR 0.89, 95% CI 0.80-0.99, p=0.04), and RAS blockade (OR 0.19, 95% CI 0.07-0.53, p=0.001). The predictive model had an area under the curve of 0.79 (95% CI 0.70-0.88) with a p-value of 0.047 and a global accuracy of 77%.

Conclusion: In conclusion, our study found that hyponatremia and proteinuria were significantly associated with a poorer outcome in terms of CKD progression and mortality in patients with cardiorenal syndrome. Conversely, higher left ventricular ejection fraction and a higher estimated glomerular filtration rate at discharge from the decompensation episode were linked to a lower risk. Our findings support the use of RAS-blocking drugs as beneficial in this population.

#6448
IMPACT OF PRE-DIALYSIS FOLLOW-UP ON OUTCOMES IN DIALYSIS PATIENTS
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Fresenius Medical Care, Argentina

Background and Aims: Pre-dialysis care aims to slow down the decline in kidney function and to prepare patients for their potential start of renal replacement therapy. Patients who received attention earlier showed reduced mortality and hospitalization, better uptake of peritoneal dialysis, and earlier placement of arteriovenous fistula for hemodialysis. The objective of this study is to analyze the impact of pre-dialysis care in dialysis patients from Fresenius Medical Care Latin America (FMEA).LAtrAm).

Method: Patients incident to dialysis that started treatment at FME LatAm between January 2019 and December 2022 were included in this retrospective observational study. They were classified according to whether they received pre-dialysis care or not as CKD (more than 10 days of follow up) or No CKD (less than 10 days). CKD group was subclassified regarding the length of stay in pre-dialysis care in 10 to 45 days (10-45), 45 to 90 days (45–90), and more than 90 days (>90). Demographic variables, vascular access, and laboratory variables were compared between CKD and No CKD, and within subgroups during the observation period. Values are expressed in mean ± SD. Values compared using Student t-test or ANOVA accordingly.
Results: CKD patients were older than No CKD (CKD: 61.5 ± 16.6 vs NoCKD: 60.6 ± 17.2; p = 0.02), with lower male prevalence (CKD: 57.5% vs NoCKD: 60.2%; p=0.001). No significative differences in prevalence of diabetes were found. Patients under pre-dialysis treatment showed a higher rate of PD referrals (CKD: 44.6% vs NoCKD: 7.3%; p <0.0001). Regarding vascular access, a higher percentage of CKD patients started dialysis with definitive access (AVF or AVG) (CKD: 47.9% vs NoCKD: 31.5%; p <0.0001). In the same way, prevalence of definitive accesses was higher in patients with longer CKD stay (10-45: 38.4%, 45-90: 57.3%, >90: 50.2%; p<0.0001). Within patients who started treatment with a catheter, a higher percentage of CKD patients already had a fistula or graft performed at treatment start (CKD: 7.3% vs NoCKD: 2.7%; p <0.0001). EPO prescription was higher as the time of follow-up was longer (10-45: 3.3%; 45-90: 7%, >90: 14.9%; p<0.0001). As expected for CKD patients haemoglobin was higher and ferritin was lower (Table 1). Though TSAT, Calcium, and Albumin were significative different between CKD and No CKD, the difference was not clinically relevant. Phosphorus and iPTH was higher in CKD patients and creatinine clearance calculated by MDRD was lower in those patients, opposite of expected (Table 1). Though older and male patients are more likely to have CKD follow-up. Pre-dialysis treatment has a deep impact on PD referral, EPO prescription, type of vascular access at admission, and ready-made vascular access at treatment start. Some laboratory results were not as expected, maybe due to non proper medication accessibility or inadequate financial support at predialysis stages. Even though, CKD follow-up is crucial to prepare patients for a better start of renal replacement therapy.

#6535
SEXUAL DIMORPHISMS OF ACUTE KIDNEY INJURY: DIVERGENT PERFORMANCES OF BIOMARKERS OR DIFFERENT MOLECULAR MECHANISMS?
Alexis Piedrafita1, Justyna Siwy2, Ana Belen Sanz3, Paul Bousquet4, Julie Klein5, Melinda Alves5, Audrey Casemayou5, Vincent Minville5, 6, 7, 8
1University Hospital of Toulouse, Department of Nephrology and Organ transplantation, Toulouse, France, 2MosaicDiagnostics, Germany, 3IIS-Fundacion Jimenez Diaz, Laboratory of Nephrology, Spain, 4University Hospital of Toulouse, France, 5INSERM U1297, Toulouse, France, 6University Hospital of Toulouse, Anesthesiology, France, 7IIS-Fundacion Jimenez Diaz, Spain and 8University Hospital of Toulouse, Nephrology and Organ transplantation, Toulouse, France

Background and Aims: Before implementing individualized strategies to prevent or treat acute kidney injury (AKI), identifying clusters of patients with common (or divergent) pathophysiological mechanisms, diagnosis criteria or outcome is of utmost importance.

Method: We compared the characteristics of 1170 male and female patients referred for cardiac surgery with cardiac bypass (CBP) using multivariate logistic regression and propensity score-based analysis. Performances of the candidate urinary biomarkers neutrophil gelatinase-associated lipocalin (uNGAL), [IGFBP7], [TIMP-2] product (Nephrocheck), and a recently developed AKI signature of 204 urinary peptides (PeptAKI) were compared, and sex-dependent individual urinary peptide changes were studied.

Results: In these patients referred for CBP-surgery, incidence and severity (K/DIGO classification) of AKI were similar in men and women (about 25%), even after adjustment of the usual risk factors of AKI including baseline estimated glomerular filtration rate, age, diabetes mellitus, length of CBP and red blood cell transfusion. Performances of uNGAL, Nephrocheck and PeptAKI strongly diverged between males and females. In the overall cohort, as well as in sub-groups of males and females, the multi-markers PeptAKI signature outperformed uNGAL and Nephrocheck. Reanalysis of peptides included in PeptAKI at the single peptide level suggested divergences of AKI mechanisms between sexes. In women, the peptide score-derived risk of AKI strongly relied on peptides indicating kidney inflammation (including SERPINs, SAA1, osteopontin, uromodulin fragments) and hemolysis (HBA1, HBB), whereas a peptide derived from a stress-responsive protective gene in kidney tubular epithelial cells (VGF nerve growth factor) was dramatically less abundant in women developing AKI.

Conclusion: In patients referred for CBP-surgery, significant clinical and biological differences between men and women, as well as sexual dimorphism of AKI biomarkers performances, were identified. Urinary peptide signatures may help to personalize prevention of AKI progression by giving both quantitative and sex-related qualitative information on molecular mechanisms underlying AKI.

#6652
ACUTE KIDNEY INJURY IN PATIENTS WITH MULTIPLE MYELOMA SUBMITTED TO AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANT: A COHORT ANALYSIS
Carolina Branco1, Natacha Rodrigues1, Filipe Marques1, Claudia Costa1, Pedro Vasconcelos1, Carlos Martins2 and José António Lopes1
1Centro Hospitalar Universitário Lisboa Norte, Nephrology and Renal Transplantation, Lisboa, Portugal and 2Centro Hospitalar Universitário Lisboa Norte, Haematology, Lisboa, Portugal

Background and Aims: The incidence of most haematological neoplasms has been increasing and with them hematopoietic cell transplantation (HCT) as it provides better survival rates to several of these malignancies. There is a wide range of acute kidney injury (AKI) reported incidence in HCT patients, mostly due to the heterogeneity of AKI definitions and study populations that include
different underlying illnesses. We aimed to evaluate incidence, severity and risk factors of AKI by KDIGO classification considering creatinine and urinary output (UO) criteria in patients with multiple myeloma (MM) submitted to autologous HCT.

**Method:** We conducted a retrospective cohort study including patients with MM submitted to autologous HCT admitted in a tertiary hospital between Jan./2005-Dec./2015 with a 3 year follow-up period. To evaluate AKI cumulative incidence, risk factors and impact on relapse, survival analysis methods considering death as competing were used. Multivariate stepwise analysis using logistic regression was used to evaluate risk factors associated with AKI.

**Results:** 143 patients were included [median age was 50.5 (59.2-63.6) years, 61.5% male and 90.9% Caucasian]. 37.1% had hypertension, 12.6% diabetes mellitus and 10.5% chronic kidney disease (CKD) [median overall baseline eGFR 100.4 (89.5-110.8) mL/min/1.73 m²]. Median percentage of plasma cells on bone marrow aspirate was 30 (17-67)%. serum M-protein 3.3 (2.2-6.6) g/dL and serum titre of the affected light chain 3560 (890-7800) mg/dL. 49 patients had cytogenetic abnormalities. 49% of patients had R-ISS stage I at diagnosis. Median number of previous lines of therapy was 1 (1-2) and the median number of cycles 4 (3-4). 34.5% were previously submitted to radiotherapy. At admission, mean haemoglobin was 11.7 (10.8-12.4) g/dL, neutrophils 3375 (2330-4765) /mm³, serum urea 33 (28-44) mg/dL, uric acid 5 (4.1-6) mg/dL, phosphate 3.4 (3.2-9) mg/dL, LDH 333 (297-390) U/L, albumin 3.9 (3.7-4.2) mg/dL and alanine transaminase 18 (14-27) U/L. Fever (77.6%), exposure to nephrotoxins (74.1%), low grade mucositis (53.9%) and sepsis (26.6%) were common during hospital admission. Cumulative incidence of AKI at 100 days was 49.7% (71 patients) with median time to event of 8 (5-13) days. 85.9% of patients had stage 1 AKI at diagnosis, although 16.4% of these (10 patients) degraded to worse stages. On univariable analysis, the predictor variables with impact on AKI were higher age (p=0.057), higher body mass index (BMI) (p=0.048), HCT-comorbidity index ≥2 (p=0.005), lower baseline eGFR (p<0.001), previous CKD (p=0.001), presence of amyloidosis (p=0.078), higher R-ISS (p=0.002), presence of cytogenetic abnormalities (p=0.055), development of sepsis (p=0.016), fever (p=0.044) and higher grade mucositis (p=0.001), exposure to nephrotoxins (p=0.007), higher neutrophils count (p=0.021), serum urea (p<0.001) and LDH (p=0.002) and lower phosphate (p=0.049), and alanine transaminase (p=0.077). Multivariable analysis showed an independent association of AKI with BMI [HR 1.08 (1.03-1.14), p=0.004], CKD [HR 3.60 (1.55-5.78), p=0.001], amyloidosis [HR 2.73 (1.40-5.33), p=0.001], high grade mucositis [HR 2.35 (1.37-4.02), p=0.002], exposure to nephrotoxins [HR 2.20 (1.08-4.47), p=0.029], leukocyte count [HR 1.01 (1.01-1.01), p<0.001] and serum phosphate [HR 0.57 (0.39-0.84), p=0.004] maintained an independent association with AKI.

**Conclusion:** Our results show that AKI occurs in almost half of the patients with MM submitted to HCT and reinforce the need for prevention, monitoring and early approach to AKI in these patients particularly in those with higher BMI, CKD, secondary amyloidosis, higher leukocyte count and lower serum phosphate at admission, as well as in those that develop mucositis and are exposed to nephrotoxins. We also believe considering both SCR and UO KDIGO criteria for AKI may have increased the reliability of our data, this being the first study to include both criteria in this population of patients.

**Background and Aims:** Several reports showed that some Covid-19 patients tend to have serious and fatal complications related to the kidney and heart. Rationale and mechanisms inducing this pathogenesis is unclear, but it’s more common to happen in patients with hemodynamic instability and refractory severe hypotension related to cytokine storm. It represents an irreversible stage of a sepsis-like illness that induces simultaneous damage to various organs as the myocardium and renal tubules alike the cardio-renal syndrome. The predictors for this injurious effect of COVID-19 on both myocardium and renal tissues might be related to the co-morbidities, late presentation and other factors which need further evaluation. The aim of this article is to study the predictors of cardio-renal syndrome in COVID-19 patients.

**Method:** Our study is a prospective observational study conducted upon confirmed 160 COVID-19 ICU patients admitted from 15th March till 20th May 2020. All patients were subjected to clinical assessment, full laboratory evaluation including PCR for COVID-19 from nasopharyngeal swab and full radiological evaluation.

**Results:** As regards the predictors for cardio-renal syndrome [15-17]; Age showed high statistically significance (P <0.0004). Furthermore, serum creatinine and serum K were statistically significant in patients with cardio-renal affection (P=0.015, 0.021) whereas GFR, D-dimer, need for mechanical ventilation and vasopressors were highly statistically significant with cardio-renal affected patients (P <0.001).

**Conclusion:** Cardio-renal syndrome was common in COVID-19 ICU patients. Hypokalemia, lower GFR on admission, mechanical ventilation, vasopressors, age and D-dimer were significant independent predictors for CRS. Moreover, CRS during hospitalization was associated with an increased risk of in-hospital death.
Figure 2:
Table 1: Demographic details for developing Cardiorenal Syndrome.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n=150)</th>
<th>No CRS (n=252)</th>
<th>CRS (n=20)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>54.8 (51.0 to 67.0)</td>
<td>57.7 (48.5 to 66.0)</td>
<td>74.5 (67.5 to 79.5)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84 (52.5%)</td>
<td>78 (51.3%)</td>
<td>12 (60.0%)</td>
<td>0.282</td>
</tr>
<tr>
<td>DM</td>
<td>58 (36.0%)</td>
<td>65 (31.8%)</td>
<td>13 (65.0%)</td>
<td>0.712</td>
</tr>
<tr>
<td>COPD</td>
<td>16 (10.0%)</td>
<td>14 (7.0%)</td>
<td>2 (10.0%)</td>
<td>0.184</td>
</tr>
<tr>
<td>CKD</td>
<td>42 (26.2%)</td>
<td>30 (25.0%)</td>
<td>12 (60.0%)</td>
<td>0.026</td>
</tr>
<tr>
<td>Marital obesity</td>
<td>7 (4.0%)</td>
<td>3 (1.4%)</td>
<td>4 (20.0%)</td>
<td>0.178</td>
</tr>
<tr>
<td>TLL</td>
<td>7.6 (7.0 to 9.1)</td>
<td>7.5 (7.5 to 9.0)</td>
<td>12.6 (7.4 to 14.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>92 (71.0%)</td>
<td>85 (70.0%)</td>
<td>7 (35.0%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>CRP</td>
<td>73 (49.0%)</td>
<td>66 (53.0%)</td>
<td>7 (35.0%)</td>
<td>0.155</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.05 (0.9 to 1.3)</td>
<td>0.9 (0.8 to 1.2)</td>
<td>1.35 (1.0 to 1.7)</td>
<td>0.0005</td>
</tr>
<tr>
<td>eGFR</td>
<td>70.5 (50.1 to 90.9)</td>
<td>74.3 (51.0 to 90.2)</td>
<td>34.3 (28.5 to 35.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>14 (8.8%)</td>
<td>18 (9.0%)</td>
<td>0 (0.0%)</td>
<td>0.454</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) or number (percentage). * Quantitative variables are compared using the Mann-Whitney U-test and categorical variables using Fisher's exact test.

Table 2: Backward multivariable regression analysis for prediction of CRS in COVID-19 patients.

<table>
<thead>
<tr>
<th>Variable*</th>
<th>B</th>
<th>SE</th>
<th>Wald</th>
<th>P-value</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.086</td>
<td>0.047</td>
<td>3.44</td>
<td>0.064</td>
<td>1.090</td>
<td>1.066 to 1.115</td>
</tr>
<tr>
<td>eGFR on admission (ml/min)</td>
<td>-0.030</td>
<td>0.008</td>
<td>6.994</td>
<td>0.006</td>
<td>0.924</td>
<td>0.881 to 0.970</td>
</tr>
<tr>
<td>Serum K+ on admission (mmol/l)</td>
<td>-0.885</td>
<td>0.006</td>
<td>7.790</td>
<td>0.006</td>
<td>0.201</td>
<td>0.164 to 0.244</td>
</tr>
<tr>
<td>Constant</td>
<td>4.735</td>
<td>4.642</td>
<td>1.040</td>
<td>0.308</td>
<td>0.479</td>
<td>0.106 to 1.987</td>
</tr>
</tbody>
</table>

HYPOCHLOREMIA AS A MARKER OF ALL-CAUSE MORTALITY AND UNPLANNED DIALYSIS STARTS IN A COHORT OF ACUTE KIDNEY INJURY: A 4-YEAR FOLLOW-UP STUDY

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Background and Aims: Serum chloride is an emerging marker of mortality in patients with hypertension, heart failure, sepsis, and chronic kidney disease. The relationship between hyperchloremia and acute kidney injury is well known, especially in critically ill patients. However, the role of baseline hypochloremia in the prognosis of hospitalized patients with acute kidney injury (AKI) remains poorly understood.

Method: Retrospective cohort type study. We included n=243 patients with AKI stage 3 from consultations received by the nephrology department of our hospital between January 1, 2017, to December 31, 2017. The sample was divided into two groups considering baseline serum chloride (Cl−) levels.

Hypochloremia was considered if Cl− < 98 mEq/L. The primary endpoint was a composite variable for unplanned dialysis starts and all-cause mortality.

Results: The mean age was 68 years. Females accounted for 39.5%. The mean baseline sodium was 137±7.2 mEq/l and the mean baseline chloride was 98.9±7.05 mEq/l (Table 1). The mean follow-up of the patients was 21±19.61 months. The incidence of the primary endpoint was n=166 (68.3%). 148 (60.9%) died, of whom 78 (32%) died during their hospital stay. The causes of death were: 30.6% cardiovascular, 12.9% tumor, 44.7% infectious, and 11.8% other. Kaplan-Meier estimates showed lower survival rates in patients with chloride levels below 98 mEq/l (p=0.006, log rank test) (Figure 1).

Conclusion: Patients with AKI stage 3 with lower baseline chloride levels (<98 mEq/L) were more likely to have higher overall mortality and unplanned dialysis starts.

#4589 Abstracts
ACUTE CORTICAL NECROSIS IN PREGNANCY IS STILL AN IMPORTANT CAUSE FOR END-STAGE RENAL DISEASE IN DEVELOPING COUNTRIES

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Background and Aims: Renal cortical necrosis (RCN) is a serious complication of acute kidney injury (AKI) and pregnancy is a clinical state closely associated with it with poor renal outcomes. The incidence is much higher in obstetrical AKI compared to other causes of RCN. Despite better medical care facilities available, this continues to be an important cause of morbidity and mortality in developing countries.

Method: This is a retrospective analysis among all pregnant females presenting with AKI from January 2000 to December 2020 at a tertiary care center in the northern part of India. We looked for the incidence of obstetrical-related RCN in our renal biopsies performed in the last 20 years and to evaluate precipitating factors responsible for RCN.

Results: RCN constituted 8.1% of pregnancy-related AKI cases in our institution. The overall incidence has been declining which was 9.09% from 2000 to 2008 to 8.7% from 2009 to 2014 and 8.1% from 2014-2020. The patient's median age was 28.4 ± 4.6 years. The average time to presentation from the day of delivery was 7.8 ± 3.0 days. The mortality was observed in 10.4% of them with sepsis and multiorgan dysfunction present in all of them. The most common etiology for RCN was found to be septic abortion and puerperal sepsis accounting for - 16.2% each. Postpartum hemorrhage was a cause in 9.67% of patients. The most important cause of RCN was postpartum thrombotic microangiopathy which was observed in 49.5% of patients. Kidney biopsy was helpful in diagnosis in 36 patients while computed tomography scan abdomen alone helped in diagnosis in five patients. Patchy cortical necrosis in histology was seen in 36.7% of patients and morbidity in terms of prolonged hospitalization was seen in 36.7% of patients and morbidity in terms of prolonged hospitalization was seen in 23.4% while dialysis dependency in 63.4% of the study population.

Conclusion: Strategies need to be implemented in reducing the preventable causes for RCN which is not only catastrophic in terms of renal outcomes but also for social and psychological perspectives as well.
#5167
RENAL PROGNOSIS IN PATIENTS WITH ACUTE KIDNEY INJURY AND COMPARISON OF THE RIFLE AND KDIGO CLASSIFICATION SYSTEMS: WHAT IS THE ROLE OF DIABETES MELLITUS?
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General Hospital of Athens Hippokratario, Greece

Background and Aims: Acute Kidney Injury (AKI) is a frequent clinical entity. There are three AKI definition classifications: RIFLE, AKIN and KDIGO. The endpoint of this study is to compare KDIGO and RIFLE regarding the prediction of AKI stage and adverse outcomes and to evaluate the renal prognosis of patients with a history of chronic kidney disease (CKD), who develop AKI during hospitalization. It is a well-known fact that Diabetes mellitus (DM) is the most common cause of end-stage chronic kidney disease (CKD). The epidemiology and outcome of diabetic patients with AKI during hospitalization, needs further study and comparison with the data of non-diabetic patients. As a secondary end point of this study we observed the progression of kidney function and severity of treatment in diabetic patients with stage III AKI (KDIGO) in comparison with the non-diabetic patients.

Method: This is a retrospective epidemiological study where data of 1083 adult patients were examined with AKI, who were hospitalized in various clinics at General Hospital of Athens Hippokratario between January 2021-September 2022.

Results: A total of 1083 patients were registered (63% male, mean age 74.5 ±12.6 years). 42% suffered from diabetes mellitus, 39% from arterial hypertension and 41% from CKD. RIFLE identified fewer patients with AKI than KDIGO (69.7% vs. 100%, p<0.001). Of all patients, 43.1% corresponded to AKI stage 1 (AKI-1), 7.3% to AKI stage 2 (AKI-2) and 46.7% to AKI stage 3 (AKI-3) according to KDIGO. 41.9% of AKI-3 patients underwent hemodialysis. Of the 214 patients on dialysis, 31.8% were not identified as AKI by RIFLE. In addition, patients with a history of CKD showed a higher percentage of AKI-3 (47.1% vs. 39.3% AKI-1, p=0.003 and 13.6% AKI-2, p=0.001) and underwent hemodialysis in a higher percentage (56.6% vs. 43.4%, p=0.002). On the secondary end point 1083 patients, 458 (42.3%) diabetic and 625 (57.7%) non-diabetic were recognized. Hemodialysis was required in 83(18%) diabetic patients and in 132(21.1%) non-diabetic patients. Patients who ended up on end stage CKD requiring chronic hemodialysis or with GFR <15ml/min/1.73 m² one month after hospital discharge were 37.7% and 51%, respectively. More specifically patients with the worst prognosis, who developed end stage CKD or ended up with GFR <15ml/min/1.73 m² one month after hospital discharge, were categorized in three groups according to CKD Stage at hospital admission: in group A) CKD Stage II out of 29, 8 (27.3%) non-diabetics and out of 19, 4 (21%) diabetic, in group B) STAGE IIIa out of 30 patients 5 (16.6%) non-diabetic and out of 15 3 (20%) diabetic and in group C) STAGE IIIb out of 17 patients 8 (47%) non-diabetic and out of 20 6 (30%) diabetic. It should be mentioned that the worst prognosis was observed in patients who were hospitalized for infection out of 30, 16(63%), with prerenal AKI out of 19 patients, 10(53%) and with a cardiovascular event out of 18 patients, 6(33%).

Conclusion: RIFLE criteria identified a lower proportion of patients with AKI compared to KDIGO, while not classifying a proportion of patients undergoing hemodialysis as AKI. Additionally, CKD was associated with worse renal prognosis in hospitalized patients with AKI. Patients with AKI on CKD who required hemodialysis during their hospitalization did not appear to have a worse prognosis at one month after discharge, comparing diabetic with non-diabetic in group A and B. On the contrary there was a significant difference between patients in group C.

REFERENCES

#5213
RELATIONSHIP BETWEEN CYTOKINE RELEASE SYNDROME AND ACUTE KIDNEY INJURY AFTER CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY IN HEMATOLOGIC NEOPLASMS
Juan Leon Román, Gloria Iacoboni, Sheila Bermejo Garcia, Cecilia Carpio, Andor Vergara Arana, Oriol Bestard Matamoros, Pere Barba and Maria Jose Soler Romeo
Vall d’Hebron University Hospital, Barcelona, Spain

Background and Aims: CAR-T cell therapy is a promising new immunotherapy to treat refractory hematologic malignancies (RHM). Despite the potential benefits, high rates of treatment related toxicity have been reported after CAR-T infusion. AKI occurs between 20-30% after treatment. The purpose of this study was to identify the relationship between the proinflammatory status (CRS, ICANs, and febrile neutropenia) and AKI development.

Method: Medical records of 115 patients treated with CD19-targeted CAR-T cells for refractory hematologic malignancies at HUVH between July 2018 and May 2021 were reviewed. Clinical data was reviewed within 30 days after CAR-T cells therapy. AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria: grade 1, 1.5 to <2-fold of baseline; grade 2, 2- to <3-fold of baseline; grade 3, ≥3-fold of baseline. We performed statistical analysis to identify risk factors for AKI development.

Results: A total of 24/115 patients presented AKI after CAR-T infusion. AKI stage 1 was diagnosed in 17 (15%) patients, AKI stage 2 was diagnosed in 4 (3.5%) patients, and AKI stage 3 was diagnosed in 3 (2.6%) patients. 4/17 patients died in the AKI stage 1 group while 2/3 patients in the AKI stage 3 group. Renal function was recovered in 19/24 (79%) patients within the first month. Chronic kidney disease was present in 13% patients. Among types of CAR-T cell infusion, “investigational product” was infused in 27.8%, tsigengencelucel in 49.6%, axicabtagen ciloleucel in 20%, and brexucabtagene autoleucel in 2.6%. The most frequent complications were cytokine release syndrome (81.9%), febrile neutropenia (67%) and neurotoxicity (28.7%). Tociluzumab was given in 31 (27%) patients for CRS grade ≥2, and 3% of patients were admitted to the intensive care unit 3/36 patients died after CAR-T infusion. Male sex, CAR T-cell construct, ICANs, CRS, and death by any cause were associated with AKI. Only AKI CRS ≥2 (p=0.001) was identified as independent risk factor for AKI.

Conclusion: AKI development is mainly transient and associated with the proinflammatory status after CAR-T cell infusion.

#11078 Abstracts
Table 1: Demographic and Clinical Characteristics of the 115 patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All (n=115)</th>
<th>AKI patients (n=24)</th>
<th>Non-AKI patients (n=91)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range, %)</td>
<td>61 (20-81)</td>
<td>16 (66.7)</td>
<td>46 (50.5)</td>
<td>0.16</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>76 (66)</td>
<td>20 (83.3)</td>
<td>56 (61.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>43 (37.4)</td>
<td>13 (54.2)</td>
<td>30 (33.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus, n (%)</td>
<td>9 (7.8)</td>
<td>3 (12.5)</td>
<td>6 (6.6)</td>
<td>0.34</td>
</tr>
<tr>
<td>Chronic kidney disease, n (%)</td>
<td>16 (13.9)</td>
<td>6 (25.0)</td>
<td>10 (11.0)</td>
<td>0.08</td>
</tr>
<tr>
<td>CAR T-cell construct, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>- Investigational product</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Tisagenlecleucel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Axicabtagene ciloleucel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Brexucabtagene autoleucel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 32 (27.8)</td>
<td>7 (29.2)</td>
<td>25 (27.5)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>- 57 (49.6)</td>
<td>14 (58.3)</td>
<td>43 (47.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 23 (20.0)</td>
<td>1 (4.2)</td>
<td>22 (24.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 3 (2.6)</td>
<td>2 (8.3)</td>
<td>1 (1.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRS, n (%)</td>
<td>95 (81.9)</td>
<td>21 (87.5)</td>
<td>74 (81.3)</td>
<td>0.56</td>
</tr>
<tr>
<td>CRS grading</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>- Grades 0-1, n (%)</td>
<td>60 (51.7)</td>
<td>6 (28.6)</td>
<td>54 (73)</td>
<td>0.001</td>
</tr>
<tr>
<td>- Grades 2-4, n (%)</td>
<td>35 (30.2)</td>
<td>15 (71.4)</td>
<td>20 (27)</td>
<td></td>
</tr>
<tr>
<td>Febrile neutropenia, n (%)</td>
<td>77 (67.0)</td>
<td>20 (83.3)</td>
<td>57 (62.6)</td>
<td>0.05</td>
</tr>
<tr>
<td>ICANS, n (%)</td>
<td>33 (28.7)</td>
<td>11 (45.8)</td>
<td>22 (24.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>ICU admission, n (%)</td>
<td>6 (5.2)</td>
<td>3 (12.5)</td>
<td>3 (3.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>- Due to disease progression</td>
<td>30 (83.3)</td>
<td>2 (33.3)</td>
<td>28 (93.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>- Treatment-related</td>
<td>3 (8.3)</td>
<td>3 (50.0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>- COVID-19 pneumonia</td>
<td>3 (8.3)</td>
<td>1 (16.7)</td>
<td>2 (6.7)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: AKI score and mortality.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All</th>
<th>Alive (n=79)</th>
<th>Deceased (n=36)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-AKI patients, n (%)</td>
<td>91 (79.1)</td>
<td>61 (77.2)</td>
<td>30 (83.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>AKI patients</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1, n (%)</td>
<td>17 (14.8)</td>
<td>13 (16.5)</td>
<td>4 (11.1)</td>
<td></td>
</tr>
<tr>
<td>- 2, n (%)</td>
<td>4 (3.5)</td>
<td>4 (5.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>- 3, n (%)</td>
<td>3 (2.6)</td>
<td>1 (1.3)</td>
<td>2 (5.6)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Adjusted OR for AKI development.

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR</th>
<th>CI 95%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>3.21</td>
<td>0.88-11.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.60</td>
<td>0.53-4.83</td>
<td>0.40</td>
</tr>
<tr>
<td>ICANs</td>
<td>2.11</td>
<td>0.68-6.49</td>
<td>0.19</td>
</tr>
<tr>
<td>CRS</td>
<td>5.12</td>
<td>1.66-15.8</td>
<td>0.004</td>
</tr>
</tbody>
</table>

#5282

ACUTE KIDNEY INJURY IN INFECTIOUS DISEASE BY CORONAVIRUS IN BRAZIL: A STUDY ON INCIDENCE, RISK FACTORS, AND PROGNOSIS

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Faculty of Medicine of Botucatu, UNESP, Brazil

Background and Aims: Although diffuse alveolar damage and acute respiratory failure are the main features of COVID-19 disease in its severe form, renal involvement is frequent (4-37%). To assess the incidence of acute kidney injury (AKI) in Brazilian patients hospitalized with COVID-19 and to identify both the risk factors associated with its onset and those associated with its prognosis.

Method: This is a prospective cohort study of patients hospitalized with COVID-19 at a public and tertiary university hospital in São Paulo from March 2020 to May 2021, encompassing the first and second waves of the pandemic. Patients were followed up until the clinical outcome (discharge or death). The evaluation of renal function was performed by measuring serum creatinine and urinary output and the diagnosis of AKI was performed according to the KDIGO 2012 criteria. The occurrence of AKI was established as the dependent variable, using the Chi-Square Test for the comparison of categorical variables and the T Test for continuous variables. Afterwards, a multivariate analysis was performed using the logistic regression model, with calculations of the Odds Ratio (OR), including in the model all the variables that showed association with the outcome (p<0.20). A similar procedure was performed after establishing death as the dependent variable.

Results: 887 patients with COVID-19 were analyzed, 54.6% were admitted to the intensive care unit (ICU) and 45.4% were admitted to the ward. The overall incidence of AKI was 48.1%, more frequent in the ICU (83.8 vs 17.1%, p<0.0001). Upon hospital admission, 487 patients were submitted to urine test I, of which 58.5% had hematuria and 51.5% had proteinuria. The overall mortality was 38.9%. The average time for the diagnosis of AKI was 6 days and AKI KDIGO 3 was the most frequent (60.2%). Acute renal support was indicated in 58.8% of patients. According to logistic regression, the risk factors for AKI were the use of diuretics (OR 2.2, CI 1.2-4.1, p<0.05), mechanical ventilation (OR 12.9, CI 4.3-38.2, p<0.05), presence of proteinuria (OR 1.6, CI 0.9-2.7, p=0.07), presence of AKI (OR 6, CI 2.9-12.2, p<0.05), mainly KDIGO 3 (OR 0.6, CI 0.2-1.3, p=0.2), high D-dimer (OR 1, CI 1, p=0.05), SOFA score (CI 1.35, CI 1.1-1.6, p<0.05) and ATN-ISIS score (OR 996.4, CI 4.8-203271, p<0.05). Finally, the variables that showed the difference in the profile of patients between the two waves of the pandemic were identified, being less frequent in the second wave male gender (OR 0.51, CI 0.35-0.74, p<0.05) and Caucasian ethnicity (OR 0.47, CI 0.2-0.8, p<0.05), and more frequent in the second wave the use of mechanical ventilation (OR 1.57, CI 1-2.3, p<0.05), proteinuria (OR 1.44, CI 1-2.1, p<0.05), higher D-dimer values (OR 1.09, CI 1-1.1, p<0.05) and ATN-ISIS score (OR 40.9, CI 1.7-948.1, p<0.05).

Conclusion: AKI associated with severe COVID-19 in Brazil was more frequent than in the Chinese, European, and North American cohorts, and the risk factors associated with its development are the use of diuretics, mechanical ventilation, VAD, dyslipidemia, proteinuria, CKD, older age, elevated CPK and D-dimer. Mortality was high and higher in patients with arterial hypertension, on mechanical ventilation, with proteinuria, with AKI, mainly KDIGO 3, high D-dimer, and higher SOFA and ATN-ISIS. In the second wave, AKI severity was greater, but mortality was similar to that of the first wave, which may reflect both the effectiveness of vaccines against SARS-CoV-2, as well as the constant learning that frontline professionals have built throughout the pandemic, to provide greater support to its patients.
The neural network achieved a performance of 0.14322 in 6 epochs. Results:

Method: The study included 86 hospitalized patients with acute renal impairment who were divided according to the stage of renal impairment at admission to hospital treatment into three groups. The assessment of acute renal impairment and the classification of disease stages were based on the diagnostic stages by the K / DIGO group. All examined patients were over 18 years of age. In the first stage of the disease it was 12.79%, in the second stage it was 15.12%, and in the third 72.09% of patients. Test methods included clinical physical examination, laboratory evaluation, functional tests, and echonographic examination. Clinical data included demographic, comorbidity and vital parameters, baseline full blood count, biochemistry tests, and echosonographic examination. Further laboratory investigations were performed as indicated clinically thereafter. Spot blood and urine samples were collected from all patients in the morning after overnight fasting. The neural network was created in feed forward back propagation of the connection between the data of 69 patients with 31 parameters. In pattern recognition, the neural network learns to recognize the conditions in which it was decided to send the patient to dialysis 10 or to send to classical treatment 01. The training function analyzed the patients separated in three special categories 80% training, 10% test and 10% validation. The algorithm of the learning function is a scaling gradient that adapts the input data to the output data.

Results: The neural network achieved a performance of 0.14322 in 6 epochs. In a test with the data of 17 patients, it was shown that the neural network indicates for which patients dialysis treatment is a better option that fits with AKI stage 3. For patients with the first and second stages of the disease, conservative treatment is a better therapeutic choice.

Conclusion: This paper deals with a current topic by analyzing data using a neural network algorithm to help assess the stage of the disease in high-risk hospitalized patients with acute kidney injury and select treatment modalities. The conclusions derived from this analysis should help with stage recognition and the selection of treatment modalities for patients with acute kidney injury. Results: A total of 1082 adult patients were recorded with median age 77 years. The majority of them had several comorbidities, 457(42%) diabetic, 424(39%) hypertensive and 442(41%) with Chronic Kidney Disease (CKD). Principal causes of AKI were cardiovascular disease (405;38%), infection (198;18%), gastrointestinal disorders (130;12%) and malignancy (103;10%). Other etiologies comprise obstructive nephropathy (45%;4%), bleeding (363%;3%), surgery (29.3%), cardiovascular surgery (13%;1%) and miscellaneous (123.12%). Management of AKI included fluid resuscitation applied in 405.37% cases, intravenous diuretic therapy applied in 241;22% patients, while 216.20% cases required hemodialysis.

The mean creatinine value at assessment was 3.9±2 mg/dl while 15% of the patients had a normal admission creatinine (<1.3mg/dl). The patients were classified in three groups according to the creatinine levels rise: A) 345 patients at baseline had a creatinine rise of 0.3-0.5 mg/dl, B) 343 had a rise of 0.6-1 mg/dl and C) 394 had a rise of type "Periodic" type "Periodic"> 1 mg/dl. The mean value of hospitalization days for each of the 3 above groups was calculated as 10.8 ± 10.3, 10.7 ± 8.1 and 14.7 ± 11.4 respectively, p<0.05 for the comparisons with the 3rd group.

In comparison, there was no significant difference in the treatment method of AKI between the 2 groups, but Hemodialysis was applied more frequent in the 3rd group (44 vs 46 vs 124 patients, p<0.05 for the comparisons with the 3rd group). Regarding the difference between the creatinine levels on admission and the creatinine levels on discharge, a statistically significant difference was found between the 3 groups (p<0.05) with prevalence of worst discharge creatinine levels to the third group. 15% exited with creatinine <1.3 mg/dl. In a multivariate linear regression model, it was also found that the difference in admission-discharge creatinine levels, diabetes mellitus was an independent factor (p = 0.035) as well as the group categorized based on the increase in creatinine during assessment (p<0.01).

Conclusion: Hospitalized patients in non-nephrology clinics may develop AKI and require different treatment plan as well as management of the primary cause. The heterogeneity of AKI and the need for dialysis as well as the days of hospitalization, underlines the need for close observation, personalized care, vigilance of other specialists and the cooperation with nephrologists.

As it is shown from this study the early nephrology assessment is associated with fewer days of hospitalization and better outcome for the patient's renal function, as well as the severity of the treatment. As the prevalence of chronic kidney disease is rising around the world is of great importance for the patients with AKI to be able to maintain their kidney function.
Septic (16.6%), Mixed Renal Tropism (16.2%), Ischemic (15.5%) and CS (10.9%). Regarding the CS, patients were more often admitted to the ICU (100%; p<0.001) made the least use of corticosteroids (51.6%; p>0.001) and diuretics (12.9%; p=0.016), they made the most use of mechanical ventilation (100%), vasoactive drugs (100%) and dialysis (74.2%; p<0.001). Paradoxically, they were the most obese (67.74% p= 0.011), but had less hypertension (48.4%; p = 0.025), less previous cardiovascular disease (6.45% p = 0.01), and less dyslipidemia (9.68%; p = 0.012). In general, the mixed etiology markedly comes closest to the CS etiology, followed by the MOF. Patients who least needed dialysis were those with septic etiology (18.18% p<0.001). Preliminary tests show an impressive mortality of 69.61%, which is associated with the AKI pathophysiological mechanisms (p<0.0001). CS (87.1%), MOF (87.0%), and Mixed Etiologies (89.1%) are the pathophysiological mechanisms associated with poor prognosis; and Viral Renal Tropism (54.3%), Sepsis (48.3%), and Ischemic Injury (34.1%) are the pathophysiological mechanisms related to the best outcomes.

Conclusion: AKI related to COVID-19 patients are mostly elderly, admitted to ICU, classified as KDIGO 3 and their mortality is notable. Nevertheless, the mortality and the need for dialysis depends on the pathophysiological mechanism their AKI, as CS, MOF and Mixed Etiologies are the pathophysiological mechanisms associated with poorest prognosis; and Viral Renal Tropism, Sepsis, and Ischemic Injury are related to the best outcomes.

#6428
PERCUTANEOUS RENAL BIOPSY (PRB) IN METASTATIC RENAL CELL CARCINOMA (mRCC) PATIENTS WITH ACUTE KIDNEY INJURY (AKI) ON SYSTEMIC ANTICANCER THERAPY
Tomaž Milanez1,2, Miha Arnol2, Vladimir Premru2, Nika Kojc3, Janja Ocvirk1, Tanja Ovcaricek1 and Edgar Jaimes4
1Institute of Oncology Ljubljana, Ljubljana, Slovenia, 2University Medical Center Ljubljana, Dept of Nephrology, Slovenia, 3Ljubljana, Slovenia and 4Memorial Sloan Kettering Cancer Center New York, Department of Medicine, New York, United States of America

Background and Aims: PRB is relatively contraindicated in patients with solitary kidney (SK) due to the perception that PRB is a risky procedure in this patient population. There are however situations in which a renal biopsy is essential to assess renal toxicity of systemic therapy and/or to identify the underlying kidney disease in the remaining kidney. Data on pathological findings of the kidney disease in mRCC patients receiving systemic anticanter therapy is scarce and it may influence the cancer treatment plan. The main aim of this study was to characterize the pathological findings of PRB in patients with SK undergoing systemic therapy.

Method: We retrospectively analyzed the pathological findings of mRCC patients with AKI who underwent PRB during systemic treatment with antiangiogenic tyrosine kinase inhibitors (TKIs) and/or immune checkpoint inhibitors (ICIs) at the Institute of Oncology Ljubljana between 2018 and 2022. All biopsies were performed under ultrasound guidance by the treating nephrologist in patients with clinical evidence of AKI and no other formal contraindications for PRB.

Results: A total of 11 PRBs were performed in 10 patients, eight of whom had SK (Table 1). Six patients were treated with TKIs and ICIs, three with ICIs and one with a TKI alone. None of the patients had major bleeding or required any additional intervention as a consequence of the PRB. Histology revealed thrombotic microangiopathy (TMA) in three, diabetic nephropathy in three, acute interstitial nephritis in two and focal segmental glomerulosclerosis in three patients. Based on pathological findings, the therapy was discontinued after seven PRBs. One patient with TMA showed progressive loss of renal function (RF) after discontinuation of antiangiogenic therapy while the other two had either stable or improved RF.

Conclusion: Our results indicate that PRB is a safe procedure in patients with SK undergoing systemic treatment for mRCC. The pathological findings in our patients guided the decision either to continue or to discontinue the treatment, which resulted in improvement or stabilization of RF in the vast majority of patients. This study suggests that in patients with SK, PRB can provide important information, which may have a significant impact on the oncological and the nephrological therapeutic approaches.

Table 1: Age and laboratory findings of mRCC patients receiving systemic anticancer treatment prior to PRB.

<table>
<thead>
<tr>
<th>No. of biopsies</th>
<th>Age at biopsy</th>
<th>No. of patients</th>
<th>Baseline Scr (μmol/L)</th>
<th>Peak Scr (μmol/L)</th>
<th>No. of patients with proteinuria ≥3.5 g/24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>69 (59-74)∗</td>
<td>10</td>
<td>122.1 (30)∗</td>
<td>280 (66.5)∗</td>
<td>4</td>
</tr>
</tbody>
</table>

SCr, serum creatinine
∗median (interquartile range)
**mean (standard deviation)
Without AKI compared to patients with AKI (22.01% vs 16.69 ± 4.5% respectively). The Kaplan-Meier curve illustrated longer survival in patients with AKI (Log-rank test: X² = 15.41; p = 0.0001).

Conclusion: Renal impairment in COVID-19 patients occurs in significant percentage, and it is a factor of poor prognosis. The severity of the disease itself is emphasized as main contributing mechanism in the occurrence of AKI, and the lower blood saturation at admission is the strongest mortality predictor, outreaching the significance of the AKI itself.

#4566
PREDICTIVE ADMISSION RISK FACTORS, CLINICAL FEATURES AND KIDNEY OUTCOMES IN COVID-19 HOSPITALISED PATIENTS WITH ACUTE KIDNEY INJURY
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University Clinic of Nephrology, Medical Faculty, St Cyril and Methodius University, Nephrology, Skopje, Republic Of North Macedonia

Background and Aims: Kidneys in COVID-19 patients demonstrate high vulnerability and acute kidney injury (AKI) is recognized as a cause of poor outcome and high mortality, in those requiring hospitalisation. The aim of our study was to assess the predictors and rate of AKI involvement among COVID-19 hospitalised patients at the day of admission, and to see the impact of AKI on patient's prognosis and life expectancy.

Method: We analysed admission data of COVID-19 patients, hospitalized in a tertiary nephrology hospital, during the first pandemic wave. Outcome data were recorded, including the need for renal replacement therapy (RRT) and inpatient mortality at 30 days.

Results: Out of 115 admitted patients included into the final analysis, 62(53.9%) presented with AKI, 21(39.3%) met KDIGO criteria for stage 1, 7(11.3%) for stage 2 and 34(54.8%) for stage 3 of AKI. RRT was required in 26 patients (22.6% of total, 41.9% of all AKI). From the discharged patients, AKI has been resolved in 76% and no need of RRT following hospital discharge was noted. Pre-existing CKD was associated with a 13-fold risk of AKI (OR 13.04; 95% CI:3.85–44.06, p = 0.009). Pre-existing CKD, that were followed by the nephro-obstetric clinical team were recorded, including the need for renal replacement therapy (RRT) and perinatal outcomes between 2011 and 2022.

Conclusion: Renal impairment in COVID-19 patients occurs in significant percentage, and it is a factor of poor prognosis. The severity of the disease itself is emphasized as main contributing mechanism in the occurrence of AKI, and the lower blood saturation at admission is the strongest mortality predictor, outreaching the significance of the AKI itself.

#4762
PREGNANCY-RELATED ACUTE KIDNEY INJURY: 10-YEAR SERIES OF A NEPHRO-OBSTETRIC CLINIC
Estela Nogueira1, Nadiesda Perez1, Iolanda Godinho1, Mónica Centeno2, Luisa Pinto2 and José António Lopes3
1 Centro Hospitalar Universitário Lisboa Norte, EPE, Nephrology and Renal Transplantation, Lisbon, Portugal and 2 Centro Hospitalar Universitário Lisboa Norte, EPE, Obstetric, Gynecology and Reproductive Medicine Department, Lisbon, Portugal

Background and Aims: Pregnancy-related acute kidney injury (P-AKI) is a rare complication of pregnancy associated with significant maternal and fetal morbidity and mortality. Its incidence has progressively decreased worldwide with the improvement of obstetric care, but recently some developed countries have noticed an increase in its incidence. Adjusted definition of AKI in pregnancy is lacking, making its incidence difficult to ascertain. Herein, the authors retrospectively evaluated the causes and outcomes of P-AKI patients surveilled by the nephro-obstetric clinical team.

Method: Retrospective analysis of maternal, obstetric and perinatal outcomes of P-AKI patients, that were followed by the Nephro-obstetric clinical team between 2011 and 2022.

Results: We evaluated 29 patients, with mean age of 32 ± 6 years [17 – 42], 19 Caucasian and 9 Black, 17 nulliparous, 16 hypertensive, 7 diabetic, 1 with HIV, and 1 with systemic lupus erythematosus. Only 12 patients had CKD and 3 were renal transplant patients. In 2/29 patients P-AKI occurred before 20 weeks [15-17] due to obstructive uropathy and pregnancy hyperfiltration in a CKD G3 patient. After 20 weeks of gestation, P-AKI occurred in 27/29 patients (mean 32 weeks; range 21-41weeks), with mean SCr of 3.1 mg/dl [1.8-4.5] in previously CKD patients and mean SCr of 2.4 mg/dl (1.2-5.8 mg/dl) in the patients with normal renal function. Regarding the severity of P-AKI, 16/27/6 patients developed AKI stage 1/2/3 (KDIGO), respectively. Causes of P-AKI after 20 weeks in patients with normal renal function were preeclampsia (PE; 8/14), HELLP syndrome (1/14), hemorrhagic shock (1/14), severe hypercalcemia (1/14), corticosteroid nephrosis due to hypervolemia and nephrotoxic agents (1/14). All patients had full renal recovery. In renal transplant patient P-AKI was related to PE (2/3), sepsis (1/3) and probable calcineurin inhibitor toxicity (1/3). Regarding CKD patients, P-AKI was caused by PE (6/10), hyperfiltration of pregnancy (3/10) and allergic interstitial nephritis (1/10). The need for renal replacement therapy occurred in 7/29, and only 2/7 became dialysis dependent (both with previous CKD diagnosis). De novo or worsening proteinuria occurred in 15/29 (3975 g/day; 431-14000 g/day) and 10/29 patients (mean 6227 mg/day; 681-14937 mg/day), respectively. Regarding fetal outcomes, there were 2 stillbirths, mean gestation duration was 33 weeks (25-41 weeks), mean birth weight 1947 g (550-3950 g) and mean Apgar 1/5/10 was 8/9/10, respectively. Cesarean was performed in 19/27 patients and 7 newborns were admitted to the neonate care unit due to prematurity.

Figure 1: Kaplan-Meier survival curve: patient in-hospital survival among patients with and without AKI.
Conclusion: In a tertiary referral center, P-AKI was associated to a wide range of causes, frequently required a multidisciplinary approach and was associated to significant worse maternal, obstetric and perinatal outcomes.

#5535
CALCICUM EXCRETION FRACTION AS AN EMERGING PARAMETER FOR AN ACCURATE DIFFERENTIAL DIAGNOSIS OF ACUTE KIDNEY INJURY
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Background and Aims: Urinary parameter determination is an essential tool for differentiating acute kidney injury (AKI) etiology. The most used ion in clinical practice is sodium (and its excretion fraction, NaEF), followed by urea (UreaEF) (that is useful in certain circumstances such as diuretic treatment). However, tubular transport includes other anions and cations that have not been widely studied. In the present study, we aim to evaluate the relation between AKI etiology (i.e. functional vs acute tubular necrosis) and calcium excretion fraction (CaEF).

Method: This is a transversal study including consecutive patients with diagnosis of AKI. Patients with suspicion of non-functional or ATN etiology (such as those with proteinuria, hematuria) were excluded. At admission, we collected epidemiological data, comorbidities and active treatments. AKI etiology was determined based on urinary parameters (sodium, urea) and recovery pattern of kidney function after treatment instauration. We compared CaEF in patients with ATN and functional AKI in the whole sample and among patients with and without previous CKD and diuretic prescription.

Results: We included 94 AKI episodes (55% female, 76±15 years). Forty-five (48%) patients had chronic kidney disease (CKD) at baseline and 56 (60%) were receiving treatment with diuretics. Of the 94 AKI, 78 (83%) presented an ATN pattern and 16 (17%) were catalogued as ATN. Median CaEF was 1.09 (0.63-2.58) %. CaEF was associated to the etiology of AKI. In patients with functional AKI, median of CaEF was 0.95 (0.60-1.84) % in contrast to ATN (2.33 [1.22-7.27] %)(p<0.001). CaEF presented a positive and significant correlation to NaEF (ρ 0.574, p<0.001) and UreaEF (ρ 0.409, p<0.001). An adjusted regression model including the presence of CKD at baseline and diuretic treatment showed that CaEF independently predicted ATN (OR per 1% increase 1.42, 95%CI [1.16-1.75], p<0.001). In patients without CKD, CaEF predicted ATN (OR 1.61, 95%CI [1.13-2.28], p = 0.008), in contrast to the cohort with CKD where only a trend was demonstrated (OR 1.29, 95%CI [0.99-1.69], p = 0.057) (Figure 1). CaEF also predicted ATN irrespective of the diuretic prescription at baseline (OR 1.35, 95%CI [1.01-1.74], p = 0.018 for diuretic users and OR 1.57, 95%CI [1.06-2.32], p = 0.025 for non-diuretic users) (Figure 1). Receiving operator curves (ROC) demonstrated a 0.712 area under the curve (AUC) of CaEF >1.6% for ATN, that was the best value for diagnosis in terms of sensitivity and specificity. CaEF>1.6% predicted ATN (OR 8.09, 95%CI [2.32-28.2], p = 0.001) after adjusting for the presence of CKD at baseline and diuretic treatment.

Conclusion: CaEF could help in the identification of the AKI etiology as higher values (i.e. >1.6%) are independently associated with ATN.

#2550
THE ANTI-AGING FACTOR, α-KLOTHO EXPRESSION DURING HUMAN PREGNANCY AND ITS COMPLICATIONS: PREECLAMPSIA AND SMALL-FOR-GESTATIONAL-AGE NEONATE
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Background and Aims: Pre-eclampsia (PE) is defined as arterial hypertension associated with proteinuria and may cause dysfunction of vital organs as kidney, liver, brain and other organs. PE is consider as the leading cause of maternal and perinatal morbidity worldwide [1,2]. IUGR definition is abnormal fetal growth compared with growth potential of a specific infant. α-Klotho (αKL) protein has three isoforms: a single transmembrane (mKL) form, a shed soluble form, and a secreted soluble circulating protein (sKL). mKL is expressed in the kidney and placenta. Nowadays, αKL levels correlation to pregnancy or pregnancy’s complications, such as pre eclampsia (PE) or intra-uterine growth restriction (IUGR) is not clear. The research goals were to monitor αKL concentrations during pregnancy and to investigate its expression alterations in correlation to pregnancy complication [3,4,5].

Method: The research included 49 participants, recruited at the Baruth Padeh Poriya medical center, Obstetric Department. The participants were divided into two groups: healthy and complicated pregnancy (PE, IUGR or both). Blood and urine samples were collected during pregnancy and post-delivery (PD). Placental samples were subjected to biochemical (WB) and Elisa, morphological (H&E) histological (IHC) staining and genetic analysis (qPCR). αKL activity was assessed using specific assigned Elisa kit.

Results: sKL during pregnancy show constant concentration that was similar in both healthy and complicated pregnancy. Significant decrease was measured in PE in sKL concentration at PD compared to its level during pregnancy. αKL activity was dramatically reduced in complicated pregnancies compared with healthy pregnancy during and PD. Placental tissue section staining presents decrease in mKL level in the placenta of complicated pregnancy group compared with healthy group. Additionally, we found significant decline in the expression of mRNA of mKL in PE/IUGR placenta compared with healthy group.

Conclusion: sKL level was similar in both healthy and complicated pregnancy, our results suggest low activity of sKL in complicated pregnancy compared with control. 2. Complicated pregnancy is manifested in decline in mKL, also with low activity of sKL compared with control, and gene expression between healthy and complicated pregnancy. 3. A dramatic and significant

Figure 1: Association between CaEF and AKI etiology in patients with and without CKD and diuretic treatment.
Figure 1: Placental klotho levels in control and PE/IUGR group. A. Representative western blots of α-Klotho protein levels in human placental lysates. Proteins were detected by immunoblotting using antibodies against α-Klotho and GAPDH as a loading control. B. Quantification of total Western blot. Placental m-klotho level was significantly reduced in placental PE/IUGR lysate compared with control. PE n=13 control n=20. The results represent the mean ± SEM. Unpaired student’s t-tests were performed to obtain the p values indicated on the graph **p <0.0001.

decline in NO molecules concentration in urine of complicated pregnancy compared with healthy pregnancy.

REFERENCES

#4185
EPISODES OF AKI FOLLOWING HOSPITALISATION AND ASSOCIATION WITH ADVERSE OUTCOMES: ANALYSIS FROM A PROSPECTIVE COHORT STUDY
Kerry Horner1,2, Daniela Viramontes-Horner1, Rebecca Packington3, Sue Shaw4, Aleli Akani5, Tim Reilly6, John Monaghan4 and Nick Selby1,2

1 University of Nottingham, Centre for Kidney Research and Innovation, United Kingdom, 2 University Hospitals of Derby and Burton NHS Foundation Trust, Renal Unit, United Kingdom, 3 University Hospitals of Derby and Burton NHS Foundation Trust, Department of Informatics, United Kingdom and 4 University Hospitals of Derby and Burton NHS Foundation Trust, Department of Chemical Pathology, United Kingdom

Background and Aims: AKI is associated with adverse long-term outcomes, including mortality, cardiovascular events and CKD development and progression. Individuals who have sustained AKI are at increased risk of developing further AKI. This analysis presents the association of long-term risk related to recent and further episodes of AKI in a prospective cohort of recently hospitalised individuals.

Method: Two matched cohorts of hospitalised individuals who had survived to at least 90 days after hospital discharge were recruited. The cohorts consisted of people who had sustained AKI during hospital admission (exposed group), and those who had not (non-exposed group), and were matched 1:1 for age, baseline eGFR stage and diabetes. Renal function, albuminuria and new AKI episodes were measured at 3 months, one, three and five years after index hospitalisation. Mortality, further AKI episodes and episodes of heart failure were recorded. Kidney disease progression was defined as decrease in eGFR of ≥25% associated with a decline in eGFR stage. Multivariable analysis was performed with binary logistic regression to assess the associations between repeated AKI episodes and outcomes.

Results: 866 exposed and non-exposed participants were recruited and successfully matched. Over the 5-year follow-up period, 138 (34%) participants in the exposed group had ≥1 further AKI compared with 67 (16%) in the non-exposed group (OR 2.71 [95% CI 1.94 to 3.77]; p <0.001). Independent associations with developing AKI during the follow-up period were AKI during index admission, baseline eGFR, albuminuria at 3 months and smoking
status. Binary logistic regression, including all matched participants, showed that AKI during follow-up was independently associated with 5-year kidney disease progression (adjusted OR 2.49, 95% CI 1.42-4.37, p = 0.002), mortality (adjusted OR 3.076 95% CI 2.039-4.639, p < 0.001) and episodes of heart failure (adjusted OR 5.234 95% CI 3.355-8.164, p < 0.001). There was an additive effect, with the frequency of adverse outcomes increasing as number of AKI exposures increased (Table 1). Exposure to AKI during index admission or follow-up episodes conferred similar risk of kidney disease progression. AKI during the follow-up period had a stronger association with mortality and heart failure episodes than AKI during the index admission in this survivor cohort.

### Table 1: Incidence of kidney disease progression, mortality and heart failure episodes after 5-years follow up, according to number of time points during index admission and follow-up in which AKI episodes occurred.

<table>
<thead>
<tr>
<th>Number of AKI episodes</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>&gt; = 3</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney disease progression n (%)</td>
<td>19 (5.4)</td>
<td>92 (26.5)</td>
<td>45 (39.1)</td>
<td>17 (65.4)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Mortality n (%)</td>
<td>57 (15.6)</td>
<td>87 (24.2)</td>
<td>41 (35.7)</td>
<td>9 (34.6)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>≥ 1 episode of heart failure n (%)</td>
<td>37 (10.1)</td>
<td>66 (18.4)</td>
<td>41 (35.7)</td>
<td>13 (50)</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>

Conclusion: Previous AKI episodes were associated with increased frequency of future AKI episodes. AKI episodes during follow up period were independent associated with adverse outcomes regardless of AKI exposure during index hospitalisation. Increasing number of exposures to AKI had an additive effect on the proportion of individuals showing kidney disease progression, mortality and heart failure episodes. In this cohort of AKI survivors, AKI during the follow-up period had a stronger associated had with these outcomes than exposure to AKI during the index admission. A strategy for improving long-term outcomes in AKI survivors may be improving the identification of those at greatest risk of future AKI and strategies to prevent or optimise early detection and management.

### #6045

**TWO-YEAR INPATIENT ACTIVITY OF A DEDICATED ONCOBASED NEPHROLOGY DEPARTMENT**

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**Background and Aims:** Oncoonephrology is a rapidly evolving nephrology subspecialty that focuses on the interaction between cancer and the kidney. Our aim was to describe the clinical activity of a Nephrology Department in a cancer care center, in a 2-year period.

**Method:** We retrospectively analyzed the patients observed by the Nephrology Department at our center between 2021 and 2022. Demographic, clinical and laboratory data were collected. The statistical analysis was performed with SPSS software.

**Results:** During the 2-year period, there were 26,015 admissions, 636 of which required a Nephrology observation. Sixty-two percent were female; the mean age was 68 years (SD 12.4) with a median Charlson Comorbidity Index of 7. Most cancers were from gastrointestinal (24.1%, n = 153) or urologic origins (22.3%, n = 142), 37% had metastatic disease. Hematologic malignancies accounted for 12.1% of patients (n = 77). Nearly 44.5% of patients (n = 283) had chronic kidney disease (CKD), 20.8% (n = 59) of which were on hemodialysis (HD). Urinary tract obstruction (23.3%), cardiovascular risk factors (17.3%) and nephron loss (10.6%) were the most common causes of CKD. The main reasons for admission were renal dysfunction (23.7%; n = 151), infectious complications (23.3%, n = 148) and elective surgery (20.3%, n = 129). Of the patients observed, 40.7% (n = 259) had acute kidney injury (AKI). 23.3% (n = 148) acute-on-chronic kidney disease and 11.8% (n = 75) hydro-electrolytic disorders. Ten patients (1.6%) were evaluated for nephritic syndrome (NS) or rapidly progressive renal failure (RPRF). Among AKI patients, intrinsic causes were the most prevalent (48.7% of all cases), with sepsis and ischemic and toxic acute tubular necrosis being the most frequent. Pre-renal and post-renal etiologies occurred in 29.7% and 21.6% of cases, respectively. Gynecological and prostate tumors were the main neoplastic cause of post-renal AKI. There were 5 TMA cases in allogenic stem cell transplanted patients or treated with gemcitabine and six cases of acute interstitial nephritis, the majority immune check-point inhibitors-related. Over 54% (n = 142) of patients presented with AKI stage 3. About 13% (n = 34) needed renal replacement therapy (RRT), mainly continuous or hybrid techniques (58.8%; n = 20), and only 38% (n = 13) recovered renal function. The group of acute-on-chronic CKD patients included mostly stage 3b and 4 CKD. Most of them (54.1%; n = 80) had an intrinsic cause for kidney dysfunction. There was an equal distribution between stages of AKI severity. About 5% (n = 8) needed RRT and only two of those recovered. Hyponatremia was the most common electrolyte disturbance (56%; n = 42), followed by hypercalcemia (17.3%; n = 13). Over 40% of all cases of hyponatremia occurred in patients with metastatic lung cancer, probably related with the high prevalence of SIADH in this population. All but two patients with NS or RPRF underwent kidney biopsy. Among the patients with NS, its etiologies were: focal and segmental glomerulosclerosis secondary to pemiprodramine (n = 2), podocytopathy related to pazopanib (n = 1), paraneoplastic membranous nephropathy (n = 1), AL amyloidosis (n = 1) and TMA secondary to gemcitabine (n = 1). The causes of RPRF were ANCA-negative small vessel vasculitis, crescentic glomerulonephritis (GN) related to pembrolizumab and TMA. We also followed two patients with acute kidney disease, one with ATN secondary to bisphosphonates therapy and other with paraneoplastic fibrillary glomerulopathy. The median duration of hospitalization was 10 days (IQ 7.0 – 20.8), with median Nephrology follow-up time of 5.5 days (IQ 3.0 – 9.0). The overall mortality rate was 21.5%, and it was even higher on the subgroup with AKI (27.4%; p = 0.03). About 44% (n = 219) of patients were referred to outpatient Nephrology follow-up, at discharge.

**Conclusion:** Our data provides a picture of the rich inward activity developed at our cancer center by the nephrology team. The complexity of these patients highlights the importance of a multidisciplinary approach in their management. No surprisingly, there was a high mortality rate, which was even higher in the AKI-patients subset.

### #6489

**UNI-494 DOES NOT SIGNIFICANTLY AFFECT RAT RESPIRATORY FUNCTION**

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**Background and Aims:** Nicorandil, a selective mitochondrial ATP-sensitive potassium channel activator, may be beneficial for several disease states, including acute kidney injury. However, its clinical use is limited by serious gastrointestinal side effects and rapid absorption and elimination. UNI-494, a novel nicorandil prodrug designed to improve its pharmacologic properties, may increase the short half-life and improve the safety profile of nicorandil. We present safety results from a safety pharmacology study evaluating the effects of UNI-494 on respiratory function in a rat model.

**Method:** The effects of UNI-494 on respiratory function (peak inspiratory and expiratory flow, inspiratory and expiratory time, minute volume, and respiratory rate) were evaluated using whole body plethysmography test in 4 groups of male Wistar Han rats (n = 8 per group). In addition to a control group, 3 test groups were administered doses of 2, 20, or 200 mg UNI-494/kg. Airway function parameter data generated were acquired using specialized EMKA Technologies software (IOX version 2.9.5; DATANLYST version 2.6.1) connected to Emka plethysmographic equipment. Recordings were taken 3 hours before and 4 hours after administration of the control and test items. Effects were reported at 0, 10, 15, 20, 30, 60, 90, 120, 180, and 240 minutes after administration.

**Results:** UNI-494 had no relevant effects on rat respiratory function over the 240-minute test period at any dose (2, 20, or 200 mg UNI-494/kg). There were small but insignificant differences in peak inspiratory and expiratory flow (Figure 1, 2), minute volume, respiratory rate, and inspiratory and expiratory time between the control group and the 200 mg UNI-494/kg group.

**Conclusion:** Rat respiratory function was not significantly affected by UNI-494. Future studies should continue to evaluate the safety and efficacy of this novel drug.
CARDIORENAL SYNDROME TYPE 1 IN CHILDREN AFTER SURGICAL TREATMENT OF CONGENITAL HEART DISEASE USING CARDIOPULMONARY BYPASS
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Background and Aims: According to recent data, acute kidney injury (AKI) after pediatric cardiac surgery is a significant postoperative complication that occurs in 35-64% of children (1,2) and is associated with increased hospital mortality and unfavorable short-term outcomes. The problem of acute kidney injury in children after cardiac surgery remains relevant, despite the development of modern technologies and methods. Complications after pediatric cardiac surgery have serious negative consequences, prolonging the days of stay in the pediatric intensive care unit (PICU) and increasing mortality (3). The aim of the study is to analyze the frequency of AKI in children after open-heart surgery for congenital heart defects (CHD) using cardiopulmonary bypass (CBP).

Method: We conducted a retrospective analysis of 402 medical records of patients hospitalized in the ICU of JSC NRCSC Astana, Kazakhstan, from January 2018 to December 2022. Inclusion criteria: Children under 18 with CHD who underwent open-heart surgery for congenital heart defects (CHD) using cardiopulmonary bypass (CBP).

Results: The analysis included the total number of patients - 402 patients. The frequency of AKI was 15.6% (63 out of 402). Among the patients who developed AKI: boys - 45 (71.4%), girls - 18 (28.5%). The age distribution is as follows: children under 1 month among AKI - 50 (79.3%), under 6 months among AKI – 13 (20.6%), under 1 year among AKI – 5 (7.9%). According to the statistical analysis results, the complication depends on the type of operation, as there is a statistical significance of the differences in the groups (p = 0.046). However, the type of operation (p = 0.35) does not matter for the outcome. Also, the children's weight (p = 0.082) has no statistical significance on the number of complications and the outcome. The sex of children has a statistical significance for complications; in boys, it is significantly higher (p = 0.05).

Conclusion: According to our data, the frequency of AKI developed in 15.6% of patients after surgical treatment of CHD using CBP. The overall mortality rate is 19.9%, with boys having a higher risk. Thus, the frequency of AKI is influenced by many factors before, during and after surgery. Therefore, developing preventive measures is a priority for improving the cardiac surgery results in children.

INITIAL EMERGENCY ROOM 6-HOUR URINE VOLUME IS AN IMPORTANT FACTOR FOR THE SURVIVAL OF CRITICALLY ILL PATIENTS UNDERGOING CRRT
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1Chungnam National University Hospital, Nephrology, Daejeon, Rep. of China, 2Chungnam National University, Medical Science, Daejeon, Rep. of China and 3Chungnam National University Sejong Hospital, Nephrology, Sejong, Rep. of China

Background and Aims: It has been little known whether initial emergency room factors affect survival or renal function in critically ill patients undergoing continuous renal replacement therapy. We examined whether...
initial factors in ER impact survival and renal recovery in critically ill patients undergoing continuous renal replacement therapy. Method: The study was a single-center, retrospective study of 332 patients for critically ill patients admitted to ICUs for continuous renal replacement therapy via emergency room from March 1, 2018 to May 31, 2021. Clinical parameters including urine output, eGFR, and serum NGAL were identified. The primary outcomes were the 30- and 90-day mortality. Secondary outcomes were the 30- and 90-day dialysis-free duration. Results: Low urine output (LUO, defined as < 0.5 mL/kg/hr x 6 hours) group was significantly associated with 30-day mortality and 90-day mortality. Multivariable Cox regression analysis showed that LUO group was significantly more associated with the increased risk of 30-day mortality and 90-day mortality (hazard ratio, 1.935 and 2.141, respectively) compared to high urine output (HOU, defined as ≥ 0.5 mL/kg/hr x 6 hours) group. There was no significant association between 30-day or 90-day mortality and initial estimated glomerular filtration rate (eGFR) plasma neutrophil gelatinase-associated lipocalin (NGAL) levels. In critically ill patients undergoing continuous renal replacement therapy, HOU group and initial eGFR ≥ 30 ml/min/1.73m2 groups was associated with decreased 30-, and 90-day dialysis-free duration. However, serum NGAL had no significant relation with 30-, and 90-day RRT free durations. Conclusion: During admission to emergency room, the initial low urine output is an important factor for 30- and 90-day mortality in Critically Ill Patients Undergoing Continuous Renal Replacement Therapy. #5974 CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF THE ONCO nephrological POPULATION: A MULTICENTRE PROSPECTIVE OBSERVATIONAL STUDY Giovanni Pintus1, Silvia La1, Alessandra Punzo1, Luca Salomone1, Adolfo Perrotta1, Silverio Rotondi1, Lida Tartaglione1, Francesca Tinti1, Sandro Feriozzi1 and Sandro Mazzaferrino1 1Sapienza University, Department of Internal Medicine, Anesthesiological and Cardiovascular Clinical Sciences, Rome, Italy; 2University of Padua, Department of Medicine - DIMED, Padua, Italy; 3Sapienza University, Department of Translational and Precision Medicine; Nephrology Unit, Rome, Italy; 4Civile Hospital, Nephrology and Dialysis Unit, Nephrology and Dialysis Unit, Viterbo, Italy Background and Aims: Onconephrology is a recently developed discipline aimed at diagnosing and managing renal disease in cancer patients. Few data are available regarding clinical and histological aspects concerning the whole population referred to an onco nephrology clinic. Our study aimed to describe the clinical and histopathological characteristics of these patients and to evaluate indices of renal function recovery, renal damage progression, and mortality; a specific aim was to determine in our cohort the prevalence of acute kidney injury (AKI), chronic kidney disease (CKD) and acute kidney disease (AKD) which included all patients meeting KDIGO criteria for AKD but not for AKI. Secondary aims were the analysis of the immunotherapy subgroup and to determine the rate of immune-related adverse events (IRAEs). Methods: In this prospective observational study, we consecutively enrolled 84 patients for the clinical analysis and 10 patients in two centres for the histopathological study. Clinical assessment in the former group were performed at the first visit (T0), 1 month (T1), 3 months (T2) and 1 year (T3) and compared with a pre-determined baseline. Complete oncological and nephrological assessments were performed. For kidney biopsies, histopathological findings were expressed with quantitative and semi-quantitative parameters. Outcomes were: AKI or AKD complete or partial recovery of renal function (respectively defined as: return to baseline; ≤ 3 mg/dl or > 25% or improvement to a lower stage of AKI); a composite of events (MAKE) based on CKD development or progression or death (only at T3). Results: Our population was predominantly elderly, hypertensive, in metastatic phase (64.2%). M-F; other factors associated with increased cardiovascular risk were: previous AKI (18.8%), diagnosis of type 2 diabetes (25.9%), history of former/current smoker (55.4% and 19.6%), hyperuricemia (mean uric acid 7 mg/dl), previous/current cisplatin treatment (15.5% and 3.6%). The estimated prevalence in our cohort was: AKI 30.1%; CKD 27.7%; AKI on CKD 25.7%; AKD 9.6%. Regarding AKI, 68.4% were stage 1; for CKD, most patients were stage 3A and 3B (28.2% and 46.2%). More than 1/3 of the patients presented with suspended anticancer treatment; complete therapy resume rates were modest. Complete and partial AKI recovery rates at T2 were both ~33%. Renal function was fully recovered in 50% of the AKD patients. During the follow-up, a new episode of AKI was observed in 15.5% of the patients, more frequently in the first 3 months. Patients receiving immunotherapy showed worse renal function (sCr 2.02 vs 1.51 mg/dl at T0, p<.001) and higher mortality (4 vs 0, p<.05); patients with IRAEs (25.8%) presented more frequently with discontinued therapy (Table 1). Of 36 patients with data available at 1 year, 21 (58.3%) presented the outcome MAKE; 11 patients died, 4 in the first three months. No nephrological conditions were found to predict MAKEs; presence of metastasis and female sex were the only predictors with Cox regression. Patients who underwent renal biopsy showed marked heterogeneity in the diagnoses (4 Membranous nephropathy, 1 drug-induced podocyte damage, 1 extracapillary GN after SARS-CoV2 vaccination, 1 Light/Heavy Chain Deposition Disease, 1 Chronic Tubulointerstitial Nephritis, 1 sclerohyalinosis, 1 nonspecific); histopathological data was unremarkable. Conclusion: AKI and CKD occur frequently in the onco nephrological population. These patients are susceptible to new AKI episodes. The absence of AKI recovery and anticancer therapy withdrawal are common, potentially holding negative prognostic value. Particular attention should be paid to patients undergoing immunotherapy, especially when associated with IRAE. A larger number of patients is needed to estimate the impact of nephrological factors in the extended follow-up. #3380 ACUTE KIDNEY INJURY IN NON-CRITICALLY ILL PATIENTS: CLINICAL CHARACTERISTICS AND OUTCOMES Marco Fiorentino, Sebastiano Nestola, Sabrina Carparelli and Loreto Gesualdo University of Bari "Aldo Moro", Nephrology Dialysis and Transplantation Unit, Department of Precision and Regenerative Medicine and Ionian Area (DMePre-I), Bari, Italy Background and Aims: Acute kidney injury (AKI) still represents a major health public concern associated with worldwide growing incidence. Although many studies have been focused on critically ill patients admitted to ICUs, AKI occurs even in non-critical care settings, with similar consequences in terms of short- and long-outcomes. However, epidemiological data and characteristics of AKI outside the ICU are not well investigated. The aim of the present study was to describe main features and outcomes of AKI observed in non-critically ill patients admitted to a teaching hospital. Method: We performed a retrospective analysis including all AKI patients referred to nephrology consultation in the period January-June 2021 at A.O.U. Policlinico, Bari, Italy. Clinical and laboratory data were collected using the hospital software to analyze the main features of AKI episodes, including their occurrence and stages, the need for renal replacement therapy (RRT), rate and factors associated to kidney function recovery (KFR) and in-hospital death. AKI was defined according to KDIGO Clinical Practice Guideline based on creatinine criteria. In addition, we further collect data on renal function after hospital discharge up to 12 months from discharge to assess the risk of AKI-to CKD transition. Results: Among 899 patients referred for nephrology consultation, 415 (46%) were evaluated for AKI. Pre-existing CKD was present in 204 patients (49%). Most of AKI episodes (52.5%) were classified as KDIGO Stage 3, and 54 patients (13%) required RRT (Table 1). In-hospital mortality in our study cohort was 36.9%, particularly higher in patients with pre-existing CKD (Figure 1a), in patients with stage 3 AKI (Figure 1b) and among patients who did not present KFR within 15 days (Figure 1c). Multivariable Cox regression analysis showed a higher mortality risk for advancing age (HR 1.032, 95% CI 1.012–1.053, p = 0.002) and pre-renal AKI (HR 2.823, 95%CI 1.219-6.536, p = 0.015), while KFR after AKI (HR 0.246, 95%CI 0.098-0.615, p = 0.003) was associated to a lower mortality. KFR was observed in 197 patients (47.5%), and the proportion was significantly higher among patients with AKI stage 1-2 compared to stage 3 (stage 1 62.6% vs stage 2 57.6% vs stage 3 36.8%, p<0.001). Higher baseline eGFR (OR 1.025, 95%CI 1.014-1.036, p<0.001) was associated with higher rate of KFR, while the development of severe AKI was independently associated with lower probability of KFR (OR 0.420, 95%CI 0.248-0.711, p = 0.001). Data on follow-up within 6 months after discharge were available in 62 patients: a
<table>
<thead>
<tr>
<th>Characteristics/Outcomes</th>
<th>All AKI Patients (n = 415)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>76 (65-84)</td>
</tr>
<tr>
<td>Gender (M/F), n(%)</td>
<td>245 (59%) / 170 (41%)</td>
</tr>
<tr>
<td>Baseline sCr, mg/dl, median (IQR)</td>
<td>1.3 (1-1.8)</td>
</tr>
<tr>
<td>Time of nephrology consultation since hospital admission, days, median (IQR)</td>
<td>2 (0-6)</td>
</tr>
<tr>
<td>Timing of AKI onset</td>
<td></td>
</tr>
<tr>
<td>CA-AKI, n (%)</td>
<td>230 (55.4%)</td>
</tr>
<tr>
<td>HA-AKI, n (%)</td>
<td>185 (44.6%)</td>
</tr>
<tr>
<td>Aetiology of AKI episodes</td>
<td></td>
</tr>
<tr>
<td>Pre-renal, n (%)</td>
<td>354 (85.3%)</td>
</tr>
<tr>
<td>Renal, n (%)</td>
<td>61 (14.7%)</td>
</tr>
<tr>
<td>Setting</td>
<td></td>
</tr>
<tr>
<td>Medical wards</td>
<td>305 (73.5%)</td>
</tr>
<tr>
<td>Surgical wards</td>
<td>110 (26.5%)</td>
</tr>
<tr>
<td>AKI stage according to KDIGO criteria</td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>92 (22.2%)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>105 (25.3%)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>218 (52.5%)</td>
</tr>
<tr>
<td>RRT-requiring AKI, n(%)</td>
<td>54 (13%)</td>
</tr>
<tr>
<td>Days on AKI, n(%)</td>
<td>16 (10-31)</td>
</tr>
<tr>
<td>Days on RRT, n(%)</td>
<td>10 (3-20)</td>
</tr>
<tr>
<td>Renal recovery after AKI, n(%)</td>
<td>197 (47.5%)</td>
</tr>
<tr>
<td>Dialysis dependence at hospital discharge</td>
<td>12 (2.9%)</td>
</tr>
<tr>
<td>Transfer to ICU, n(%)</td>
<td>30 (7.2%)</td>
</tr>
<tr>
<td>Length of hospital stay, days, median (IQR)</td>
<td>15 (8-26)</td>
</tr>
<tr>
<td>In-hospital death, n(%)</td>
<td>153 (36.9%)</td>
</tr>
</tbody>
</table>

Legend: AKI acute kidney injury; CA-AKI community-acquired AKI; CKD chronic kidney disease; HA-AKI hospital-acquired AKI; IQR interquartile range; sCr serum creatinine.

Further reduction of eGFR compared to the discharge was documented in 30 patients (48.4%).

**Conclusion:** AKI represents the main nephrologist’s activity as consultants at our teaching hospital. AKI episodes referred to nephrologists are usually severe and associated with a high mortality rate even outside the ICU. A timely nephrologist consultation is important to limit the incidence and severity of AKI.

Figure 1: In-hospital survival curve stratified according to baseline eGFR (a), severity of AKI (b) and kidney function recovery (c).
#3709 KIDNEY IMPAIRMENT AT DIAGNOSIS IN MULTIPLE MYELOMA: THE NEPHROLOGIST PERSPECTIVE

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**Background and Aims:** Kidney impairment (KI) at multiple myeloma (MM) diagnosis ranges between 20 and 50% and is associated with high mortality. Therefore, an important percentage of the newly diagnosed cases of MM come from nephrologists. We aimed to evaluate the new cases of MM with KI diagnosed in our nephrology tertiary care center for presentation features, initial treatment, and survival.

**Methods:** We performed a unicentric retrospective study on 89 consecutive patients newly diagnosed with MM (median age 66 years, 38% male) between 2015-2020. Patients were followed until death or end of study (September 2022), whichever came first.

**Results:** The most common MM type was free light chain (FLC) only (55%) followed by IgG (30%), IgA (14%) and IgM (1%). Kappa FLC was more frequent than lambda FLC (53 vs 47%); the median FLC level was 1760 (IQR 450, 7373) mg/L, and the median narrow plasmocytosis was 30 (IQR 15, 60) %. Among the 89 patients, 81% presented with acute kidney injury, 12% with chronic kidney disease, 5% with isolated proteinuria and 2% with nephrotic syndrome. Baseline median serum creatinine and eGFR were 5 mg/dL and 9 ml/min, respectively. Median proteinuria was 3.3 (IQR 1.3, 6) g/g with median albuminuria of 0.27 (IQR 0.11, 0.66) g/g. More than one third (34%) of the studied patients needed hemodialysis (HD) at diagnosis, and 50% progressed to renal replacement therapy by the end of the follow up period (CKD5D). The most frequent clinical features at presentation were asthenia (75%), followed by bone pain (51%), orthostatic hypotension (14%), peripheral neuropathy (10%), edema (10%) and dyspnea (6%). Arterial hypertension (71%), systemic atherosclerosis (58%), ischemic heart disease (44%) and diabetes mellitus (12%) were the most frequent recorded comorbidities. Treatment with dexamethasone was started by the nephrologist in 74% of the patients at a median dose of 128 (IQR 96, 160) mg, afterwards the patients were referred to hematology for a bortezomib based regime. During the follow up period 58 (65%) patients died; they had higher serum creatinine (5.8 vs 2.5 mg/dL, p = 0.02), needed HD at diagnosis more often (41 vs 20%, p=0.01), had lower serum albumin (3.7 vs 4.4 g/dL, p = 0.001), higher LDH (236 vs 201 U/L, p=0.01) and increased inflammation (C-reactive protein: 13 vs 3 mg/L, p = 0.001). In univariate logistic regression, the risk factors at diagnosis associated with mortality were increased age (OR 1.07, 95% CI 1.03-1.12), atherosclerotic burden (OR 5.51, 95% CI 2.13-14.22), low serum albumin (OR 0.28, 95% CI 0.13-0.63), inflammation (OR 1.05, 95% CI 1.01-1.09), increased LDH (OR 1.01, 95% CI 1.00-1.02) and the need for HD at diagnosis (OR 2.94, 95% CI 1.94-8.26). However, in multivariate analysis only low serum albumin (OR 0.22, 95% CI 0.05-0.90) and the need for HD at diagnosis (OR 10.64, 95% CI 1.71-66.14) were significantly associated with mortality.

**Conclusion:** Patients with MM and kidney impairment at diagnosis are more frequent kappa FLC, present most often as AKI, around one third of them require HD at diagnosis, and half of them progress to CKD5D. Therefore, these patients are a distinct group of MM with a high mortality rate (>60% at five years) who need interdisciplinary care.

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#3640 IMMUNORELATED RENAL ADVERSE EFFECTS IN PATIENTS TREATED WITH CHECKPOINT INHIBITORS

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**Background and Aims:** Checkpoint Inhibitors (CPI) use has revolutionized cancer treatment. However, Immuno-Related Adverse Effects (IRAE) occur in more than 50% of patients. At renal level, the initial incidence of IRAE was considered low and later studies suggest between 1.4–4.9%. The aim of the study was to describe the incidence of IRAE in a single center, and their outcomes after initiation of treatment.

**Methods:** We retrospectively studied 28 patients (72.4% male, median age 71.1 years, IR: 40.1–87.3), with metastatic neoplasms (22 advanced lung cancer, 4 melanomas, 1 renal and 1 colon) treated with CPI (Pembrolizumab 75%, 21.4% Nivolumab and 3.6% with Pembrolizumab + Iplimumab combination) who developed AKI after CPI use, at the Complejo Hospitalario Materno Insular from January 2016 to March 2022. Demographic, clinical and analytical data were collected, as well as, the evolution of kidney function.

**Results:** Immuno-related AKI occurred after a median of 3.7 months (IR: 0.23–24.0). The median plasma creatinine prior to receiving treatment with CPI was 0.9 mg/dl [IQR: 0.67-1.65]. After initiation of steroids (1mg/kg/day), 85.7% showed recovery of kidney function. Seventeen patients (60.7%) presented complete remission, 8 (26.6%) partial remission, while 3 patients (10.7%) did not recover from kidney function. In patients who did not respond initially to steroid therapy, a renal biopsy was performed (n = 7; 25.9%) showing tubulointerstitial nephritis (TIN) in 5 patients, 1 granulomatous nephritis with poor kidney function evolution, and 1 endocapillary glomeru- lonephritis together with TIN. More than half of the patients who developed immuno-related ARF presented toxicity in other organs (n = 13; 56.3%); being thrombosis the most frequent (n = 3; 10.7%).

At the end, two patients (7.1%) presented complete remission of neoplasms, 6 (21.4%) partial remission, stability was observed in 8 patients (28.6%), the neoplasm progress in 4 (14.3%) and 8 (28.6%) patients died during the follow-up. Finally, the patient median survival was 36.7 months ([IQR 5.7–79.6) post CPI treatment.

**Conclusion:** Immuno-related AKI after use of CPI is low; over two-thirds of patients recovered from total or partial renal function after initiation of steroids. The presence of granulomas in renal biopsy may confer poor prognosis.

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#4870 MORTALITY OF ELDERLY PATIENTS WITH ACUTE KIDNEY INJURY UNDERGOING CONTINUOUS RENAL REPLACEMENT THERAPY: IS AGE A RISK FACTOR?

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**Background and Aims:** The incidence of elderly patients with acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT) is increasing. However, there is little evidence on the difference of mortality rates according to age in elderly patients. This study aimed to evaluate the age effect and predictors for mortality in elderly patients with AKI requiring CRRT.

**Method:** A retrospective analysis was performed in elderly patients with AKI who underwent CRRT. A total of 480 patients aged ≥ 65 years were stratified into three groups according to age: youngest-old (age 65 - 74 years, n = 205), middle-old (age 75 - 84 years, n = 217), and oldest-old (age ≥ 85 years, n = 58). The 28-day and 90-day survival rates were compared between three groups and predictors for mortality were analysed.

**Results:** The 28-day and 90-day survival rates were not different between three age groups (P = 0.156 and P = 0.189, respectively). The oldest-old group did not show an inferior survival rate to other two groups. For 28-day mortality, prothrombin time [hazard ratio (HR) = 1.37, 95% confidence interval (CI) = 1.01 – 1.88, P = 0.046] and urine output at the start of CRRT (HR = 0.999, 95% CI = 0.998 – 1.000, P = 0.012) and CRRT duration (HR = 0.89, 95% CI = 0.83 – 0.95, P = 0.001) were predictors. For 90-day mortality, mean arterial pressure (HR = 1.02, 95% CI = 1.00 – 1.03, P = 0.019), admission duration (HR = 0.97, 95% CI = 0.95 – 0.99, P < 0.001) and CRRT duration (HR = 0.96, 95% CI = 0.91 – 0.99, P = 0.036) were predictors. The middle-old group or the oldest-old group did not exhibit higher risk compared to the youngest-old group for 28-day and 90-day mortality.

**Conclusion:** An older age was not a risk factor for mortality in elderly patients with AKI undergoing CRRT. This implicates the importance of active management and application of CRRT in critically ill elderly patients with AKI.

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#4893 THE INCIDENCE, RISK FACTORS AND OUTCOMES OF ACUTE KIDNEY INJURY AFTER MINOR LOWER LIMB AMPUTATIONS

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**Background and Aims:** Minor lower limb amputations (to amputations distal to or through the tarsometatarsal joint), are limb and
**Method:** This was a single centre retrospective study involving patients who underwent minor lower limb amputations at Mater Dei Hospital Malta between January and December 2019. Patient and procedure details were obtained from hospital records. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula. Chronic kidney disease (CKD) was defined as per Kidney Disease: Improving Global Outcomes (KDIGO) criteria. AKI was defined using Acute Kidney Injury Network (AKIN) criteria or KDIGO criteria if day 7 serum creatinine was available. Statistical analysis was performed using SPSS Statistics for Windows v21.0 (IBM Corp.).

**Results:** A total of 201 patients were included; males 69.7%, mean age 70.4 ±11.5 years, 87.1% had diabetes mellitus, 71.1% hypertension and 26.4% had ischemic heart disease. Pre-existing CKD was identified in 35.8%; 16.4% CKD stage 3a, 13.4% CKD stage 3b, 5.5% CKD 4 and 1 patient CKD 5. The majority (76.1%) underwent single toe amputations. Surgery was performed under loco-regional anaesthesia in 90% of patients, mostly in view of lower limb ulcers (64.7%) or gangrene (29.4%). A cohort of 54 (26.9%) patients received iodine based contrast within 7 days of procedure, including those who underwent bypass surgery (8%) and endarterectomy (4%). The incidence of AKI after minor lower limb amputations using AKIN criteria was 18.9%. An additional 12 patients were identified using KDIGO criteria (24.9%), however KDIGO criteria could only be applied for 123 patients as the rest did not have a day 7 serum creatinine. Most developed stage 1 AKI (18.4%), one patient developed stage 2 AKI and none developed stage 3 AKI using AKIN criteria. Only 1 patient needed temporary haemodialysis having developed AKI after day 3 post-operatively fulfilling KDIGO but not AKIN criteria. Recovery of kidney function occurred in all patients. All-cause mortality at 30 days, 60 days and 18 months (end of follow-up) was 2.0%, 5.5% and 19.9% respectively. None of the deaths were directly related to the AKI-amputation event. Patients who developed AKI, compared to those who did not, were more likely to have an eGFR <45ml/min/1.73 m² at the time of procedure (39.5% vs. 14.7%, p = 0.001). They were significantly older (73.0 ±10.4 vs. 68.5 ±11.8 years, p = 0.033), and more likely to have underlying chronic obstructive pulmonary disease (COPD) (28.9% vs. 13.5% p = 0.028). Use of loop and/or thiazide diuretics (68.4% vs. 49.1%, p = 0.049), fluorquinolones (71.1% vs. 52.8% p = 0.047) and/or carbapenems (10.5% vs. 2.5%, p = 0.043) was also more frequent in this group. Use of iodine based contrast within 7 days of procedure did not effect incidence of AKI. Hospital length of stay and all-cause mortality were not significantly higher in patients with AKI. An eGFR <45ml/min/1.73 m² was established as a strong independent predictor for the development of AKI (odds ratio [OR] 3.24, confidence interval [CI]: 1.40–7.52, p = 0.006), as were use of fluorquinolones (OR: 3.19, CI: 1.30–7.82, p = 0.012) and day 1 C-reactive protein (CRP) (OR: 1.01, CI: 1.00–1.01, p = 0.009). Cumulative survival censored at the end of follow-up was not significantly lower in patients who developed AKI (log rank: 0.45, p = 0.50).

**Conclusion:** In our study, 18.9% of patients developed AKI after minor lower limb amputations using AKIN criteria. One patient required acute haemodialysis. Age, COPD, diuretics, fluorquinolones and carbapenems were associated with increased incidence of AKI. An eGFR <45ml/min/1.73 m², day 1 CRP and fluorquinolone use were independent risk factors for the development of AKI. In this small patient cohort, AKI was not associated with higher all-cause mortality, and none of the deaths were directly related to the AKI-amputation event.

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**Method:** This is a retrospective observational study amongst adult hospitalized Dengue patients admitted at a tertiary care hospital between January 2019 and December 2019. We estimated the prevalence of Acute Kidney Injury (AKI) using KDIGO AKIN (Acute Kidney Injury Network) criteria. Outcomes were analyzed during the time of discharge.

**Results:** Out of the 1550 hospitalized patients, majority of the patients were males – 1005 (64.9%). Most common age group was between 20 to 40 years. 85 (5.48%) of the total study patients developed AKI. Older age groups were found to be more at risk for concurrent bacterial infections and higher mortality rate. Most patients had stage 1 AKI (70.1%). Overall mortality in patients with AKI was 20.3% and 80.5% in those requiring dialysis. The incidence of AKI risk was increased by as much as 4.5-fold in the presence of hemocoagulation (or hematocrit > 46.5%). Older age, Male sex, co-existing viral hepatitis, Dengue Hemorrhagic Fever, Dengue Shock Syndrome, Rhabdomyolysis, Multiple Organ Dysfunction Syndrome were found to be independent risk factors for DAKI. Presence of DAKI was associated with higher mortality and longer hospital stay.

**Conclusion:** In our study population, we found a low prevalence of AKI but Mortality was high in patients requiring ICU care and dialysis. Prompt recognition and identification of the at-risk population and administration of appropriate supportive treatment should be aimed to reduce the morbidity and mortality associated with this common and very important tropical disease.
ASSOCIATION OF TRADITIONAL AND NON-TRADITIONAL LIPID ABNORMALITIES WITH RENAL FUNCTION: A SURVEY IN A RURAL POPULATION OF BANGLADESH

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Background and Aims: The traditional and non-traditional lipid have been recognized to be involved in various atherosclerotic disease process. Several studies showed that, there is relation with renal function and dyslipidemia. Early detection of these modifiable risk factors and initiation of treatment may prevent or retard the progression of renal disease. Aim of this study was to evaluate the association of the traditional and non-traditional lipid abnormalities with renal function.

Methods: This cross sectional study was carried out in a rural area of Bangladesh. Renal function was evaluated by estimation of enzymatic creatinine, eGFR (CKD-EPI) and spot ACR. Total cholesterol (TC), triglyceride (TG), LDL and HDL was measured as traditional lipids and Apo-A1, APO-B, Lipo (a) as non-traditional lipids. Traditional dyslipidemia (TDLP) and non-traditional dyslipidemia (nTDLP) means abnormality in any of their components. Other tests include urine microscopy, Hb%, FBS, HbA\textsubscript{1c}, serum albumin and uric acid as additional risk marker.

Results: Total 201 patients were included for analysis. The mean age was 41±13 years and male/female ratio 48:52. Around 48% were overweight. Among these 20% were hypertensive, 14% diabetic, nephropathy in 13% and rest 53% had no known chronic disease. The mean value of creatinine was 0.8±0.5 mg%; eGFR was 94±23 ml/min/1.73m\textsuperscript{2}, ACR was 9.70 (median), TG 182±104 mg/dl, TC 96 ±47 mg/dl; LDL 121 ±39 mg/dl and HDL 38±6. The value of Apo-Al was 1.3 g/l (0.2-13.9), Apo-B 1.04 g/l (0.2-2.6) and Lipoprotein (a) was 17.3mg/dl (1.1-81.8). Mean value of FBS was 6.2 ±2.3 mmol/L, HbA\textsubscript{1c} 6.1 ±1.5%, Hb% 13.5 ± 1.6 g% and albumin was 4.8 ±0.5 mg%. When measured the TDLP was present in 81% and normal traditional lipids present in 19%. Similarly as a whole 50% had nTDLP and non-traditional lipids were normal in other half. Around 16% were free from both TDLP and nTDLP. The eGFR was lower in – TG >150 group than in < 150 (90 ±24 vs. 98 ±21 mg%, p=0.02); TC >200 than <200 (91 ±23 vs. 100 ± 22 mg%, p=0.001); LDL >100 and < 100 (91 ±23 vs. 100 ± 22 mg%, p=0.015) but no difference for components of nTDLP. The ACR was higher (> 30 mg/g) in 76% vs 24% (p<0.001) when TG is > 150 and < 150 mg%; 60% vs. 40% (p=0.05) when TC is > 200 and < 300mg%; and 81% vs. 19% (p<0.04) when LDL > 100 and < 100mg%. No such difference for renal functional parameters for non-traditional lipid components. In this study, eGFR had significant negative correlation with TG (r = -0.34 & p<0.001), TG (r = -0.24 & p=0.001), LDL (r = -0.25 & p<0.001) and only ACR had positive correlation with TG (r = 0.17 & p = 0.012). The nTDL wasn’t associated with altered eGFR or ACR.

Conclusion: In this study it was observed that traditional lipid components were altered in 81% whereas non-traditional lipids were altered in 50% rural subjects. Only the traditional dyslipidemia was associated with lower eGFR and higher ACR.

PLATELET TO LYMPHOCYTE RATIO AND SICKLE CELL NEPHROPATHY

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Background and Aims: Platelet-to-lymphocyte ratio (PLR) was introduced as cheap and readily assessed biologic markers of subclinical inflammation in sickle cell disease. Microalbuminuria and hyperfiltration, early markers of Sickle cell nephropathy (SCN) have been reported to be associated with platelet-to-lymphocyte ratio (PLR). This association has not yet been assessed in Congolese Sickle cell disease (SCD) children. Therefore, the aim of the present study was to assess the association between PLR and early markers of kidney disease in SCD children living in the Democratic Republic of Congo (DRC).

Method: In this cross-sectional study, we have investigated 175 SCD children from four centers (Kinshasa university clinics, CMMASS, CMD Diamond, and Baiamba Marie Mutumbo Dikembe) that give a comprehensive care to SCD patients. The PLR were calculated from full blood count. Elevated albuminuria and hyperfiltration, as the main outcomes of the study, were defined by urinary albumin/creatinine ratio (ACR) >30 mg/g and estimated glomerular filtration ratio (eGFR) > 130 ml/min per 1.73 m\textsuperscript{2} for females and > 140 ml/min per 1.73 m\textsuperscript{2} for males, respectively. Logistic regression analysis was used to assess the relationship between RPL and early sickle cell nephropathy.

Results: Of the 175 SCD children enrolled, 41(23.4%) and 67(38.3%) of them presented with abnormal albuminuria and hyperfiltration, respectively. RPL > 130 was observed in 90 (51.4%) patients. RPL was strongly, significantly and independently associated with both abnormal albuminuria (aOR 3.381; IC95\% 2.22-2.68; p = 0.000) and hyperfiltration (aOR 2.19; 95\%IC 2.09 - 22.25; p = 0.010).

Conclusion: The present study has shown that nearly fifty two out of one hundred SCD children bear a high platelet to lymphocyte ratio that is strongly and significantly associated with early markers of kidney disease.

REFERENCE
**MANAGEMENT AND OUTCOMES OF SEPSIS ASSOCIATED ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS**

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**Background and Aims:** Sepsis-associated acute kidney injury (AKI) remains a major cause of mortality in patients with critical illness and has an especially high health-related burden in developing countries. However, only a few clinical studies have focused on the clinical characteristics and prognosis of septic AKI, especially in low-income settings. Therefore, the aim of our study was to describe the clinical profile, management and outcome of critically ill patients with sepsis-associated AKI.

**Methods:** A retrospective observational study of critically ill patients with septic AKI was performed from March 2020 to June 2021 at our university hospital. Sepsis was diagnosed clinically by the presence of acute infection and new organ dysfunction. The presence of AKI was evaluated using the Acute Kidney Injury Network (AKIN) criteria. Patients with preexisting ESRD and those who did not fulfill at least one predefined criterion for AKI were excluded.

**Results:** A total of 105 patients with a median age of 58.9 years (31-78) were enrolled, including 69 and 36 patients with persistent and transient AKI, respectively. The mean SAPS II score was 51.8 (38-77). The primary source of sepsis was mainly abdominal (42.8%). AKI was defined by oliguria in 18 patients (17.1%), by creatinine elevation in 65 patients (61.9%), and by both criteria in 22 patients (21%). Septic AKI was associated with great aberrations in hemodynamics, with 71 patients (67.6%) requiring vasoactive therapy and 65 patients (61.9%) requiring mechanical ventilation. AKI severity according to the AKIN classification scheme was determined to be stage 1 in 32 patients (30.5%), stage 2 in 22 patients (20.9%), and stage 3 in 51 patients (48.6%). Overall, 75.2% of the cohort required renal replacement therapy (RRT). Hospital survival was 63.8% (n = 23) in patients with transient AKI and 43.5% (n = 30) in patients with persistent AKI.

**Conclusion:** Sepsis is the main cause of AKI in intensive care units, accounting for up to 50% of cases. Our results suggest that septic AKI is associated with higher disease severity scores at admission, requirement of vasoactive drugs, need for mechanical ventilation and increased hospital mortality. Further studies are required, especially in developing countries, to implement more preventive measures and therapeutic interventions to decrease CKD progression and mortality in these patients.

**CHANGES OF MEDICAL COSTS AND NUMBER OF USES OF CONTINUOUS RENAL REPLACEMENT THERAPY UNTIL RECENT SIX YEARS IN SOUTH KOREA**

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**Background and Aims:** Continuous renal replacement therapy (CRRT) is a necessary dialysis treatment method applied to patients with acute renal injury at intensive care unit. In South Korea, the use of such CRRT is increasing, and the cost of health insurance used for CRRT is also increasing. In this study, the pattern and medical costs increase of CRRT usage until recent 6 years were investigated.

**Method:** From 2016 to 2021, the number of CRRT claims was investigated using data from the National Health Insurance Review and Assessment Service. CRRT costs is applied by a resource-based relative value score in Korea. CRRT can be charged as continuous venovenous hemodialysis, continuous venovenous hemofiltration, and continuous venovenous hemodiafiltration depending on the treatment mode. The CRRT cost differs from the very day and the next day’s cost, and the cost of the very day includes the femoral hemodialysis catheter insertion cost, which is higher than the next day’s cost.

**Results:** CRRT medical practice is gradually increasing. The number of CRRT the very day increased from 15,640 cases in 2016 to 20,883 cases in 2021, and it continues to increase from 81,649 cases CRRT the next day in 2016 to 121,376 cases CRRT the next day in 2021. The CRRT relative value score is higher than the conventional hemodialysis (HD) and the CRRT relative value score is 9715 points higher than the conventional HD 1065 points. The total cost of CRRT increased by about KRW 52.5 billion (approximately 38,363,171 dollars) in 2021 from about KRW 17.3 billion (approximately 12,641,578 dollars) in 2016. In addition to CRRT medical practice costs, dialysis fluid, anticoagulant costs, and material costs are added, and so actual CRRT-related costs are more expensive.

**Conclusion:** CRRT is essential and it seems necessary to consider medical practices or medical costs that are important for essential medical care. CRRT is a high-cost treatment method that requires definitive guidelines or consensus on the initiation and discontinuation of CRRT.
COVID-19, RENAL DAMAGE AND ITS EVOLUTION IN HOSPITALISED PATIENTS IN THE FIRST WAVE OF THE PANDEMIC: EXPERIENCE OF ONE CENTRE

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Hospital San Pedro, Nefrología, Logroño, Spain

Background and Aims: The damage that SARS Cov2 virus exerts at the renal level has been the subject of analysis in many studies. We analysed the extent of Acute Kidney Injury (AKI), possible factors involved and mortality in patients hospitalised with Covid-19 during the first wave of the pandemic. We reassessed renal function, as well as inflammatory and nutritional status of patients 18 months after admission, together with the capacity for recovery of renal function.

Method: Observational and retrospective study of patients admitted to the ward or intensive care unit (ICU) for Covid-19 during the month of March 2020. We defined the stage of renal damage according to the KDIGO guidelines. Among the possible risk factors associated with AKI and mortality in patients hospitalised with Covid-19 during the first wave of the pandemic. We reassessed renal function, as well as inflammatory and nutritional status of patients 18 months after admission, together with the capacity for recovery of renal function.

Results: A total of 576 patients were admitted during the study period, of whom 10.6% were admitted to the ICU (n 61). A total of 45.9% (n 28) had some degree of AKI, the most frequent being grade 2 (22.9%), followed by grade 3 (18%) and grade 1 (4.9%). Of all patients requiring admission to the ICU, 78.6% of those with AKI died. The Odin scale was significantly associated with AKI and mortality, but the Charlson scale was not. The maximum dose of Cisatracurium was significantly associated with AKI. Among the patients admitted to inpatient areas (n 515), 9.9% (n 51) had AKI and 31.4% of these patients died. In most cases the degree of renal damage was mild (82.4% grade 1 vs. 13.7% grade 2 and 3.9% grade 3). When we studied the patients who presented with AKI (n 79), we observed that CK and LDH values were significantly higher, indicating a more inflammatory state. Of the 79 patients, 48.1% (n 38) died, with significant differences in serum CRP and D-dimer levels. Of the 41 patients who survived, we conducted an 18-month follow-up study that only 36.6% (n 15) completed, with a mean age of 69.7 years, 73.3% being male and 20% with previous chronic kidney disease (CKD). At the end of follow-up 86% of them recovered renal function, according to pre-admission figures, including those patients with baseline CKD. Only 13% of the patients who completed follow-up showed a slight worsening of renal function with respect to their baseline situation. We observed differences in the values of calcium, vitamin B12 and vitamin D in the group of patients who recovered renal function compared to those who showed deterioration with respect to their situation prior to admission (p < 0.02). We observed differences in the values of calcium, vitamin B12 and vitamin D in the group of patients who recovered renal function compared to those who showed deterioration with respect to their situation prior to admission (p < 0.02).

Conclusion: The incidence of AKI in COVID patients requiring admission to the ICU was four times higher than in patients admitted to the ward. The severity of renal damage was greater in the ICU, predominantly AKI 2-3 vs AKI 1, with mortality 2.5 times higher than in the ward. The group of patients who develop AKI have an elevation of inflammatory markers, which increases in the group of deceased patients. In ICU, the Odin scale was significantly related to AKI and mortality. - The mortality rate in the group of patients with AKI was high. Most of the patients have recovered pre-admission renal function after 18 months of follow-up, with differences in nutritional parameters such as calcium, vitamin B12 and vitamin D.
SIZE MATTERS: EFFECT OF NUMBER OF TRANSFUSIONS ON ADVERSE RENAL AND CLINICAL EVENTS IN PATIENTS WITH AKI

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1Hospital Clínico Universitario de Valladolid, Nephrology, Valladolid, Spain and 2Hospital Clínico Valladolid, Hematology, Valladolid, Spain

Background and Aims: AKI and anemia independently worsen the prognosis of hospitalized patients, but their association and adverse effects have been slightly studied. We aimed to investigate the effect of transfusions during hospitalization on hard renal and clinical outcomes of patients with AKI. In addition, we tested the influence of the number of transfusions on mortality between pure AKI (pAKI) and AKI-on-CKD (AoCKD) patients.

Method: Retrospective cohorts’ study, of in-patients with AKI attended by nephrology during a 12-month period. AKI severity was categorized by KDIGO-2012 criteria; we searched in a Hematology administrative data base for transfusions (and their number) during the hospitalization period. We analyzed epidemiological and clinical variables and compared the rates of the hard outcomes Length of Stay (LoS), Acute Hemodialysis (aHD), Dialysis Dependence at Discharge (DDD), and in-hospital Mortality (IHM) between individuals that didn’t and received transfusions.

Results: We included 275 individuals, 134 (49%) were transfused; they were older and suffered more DM; with no differences in the ICU hospitalization and Charlson’s Index. See Table 1A. We observed that transfused patients were classified more frequently in AKI Stage-3, had longer LoS, aHD, were more frequently dialysis dependent and their mortality rate was higher. See Table 1B. We compared patients with less or more than 5 transfusions; the latter group showed a higher rate of adverse events than the group of ≤4 transfusions. See table 1C. Figure 1 plots the K-M curve for survival between pAKI and AoCKD groups showing an excess mortality associated with the number of transfusions, especially in the AoCKD individuals.

Conclusion: In our study, we found that patients that received transfusions showed worst clinical and renal results including more severe AKI, longer hospital stay, higher rate of acute HD, dialysis dependence at discharge and mortality. We observed that the appearance of these adverse events was associated in a dose dependent manner with the number of transfusions; for these reasons, we consider that number of transfusions should be included in AKI risk models and calculators. Could optimizing the number of transfusions improve the rate of adverse renal and clinical events? We will need prospective and well-powered studies in order to answer this question and to deepen on the issue of AoCKD and worst clinical outcomes if transfused.

Table 1: A. B Comparison Between Transfused and Not transfused individuals. Part C Comparison of Results in Patients that Received More or Less than 5 Blood Packs during Hospitalization.

<table>
<thead>
<tr>
<th></th>
<th>Not Transfused</th>
<th>Transfused</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>141 (51)</td>
<td>134 (49)</td>
<td></td>
</tr>
<tr>
<td>A. Features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age – ys</td>
<td>69 (±16)</td>
<td>73 (±11)</td>
<td>0.006</td>
</tr>
<tr>
<td>Sex (Masc)</td>
<td>101 (72)</td>
<td>88 (66)</td>
<td>0.18</td>
</tr>
<tr>
<td>Hypertension</td>
<td>116 (82)</td>
<td>117 (87)</td>
<td>0.16</td>
</tr>
<tr>
<td>DM</td>
<td>48 (34)</td>
<td>66 (49)</td>
<td>0.007</td>
</tr>
<tr>
<td>CKD</td>
<td>73 (52)</td>
<td>75 (56)</td>
<td>0.28</td>
</tr>
<tr>
<td>Charlson’s Index</td>
<td>3.2 (±2.2)</td>
<td>3.7 (±2.2)</td>
<td>0.50</td>
</tr>
<tr>
<td>ICU</td>
<td>38 (27)</td>
<td>31 (23)</td>
<td>0.23</td>
</tr>
<tr>
<td>B. Results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KDIGO Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>62 (44)</td>
<td>24 (18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>12 (9)</td>
<td>17 (13)</td>
<td>0.18</td>
</tr>
<tr>
<td>3</td>
<td>67 (47)</td>
<td>93 (69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LoS</td>
<td>13 (±11)</td>
<td>22 (±16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute HD</td>
<td>12 (9)</td>
<td>31 (23)</td>
<td>0.001</td>
</tr>
<tr>
<td>HD Dependence</td>
<td>9 (6)</td>
<td>15 (11)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mortality</td>
<td>21 (17)</td>
<td>38 (28)</td>
<td>0.03</td>
</tr>
<tr>
<td>C. # Transfusions</td>
<td>≤ 4</td>
<td>≥ 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>92 (68)</td>
<td>42 (31)</td>
<td></td>
</tr>
<tr>
<td>CKD</td>
<td>57 (62)</td>
<td>18 (43)</td>
<td>0.03</td>
</tr>
<tr>
<td>KDIGO Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>20 (22)</td>
<td>4 (10)</td>
<td>0.07</td>
</tr>
<tr>
<td>2</td>
<td>10 (11)</td>
<td>7 (18)</td>
<td>0.25</td>
</tr>
<tr>
<td>3</td>
<td>62 (67)</td>
<td>31 (74)</td>
<td>0.30</td>
</tr>
<tr>
<td>LoS</td>
<td>19 (±13)</td>
<td>31 (±19)</td>
<td>0.02</td>
</tr>
<tr>
<td>Acute HD</td>
<td>15 (16)</td>
<td>16 (38)</td>
<td>0.006</td>
</tr>
<tr>
<td>HD Dependence</td>
<td>7 (8)</td>
<td>8 (19)</td>
<td>0.05</td>
</tr>
<tr>
<td>Mortality</td>
<td>15 (16)</td>
<td>17 (53)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Figure 1: K-M Curve Analysis of Survival, Number of Transfusions in AKI and AoCKD individuals.
Acute Kidney Injury (AKI) is a syndrome characterized by an abrupt drop in glomerular filtration and/or a decrease in urinary output. The awakening to a different kind of AKI that also occurs outside the hospital named community-acquired AKI (CA-AKI) occurred in 1991, however, few data have been published about its epidemiology, risk factors and outcome, especially in low-income countries. The recognition of risk factors for CA-AKI and development of symptom-based risk tool that aims to predict the risk of AKI might be able to avoid delays in its recognizing, improve the timely diagnosis and patient outcomes in this frequent syndrome. We aimed to assess CA-AKI incidence, characteristics and independent risk factors associated with CA-AKI; to evaluate the discriminatory capacity of a clinical score tool to AKI prediction to predict CA-AKI in our sample.

**Method:** We conducted a prospective observational study of general medical admissions to a tertiary hospital in Campinas (São Paulo) between 10th January 2019 and 16th September 2021; we included patients ≥ 14 years, medical suspicion of infection (or confirmed) and/or presence of at least one of the signs or symptoms on admission: fever, dyspnea, decrease in urine output, edema, hypotension, hemodynamic shock, jaundice, petechiae, ecchymosis or decreased level of consciousness. We excluded patients with stage 5 chronic kidney disease at baseline and pre-existing renal replacement therapy (undergoing dialysis and renal transplantation), and also patients with COVID diagnosis. All patients included were assessed utilizing a symptom-based risk score to predict the development of severe AKI, the need for dialysis and mortality. Patients were subjected to complete history taking, socioeconomic and education data were collected. Healthy literacy was assessed using the test of functional health literacy in adults – short version (S-TOFHLA). Predictors of CA-AKI risk were assessed using multivariate logistic regression analysis. Patients were followed up until discharged hospital. The study outcomes were development of CA-AKI, hospital mortality, dialytic need.

**Results:** We enrolled 261 patients. CA-AKI was diagnosed in 65 (25%) patients. The CA-AKI patients were older [59 (51-66) vs. 54 (38-65) years, p = 0.02], had higher basal serum creatinine [0.7 (0.5–0.9) vs. 0.6 (0.5–0.8) mg/dL; p = 0.01], lower baseline estimated glomerular filtration rate (eGFR) [103 (88-113) vs. 109 (97–121) mL/min/1.73 m²; p = 0.01] and lower eGFR on admission [64 (44 – 81) vs. 104 (82 – 116) mL/min/1.73 m²; p = 0.0001]. Liver and heart disease were most common comorbidities in the group CA-AKI [10 (16%) vs. 14 (7%) patients, p = 0.04 and 21 (33%) vs. 39 (20%), p = 0.03, respectively]. The risk score did not show significant accuracy to predicting CA-AKI, however, logistic regression showed that scores ≥ 7 points (OR 95% CI 1.007, 1.044 < 0.01), albuminuria (OR 95% CI 1.282, 6.133 p = 0.010) followed by age (OR 95% CI 1.007, 1.044 p = 0.008) and liver disease (95% CI 1.063, 6.379 p = 0.036) were independent factors associated with increased risk for CA-AKI in our population. A higher percentage of patients in our sample declared household income < $ 719.73 (month) and the CA-AKI group maintained the same distribution. Only 41 percentage of patients in our sample declared household income < $ 719.73.

**Conclusion:** Healthy literacy, education, and social class did not show association with CA-AKI; dialysis needed and mortality were not different between the groups CA-AKI or without CA-AKI. Covariates and factors associated with risk for CA-AKI were age, liver disease and scores ≥ 7 points. The main limitation of our study was not feasible to screen all the patients due to the high numbers seen daily.

**#5624 REMDESIVIR IN COVID-19 PATIENTS WITH KIDNEY DISEASE: A STUDY ON THE RENAL FUNCTION AND OUTCOMES**

Crystal Faye Lagura

Southern Philippines Medical Center, Internal Medicine, Davao City, The Philippines

**Background and Aims:** The COVID-19 pandemic has created a global catastrophe with mortality rates higher in older adults and people with chronic comorbid conditions. In which patients with chronic kidney disease were the most vulnerable population. Remdesivir, an antiviral nucleotide, showed promising results in individuals with COVID-19 infection. However, despite its shortened time to recovery in adults hospitalized with COVID19, individuals with ESRD and high stage AKI were not included in clinical trials, thus when granted an emergency use authorization it was recommended to avoid use in patients with eGFR <30mL/min “unless benefit outweighs the risk”. In this study, in the absence of Molnupiravir, the current drug of choice, we wished to study its safety by determining its effects on renal status of individuals with known kidney dysfunction. The study aims to determine the effect of Remdesivir on renal function and outcomes among COVID19 patients with kidney disease.

**Method:** The study utilized a retrospective research design. The study included patients who were 19 years old and above, with RT-PCR confirmed COVID19 infection treated with Remdesivir and who were confirmed to have kidney disease.

**Results:** 106 patients were included; the mean age was 62.25±13.96 years old, more than half of the population were males. The majority of the population had AKI while the rest had CKD and 25% underwent renal replacement therapy. Most of them were classified with severe and critical COVID infection (Table 1). To determine effects on renal function laboratory parameters were determined at baseline and after completion of treatment. There was an overall significant improvement in eGFR (<0.01), albuminuria (0.013) and in acid-base balance (0.003) and odds ratio showed that none of the demographic, clinical and laboratory profile significantly in-creased the chance of death in terms of overall clinical outcome (Table 2). To determine risk factors of patients that may contribute to patients outcome, odds ratio showed that none of the demographic, clinical and laboratory profile significantly increased the chance of death among patients who took Remdesivir. (Table 3). In terms of overall clinical outcome, this study had a mortality rate of 4.9% (Table 4).
Table 2: Laboratory Parameters Before and After Remdesivir Administration.

<table>
<thead>
<tr>
<th>Laboratory Parameters</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>0.103</td>
</tr>
<tr>
<td>Bun</td>
<td>0.399</td>
</tr>
<tr>
<td>Serum Albumin</td>
<td>0.287</td>
</tr>
<tr>
<td>Egfr</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>0.013</td>
</tr>
<tr>
<td>Electrolytes</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>0.02</td>
</tr>
<tr>
<td>Potassium</td>
<td>0.305</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.096</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.206</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>0.003</td>
</tr>
<tr>
<td>pH</td>
<td>0.02</td>
</tr>
<tr>
<td>Base Excess</td>
<td>0.344</td>
</tr>
</tbody>
</table>

Table 3: Parameters associated with Patients Outcomes after Treatment with Remdesivir.

<table>
<thead>
<tr>
<th>Demographic Profile</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 60</td>
<td>0.276</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>0.146</td>
</tr>
<tr>
<td>Type of Kidney Diseases</td>
<td></td>
</tr>
<tr>
<td>AKI</td>
<td>0.453</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>Severity of COVID</td>
<td>0.525</td>
</tr>
<tr>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>0.386</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td>Critical</td>
<td></td>
</tr>
<tr>
<td>Laboratory Parameters</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.845</td>
</tr>
<tr>
<td>Bun</td>
<td>0.375</td>
</tr>
<tr>
<td>Serum Albumin</td>
<td>0.854</td>
</tr>
<tr>
<td>Egfr</td>
<td>0.822</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>0.153</td>
</tr>
<tr>
<td>Electrolytes</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>0.374</td>
</tr>
<tr>
<td>Potassium</td>
<td>0.376</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.138</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.584</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>0.762</td>
</tr>
<tr>
<td>pH</td>
<td>-</td>
</tr>
<tr>
<td>Base Excess</td>
<td>0.287</td>
</tr>
</tbody>
</table>

Table 4: Clinical outcome after Remdesivir Treatment.

<table>
<thead>
<tr>
<th></th>
<th>101</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>Dead</td>
<td>5</td>
</tr>
<tr>
<td>Covid Critical</td>
<td>4</td>
</tr>
<tr>
<td>Covid Severe</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusion: Use of Remdesivir in patients with AKI, CKD and ESRD on dialysis was not associated with further renal function deterioration. Contrary to concerns there was rather an overall significant improvement in EGFR, degree of albuminuria and acid-base balance after treatment regardless of their disease severity and its use in patients on hemodialysis have not shown any detrimental impact on mortality.

#4725

INCIDENCE OF ACUTE KIDNEY INJURY IN PATIENTS WITH COVID-19 AND ITS IMPACT ON THE COURSE OF THE ACUTE INFECTION AND POST-COVID PERIOD

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1National Institute of Health after academician S. Avdalbekyan, Erevan, Armenia, 2Eurasian Association of Internal Medicine, “ACTIV SARS-CoV-2” Working Group, Erevan, Armenia, 3Eurasian Association of Internal Medicine, “ACTIV SARS-CoV-2” Working Group, Sochi, Russia, 4Eurasian Association of Internal Medicine, “ACTIV SARS-CoV-2” Working Group, Moscow, Russia, 5Eurasian Association of Internal Medicine, “ACTIV SARS-CoV-2” Working Group, Rostov-on-Don, Russia, 6Eurasian Association of Internal Medicine, “ACTIV SARS-CoV-2” Working Group, Nizhny Novgorod, Russia and 7Eurasian Association of Internal Medicine, “ACTIV SARS-CoV-2” Working Group, Saint Petersburg, Russia

Background and Aims: It is known that SARS-CoV-2 virus infection can contribute to kidney damage. In the literature, the incidence of acute kidney injury (AKI) during the acute period of COVID-19 is estimated to range from 5 to 36.6%. This complication significantly aggravates the course of both the acute phase and post-COVID period. However, the number of studies investigating these interactions is currently insufficient. To determine the incidence of AKI in the acute phase of COVID-19 and to assess the impact of this complication on the post-COVID period.

Method: The international register “Dynamics analysis of comorbidities in SAES-CoV-2 survivors” (“ACTIV”) (NCT04492384) was established to assess the course of COVID-19 in the Eurasian region and involved specialists from 7 countries. ACTIV is a multicenter, non-interventional, real-world clinical practice register that included men and women over 18 years of age with a confirmed diagnosis of COVID-19. The analysis included 9206 patients with reported evidence of kidney damage or its absence. In the register, the presence of AKI was determined from the attending physician’s notes in the medical records (according to modern diagnostic criteria) and the difference in serum creatinine levels $\geq 26.5 \mu mol/l$ during inpatient treatment for COVID-19. The post-COVID period was analyzed using telephone surveys of 3099 patients at 3 months, 2493 patients at 6 months and 1782 patients, at 12 months after recovery from COVID-19.

Results: AKI was detected in 11.6% (n = 1068) of cases during the inpatient treatment of the acute SARS-CoV-2 infection. Among markers of severe infection, AKI was more common (p < 0.001) than cytokine storm (7.46% of patients) or sepsis (0.17% of patients). Analysis showed that AKI occurred in patients with higher average body mass index (BMI) (29.6 kg/m² (25.1; 33.5) vs. 27.8 kg/m² (24.8; 31.6) without AKI, p = 0.018) and serum glucose levels (6.0 (5.2; 8.55) mmol/l vs. (5.8 (5.0; 7.0) mmol/l without AKI, p = 0.011). AKI increased the odds of death in the acute period of COVID-19 by 3.94 times (95% confidence interval (CI) 3.24–4.78; p = 0.0001). Similar results were recorded 3 months after recovery (Table 1).

Conclusion: AKI was reported in 11.6% of patients with COVID-19 who were hospitalized for treatment of acute infection. Kidney damage occurred in patients with higher BMI and serum glucose levels. Patients with AKI during SARS-CoV-2 infection had a significantly higher risk of death in the first 3 months after recovery.
Table 1: Analysis of the probability of death within 12 months after recovery from SARS-CoV-2, depending on the presence/absence of AKI in the acute phase of infection.

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Characteristic</th>
<th>Without acute kidney injury</th>
<th>History of acute kidney injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months after recovery (n = 3161)</td>
<td>Survivors (n = 3103)</td>
<td>2849 (91.8%)</td>
<td>254 (8.2%)</td>
</tr>
<tr>
<td></td>
<td>Deceased (n = 58)</td>
<td>44 (75.9%)</td>
<td>14 (24.1%)</td>
</tr>
<tr>
<td></td>
<td>Odds ratio (OR) (95% confidence interval (CI))</td>
<td>Ref.</td>
<td>3.59 (1.87–6.50)</td>
</tr>
<tr>
<td></td>
<td>p-ratio</td>
<td>Ref.</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>p overall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months after recovery (n = 2506)</td>
<td>Survivors (n = 2493)</td>
<td>2294 (92%)</td>
<td>199 (8%)</td>
</tr>
<tr>
<td></td>
<td>Deceased (n = 13)</td>
<td>11 (84.6%)</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td></td>
<td>Odds ratio (OR) (95% CI)</td>
<td>Ref.</td>
<td>2.22 (0.31; 8.50)</td>
</tr>
<tr>
<td></td>
<td>p-ratio</td>
<td>Ref.</td>
<td>0.360</td>
</tr>
<tr>
<td></td>
<td>p overall</td>
<td></td>
<td>0.280</td>
</tr>
<tr>
<td>12 months after recovery (n = 1794)</td>
<td>Survivors (n = 1782)</td>
<td>1649 (92.5%)</td>
<td>133 (7.5%)</td>
</tr>
<tr>
<td></td>
<td>Deceased (n = 12)</td>
<td>12 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td>Odds ratio (OR) (95% CI)</td>
<td>Ref.</td>
<td>8.36 (1.73; 29.3)</td>
</tr>
<tr>
<td></td>
<td>p-ratio</td>
<td>Ref.</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>p overall</td>
<td></td>
<td>1.00</td>
</tr>
</tbody>
</table>

#3783
INCIDENCE AND PREDICTORS OF MAJOR ADVERSE KIDNEY EVENTS IN ICU PATIENTS WITH SEPSIS: A PROSPECTIVE COHORT STUDY FROM A DEVELOPING COUNTRY

Indu Ramachandra Rao, Saurabh Thanekar, Shankar Prasad Nagaraju and Ravindra Attur Prabhu

Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India, Department of Nephrology, India

Background and Aims: Acute kidney injury (AKI) occurs in 15-60% of intensive care unit (ICU) admissions and is associated with higher mortality, morbidity and increased healthcare costs. Major adverse kidney events (MAKE) is a clinically meaningful patient-centred outcome for AKI which includes mortality, need for renal replacement (RRT) and persistent kidney dysfunction. There is a paucity of data on the incidence and risk factors of MAKE, particularly from developing countries. We sought to examine the incidence of MAKE at day 30 (MAKE30) and its predictors in a cohort of critically ill patients with sepsis.

Method: This was a prospective cohort study conducted in the medical ICUs of a tertiary-care hospital in India. Ethical clearance was obtained from the Institutional Ethics Committee. Adult patients (≥ 18 years) admitted in the medical ICUs between 1st September, 2022 and 31st December, 2022 with sepsis (as defined by Sepsis-3 criteria) were included. Those with chronic kidney disease stage 5/5D, those requiring dialysis within 72 hours of admission and with an ICU stay of <72 hours were excluded. Baseline clinical and demographic data were recorded on the day of admission. AKI was defined as per KDIGO 2012 guidelines. Patients were followed up till hospital discharge or day 30 (whichever was earlier) and clinical outcomes were noted. The primary outcome measure was MAKE30 (defined as a composite of death, provision of RRT, or sustained loss of kidney function i.e., a final inpatient creatinine ≥200% of the baseline value, at hospital discharge or at 30 days, whichever comes first).

Results: A total of 250 patients admitted in the medical ICUs during the study period were included for analysis. The baseline characteristics are tabulated below (Table 1). Over the 30-day follow-up period, AKI was noted in 185 (74%) patients, with stage 1 AKI in 38 (15.2%), stage 2 AKI in 29 (11.6%) and stage 3 AKI in 118 (47.2%). Renal replacement therapy was initiated in 86 (34.4%) patients. Mortality occurred in 58 (23.2%). Overall, MAKE30 was seen in 102 (40.8%) patients. Serum lactate (OR 1.04, 95% CI:1.01-1.06; P = 0.010) and SOFA score (OR 1.38, 95% CI:1.27-1.56; P <0.001) at admission were independently associated with MAKE30 (Table 2). There was no association with age, gender, diabetes, type of resuscitation fluid or cumulative fluid balance (at 72 hours) with MAKE30.

Conclusion: In this cohort of critically ill patients with sepsis, MAKE30 was observed in 40.8%. Serum lactate and SOFA score at admission were independent predictors of MAKE30.

**Table 1: Baseline characteristics.**

<table>
<thead>
<tr>
<th>Total number (N = 250)</th>
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<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male, N (%)</td>
</tr>
<tr>
<td>Female, N (%)</td>
</tr>
<tr>
<td>Co-morbidities</td>
</tr>
<tr>
<td>Diabetes mellitus, N (%)</td>
</tr>
<tr>
<td>Hypertension, N (%)</td>
</tr>
<tr>
<td>Ischemic heart disease, N (%)</td>
</tr>
<tr>
<td>Chronic kidney disease, N (%)</td>
</tr>
<tr>
<td>Chronic liver disease, N (%)</td>
</tr>
<tr>
<td>Clinical presentation</td>
</tr>
<tr>
<td>Pneumonia, N (%)</td>
</tr>
<tr>
<td>Abdominal focus, N (%)</td>
</tr>
<tr>
<td>Skin and soft tissue abscess, N (%)</td>
</tr>
<tr>
<td>Others, N (%)</td>
</tr>
<tr>
<td>Severity of involvement</td>
</tr>
<tr>
<td>Inotrop support, N (%)</td>
</tr>
<tr>
<td>Mechanical ventilation, N (%)</td>
</tr>
<tr>
<td>SOFA score (median, IQR)</td>
</tr>
<tr>
<td>Lab parameters</td>
</tr>
<tr>
<td>Hb (mean ± SD)</td>
</tr>
<tr>
<td>Serum creatinine (median, IQR)</td>
</tr>
<tr>
<td>Serum lactate (median, IQR)</td>
</tr>
</tbody>
</table>
Abstracts i1099

Division of Nephrology, Guangzhou, P.R. China

National Clinical Research Center for Kidney Disease, State Key Laboratory of Organ Failure Research, Nanfang Hospital, Southern Medical University, Division of Nephrology, Guangzhou, P.R. China

Background and Aims: Antiviral therapy is commonly used to treat herpes zoster. Though antivirals are generally considered nephrotoxic, few studies compared the relative risk of acute kidney injury in patients with herpes zoster that is attributable to different antivirals. We aim to examine the association of use of different antivirals with hospital-acquired acute kidney injury (HA-AKI) among Chinese adults with herpes zoster.

Method: The study population was derived from the China Renal disease System (CRDS), a retrospective cohort of hospitalized patients from 19 medical centers throughout China. We selected from CRDS 3,847 adults who received antiviral therapy for herpes zoster during hospitalization. We identify and stage AKI using patient-level serum creatinine data according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria. We compared the relative risks of HA-AKI among patients treated with different antivirals using Cox proportional hazards model, and explored the non-linear association between the accumulative dose of antivirals and the risk of HA-AKI using a penalized smoothing spline.

Result: Among 3,847 patients, 1,585 (41.2%), 699 (18.2%), 599 (15.6%) and 964 (25.1%) were treated with acyclovir/valacyclovir, ganciclovir, penciclovir/famciclovir, and fosacarnet, respectively. The incidence of HA-AKI was 4.9%, 2.9%, 2.8% and 0.8%, respectively, in the patients treated with acyclovir/valacyclovir, ganciclovir, penciclovir/famciclovir, and fosacarnet. Compared with acyclovir/valacyclovir therapy, use of foscarnet was associated with a 69% reduction in the risk of HA-AKI (hazard ratio [HR], 0.31; 95% CI, 0.14-0.66), while use of other nucleoside analogues was associated with a marginally lower risk of HA-AKI, with a HR (95% CI) of 0.31 (0.14-0.68). The incidence of HA-AKI was 4.9%, 2.9%, 2.8% and 0.8% in the patients treated with acyclovir/valacyclovir, ganciclovir, penciclovir/valamivucir, and fosacarnet, respectively. The incidence of HA-AKI was 4.9%, 2.9%, 2.8% and 0.8%, respectively, in the patients treated with acyclovir/valacyclovir, ganciclovir, penciclovir/famciclovir, and fosacarnet.

Conclusion: Antiviral therapies for herpes zoster, acyclovir/valacyclovir was associated with the highest relative risk of HA-AKI, and the association appears to be dose dependent. Clinicians should exercise rational drug use according to the different renal toxicity associated with a particular antiviral drug.

#4815

COMPARISON OF DIFFERENT ANTIVIRALS REGARDING THEIR ASSOCIATION WITH HOSPITAL-ACQUIRED ACUTE KIDNEY INJURY AMONG ADULTS WITH HERPES ZOSTER

Ruqi Xu, Xu Xin and Sheng Nie

National Clinical Research Center for Kidney Disease, State Key Laboratory of Organ Failure Research, Nanfang Hospital, Southern Medical University, Division of Nephrology, Guangzhou, P.R. China

Background and Aims: Antiviral therapy is commonly used to treat herpes zoster. Though antivirals are generally considered nephrotoxic, few studies compared the relative risk of acute kidney injury in patients with herpes zoster that is attributable to different antivirals. We aim to examine the association of use of different antivirals with hospital-acquired acute kidney injury (HA-AKI) among Chinese adults with herpes zoster.

Method: The study population was derived from the China Renal disease System (CRDS), a retrospective cohort of hospitalized patients from 19 medical centers throughout China. We selected from CRDS 3,847 adults who received antiviral therapy for herpes zoster during hospitalization. We identify and stage AKI using patient-level serum creatinine data according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria. We compared the relative risks of HA-AKI among patients treated with different antivirals using Cox proportional hazards model, and explored the non-linear association between the accumulative dose of antivirals and the risk of HA-AKI using a penalized smoothing spline.

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Conclusion: Antiviral therapies for herpes zoster, acyclovir/valacyclovir was associated with the highest relative risk of HA-AKI, and the association appears to be dose dependent. Clinicians should exercise rational drug use according to the different renal toxicity associated with a particular antiviral drug.
The age of our patients varied between 24 and 64 years for an average of 42 years. The male sex was predominant (78.57%) 11 men versus 3 women with no history of previous kidney disease. The average hospital stay was 20 days [12-42 days]. The most common clinical signs were oligo-anuria (85.7%), abdominal pain (57.1%), nausea and vomiting (42.8%), flank pain (42.8%) and muscle pain (14.2%), hypertension in 5 patients (35.7%), while 4 were hypotensive. The average creatinine on admission was 22mg/l [14-42.3], the average CPK level was 6240UI/L [2225-12570], the myoglobin was assayed in a single patient which returned on admission was 22mg/l [14-42.3], the average CPK level was 6240UI/L [2225-12570], the myoglobin was assayed in a single patient which returned.

**Table 1: Risk of Hospital-Acquired Acute Kidney Injury (HA-AKI) by different antiviral drugs.**

<table>
<thead>
<tr>
<th>Drug group</th>
<th>Total, No.</th>
<th>HA-AKI, No. (%)</th>
<th>No. of Person-Days (Incidence Rate, per 1,000 person-days)</th>
<th>Crude HR [95% CI]</th>
<th>P value</th>
<th>Adjusted HR [95% CI]</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antivirals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acyclovir/Valacyclovir</td>
<td>1,585</td>
<td>78 (4.9)</td>
<td>11,300 (6.9)</td>
<td>ref</td>
<td>-</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td>Penciclovir/Famiclovir</td>
<td>599</td>
<td>17 (2.8)</td>
<td>3,781 (4.5)</td>
<td>0.68</td>
<td>0.146</td>
<td>0.62</td>
<td>0.095</td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>699</td>
<td>20 (2.9)</td>
<td>5,668 (4.1)</td>
<td>0.59</td>
<td>0.033</td>
<td>0.67</td>
<td>0.117</td>
</tr>
<tr>
<td>Foscarnet</td>
<td>964</td>
<td>8 (0.8)</td>
<td>5,668 (1.4)</td>
<td>0.22</td>
<td>&lt;0.001</td>
<td>0.31</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Antivirals</strong></td>
<td></td>
<td></td>
<td></td>
<td>ref</td>
<td>-</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td>Acyclovir/Valacyclovir</td>
<td>1,585</td>
<td>78 (4.9)</td>
<td>11,300 (6.9)</td>
<td>4.59</td>
<td>&lt;0.001</td>
<td>3.24</td>
<td>0.002</td>
</tr>
<tr>
<td>Foscarnet</td>
<td>964</td>
<td>8 (0.8)</td>
<td>5,668 (1.4)</td>
<td>ref</td>
<td>-</td>
<td>ref</td>
<td>-</td>
</tr>
<tr>
<td><strong>Nucleoside analogues</strong></td>
<td>2,883</td>
<td>115 (3.4)</td>
<td>20,016 (5.8)</td>
<td>3.80</td>
<td>&lt;0.001</td>
<td>2.72</td>
<td>0.008</td>
</tr>
</tbody>
</table>

1 HR: hazard ratio.
2 Acyclovir/valacyclovir, penciclovir/famiclovir, and ganciclovir were combined as one group, given that we found no statistically significant differences in the risk of HA-AKI between nucleotide analogues.

Cox model was adjusted for age, gender, co-morbidities, mechanical ventilation, ICU admission, other nephrotoxic drugs and operations.

**#6665**

**NON TRAUMATIC RHABDOMYOLYSIS AND ACUTE RENAL FAILURE: WHICH INDICATIONS OF RENAL REPLACEMENT THERAPY?**

Zineb Aboudar, Sara Masrour, Mariam Chettati, Wafaa Fadili and Inass Laouad

Centre Hospitalo-Universitaire Mohammed VI Marrakech, Marrakech, Morocco

**Background and Aims:** The aim of our study is to identify the causes of non-traumatic rhabdomyolysis in our context, to study the clinical and biological presentation of patients and the indications of renal replacement therapy in the management of this entity.

**Method:** Our study is a monocentric retrospective study conducted at the university hospital Mohamed VI of Marrakech including 14 patients who presented rhabdomyolysis complicated by acute kidney injury (AKI) with no traumatic context. Those patients were followed up at intensive care unit and nephrology department over a period of 10 months from March to December 2022.

**Results:** The age of our patients varied between 24 and 64 years for an average of 42 years. The male sex was predominant (78.57%) 11 men versus 3 women with no history of previous kidney disease. The average hospital stay was 20 days [12-42 days]. The most common clinical signs were oligo-anuria (85.7%), abdominal pain (57.1%), nausea and vomiting (42.8%), flank pain (42.8%) and muscle pain (14.2%), hypertension in 5 patients (35.7%), while 4 were hypotensive. The average creatinine on admission was 22mg/l [14-42.3], the average CPK level was 6240UI/L [2225-12570], the myoglobin was assayed in a single patient which returned on admission was 22mg/l [14-42.3], the average CPK level was 6240UI/L [2225-12570], the myoglobin was assayed in a single patient which returned.

**Conclusion:** The management of non traumatic rhabdomyolysis is based above all on rehydration in order to establish blood volume and eliminate the myoglobin pigment. The use of RRT is necessary in some cases such as severe acute renal failure, threatening hyperkalaemia, acidosis or persistent anuria. Several studies suggest the benefit of its early initiation, which still remains to be demonstrated.

**#3091**

**A STUDY FOR HOSPITALIZED PATIENTS WITH COVID-19 WITH/WITHOUT IMMUNOSUPPRESSION AND RENAL FAILURE: DOES THE SURVIVAL RATE CHANGE?**

Styliani Vakiani1, Maria Triantafyllidou2, Dimitris Katsanos3, Klaoudia Lakoniti3 and Panteleimon Vakianis3

1 General Hospital of Corfu, Nephrology, Corfu, Greece, 2Corfu Gen Hosp, Nephrology, Corfu, Greece and 3Corfu Gen Hosp, ICU DEP, Corfu, Greece

**Background and Aims:** Introduction The purpose of our research topic was to study the survival of immunocompromised or non-immunosuppressed patients as well as patients with Chronic Kidney Disease who were hospitalized due to covid-19 infection during a two-year period (2020-2022).

**Method:** Material and Methods A total of 1270 patients (of whom 570 were women) with a mean age of 63 years (+/- 24 years) were studied. From these, 1000 patients were without immunosuppression and 270 were theoretically and practically immunosuppressed, including 30 patients with Chronic Kidney Disease and of these 10 were with end-stage Chronic Kidney Disease. It is important to mention that 87 patients had to be hospitalized in the ICU, of which 74 died. The rest were hospitalized in the Bioccontainment Unit, where
**#3404**

**UTILITY OF RENAL BIOPSY IN THE ETOLOGY, MANAGEMENT AND OUTCOME OF POSTPARTUM ACUTE KIDNEY INJURY**

Manoj Jain¹, Dharmander Bhadauria², Narayan Prasad² and Anupma Kaul²

¹Sanjay Gandhi Postgraduate Institute of Medical Sciences, Department of Pathology, Lucknow, India and ²Sanjay Gandhi Postgraduate Institute of Medical Sciences, Department of Nephrology, Lucknow, India

**Background and Aims:** Acute kidney injury (AKI) is a serious complication during pregnancy and postpartum period resulting in significant maternal morbidity, mortality and fetal loss. Pregnancy related acute kidney injury is still more prevalent in developing countries. This study aims to evaluate renal biopsies in postpartum period AKI (PPAKI) with etiology and its management and outcome.

**Method:** Retrospective analysis of 83 native renal biopsies received in the department of pathology, SGPGIMS, Lucknow, a tertiary care center in India with PPAKI from January 2007 to December 2021 were analyzed. Clinical and laboratory data were retrieved and renal biopsy histology slides were reviewed.

**Results:** Eighty-three patients with mean age 27.5±4.6 years had biopsy proven PPAKI. Cesarean section, vaginal delivery, hysterectomy and abortion were performed in 51, 19, 2 and 11 patients respectively. The cause of AKI was sepsis (38.6%), postpartum hemorrhage (26.5%), thrombotic microangiopathy (TMA) (11%), pre-eclampsia (3.7%) and other (20%). Duration of onset of AKI after delivery/abortion ranged from 0 to 30 days (mean 4.5±6.3 days). Fetal loss was seen in 31.7% patients. Biopsy showed partial/complete renal cortical necrosis (56.6%), TMA (24.1%), acute tubular injury (ATI) (4.8%), Lupus nephritis flare in 3.6% and other glomerular diseases (8.4%) and Tubulointerstitial nephritis in (1.2%) patient. All received multiple sessions of haemodialysis and 10 patients also had plasmapheresis. During hospital stay one died due to sepsis and shock, remainder were discharged in a stable condition with complete recovery in (5), partially recovery in (7); and 61 (71%) patients required continued renal replacement therapy. Two patients died and two had subsequent live related renal transplantation had a follow up follow-up.

**Conclusion:** AKI is a serious complication in postpartum period and require early and prompt attention to reduce fetal and maternal morbidity. Sepsis is the commonest cause of postpartum AKI.

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**#3485**

**IMPROVING THE DIAGNOSIS OF MYOCARDIAL INFARCTION IN CHRONIC KIDNEY DISEASE**

Marrica Mcdonald-Coley and Marilyn Lawrence-Wright

University of the West Indies, The Department of Medicine, Kingston 7, Jamaica

**Background and Aims:** Chronic Kidney Disease has significant morbidity and mortality owing to the increased prevalence in cardiovascular disease. This increase in morbidity and mortality is seen more so as glomerular filtration rate (GFR) declines, that is, advanced kidney failure with GFR equal to or less than 30ml/min/1.73m². Hence, it is important to control risk factors and accurately diagnose myocardial infarction in this cohort of patients.

**Secondary objectives showed that social isolation was significantly associated with confirmed myocardial infarction. Additionally, ST changes, and T-QRS discordance on electrocardiogram were found more commonly in the myocardial infarction group. Other diagnostic tools such as angiography proved to be an underutilized investigation with a prevalence of 13% in the kidney disease cohort at the University of the West Indies during the years 2018 to 2020.**

**Method:** In this retrospective cross-sectional study, data was collected from the hospital records system at the University of the West Indies. Patients with an admission diagnosis of acute coronary syndrome, unstable angina, non-ST elevation myocardial infarction, ST elevation myocardial infarction and chronic kidney disease were included in the study population. Cases were assigned based on whether or not myocardial infarction was confirmed on echocardiogram.

**Results:** Of the total number of 102 cases, 58 were chosen based on fulfillment of diagnostic criteria. 13 (22.4%) had echocardiographic evidence of a new myocardial infarction while 44 (75.9%) had no echocardiographic evidence of new myocardial infarction. Receiver Operator Characteristic Curves (ROC) used to evaluate the diagnostic performance of high sensitivity cardiac troponin T and interval/ delta changes showed an ideal value 141.50ng/L on first troponin T and 100.75ng/L on serial troponin T with delta change of 20.5% (sensitivities of 61.5%, 72.7% and 72.7% respectively). Area under the Receiver-Operating Characteristic Curve (AUC) used to determine the diagnostic accuracy of the highly sensitivity cardiac troponin T and interval delta change demonstrated high accuracy of 0.708 for the first troponin T; 0.750 for the second troponin T and 0.767 for the interval or delta change.

**Conclusion:** Overall, we showed that serial troponin measurements in kidney disease patients increase sensitivity for predicting myocardial infarction and that the values are nearly 10 times that used for the general population. An interval change of 20.5% was also predictive of myocardial infarction.
THE ROLE OF EARLY ACUTE KIDNEY REPLACEMENT THERAPY (AKRT) IN THE PROGNOSIS OF PATIENTS WITH COVID-19: A RANDOMIZED CLINICAL TRIAL

Paula Gabriela Sousa de Oliveira, Lais Gabriela Yokota, Welder Zamoner, Andre Balbi and Daniela Ponce

São Paulo State University (Unesp), Medical School, Botucatu, Brazil

Background and Aims: The COVID-19 pandemic has increased the burden of morbidity and mortality worldwide and in its moderate to severe forms is associated with serious complications such as Acute Kidney Injury (AKI). AKI related to COVID-19 appears to be multifactorial and the AKI incidence is around 20%, with the need for dialysis in up to 40-50% of critically ill patients. So far, there has been no evidence of benefit from early dialysis in different contexts of AKI. In the context of COVID-19 it is possible that the indication of early dialysis support can help and improve outcomes with inflammation and volume control. The objective of the study was to evaluate the role of early acute kidney replacement therapy (AKRT) in the context of COVID-19.

Method: We analyzed 108 patients from a randomized open-label clinical trial with AKI 3 according to the KDIGO 2012 criteria, with severe acute respiratory syndrome with confirmed COVID-19 (RT-PCR technique or serology), admitted from March 2020 to May 2021 in a reference public hospital in the State of São Paulo (Brazil). Patients were randomized to early AKRT indication (either cytokine storm or fluid balance cumulative greater than 3% of body weight) or standard indication (classic indications or systemic demand and renal capacity imbalance). Cytokine storm was characterized as uninterrupted fever (38°C or more) for at least 12 hours and exclusion criteria were patients younger than 18 years, pregnant women, chronic kidney disease (CKD) stages 4 and 5, kidney transplant recipients. Patients were randomized in blocks for allocation to groups and the primary outcome was hospital mortality. The study was approved by the research ethics committee, registered in the Brazilian Clinical Trials Registry. Seeking a detection of a 20% mortality difference between the standard and early groups, the required sample size would be 48 patients per group and was assumed an alpha error of 5%. All analyses were performed using SPSS 28.0.1.1 (15).

Results: 108 patients were included in the intention-to-treat analyses (41 in the early group and 67 in the standard group). 66.7% were men, 86.9% white, mean age of 62.56 ± 14.25 years, 93.9% in intensive care unit, 100% in mechanical ventilation (MV) and 93.5% in use of vasoactive drugs. The most common comorbidities were hypertension (68.5%), diabetes (39.8%) and obesity (52.8%). Hematiauria (47.9%) and proteinuria (74.7%) were common. The P/F ratio. ATN-SS e APACHE II scores were mean, respectively, 145.40 ± 67.70; 0.75 ± 0.12 ± 20.04 ± 6.64. 51.9% of the sample had a cytokine storm and the overall mortality was 87%. The standard and early groups were similar in gender, race, comorbidities, severity, medications, and laboratory markers of severity as well as catheter site, system coagulation, number of dialysis sessions and mortality (63.8% in the standard vs 36.2% in the early, p = 0.32). There was a difference in age e modality of dialysis between the groups (higher mean of age (57.78±14.24 years vs 65.49±13.54) and more continuous dialysis (66.7% vs 33.3%, p < 0.01) in the early group. Hypertension (68.9% vs 31.1%, p = 0.051), CKD (80% vs 20% p = 0.038) and dlysidipemia (80.8% vs 19.2%, p = 0.52) were more common in the standard. The early group had a longer ICU stay (20.26±20.93 days vs 13.22±11.34, p = 0.053), lower maximum creatinine (3.88±1.88 vs 5.24±2.46, p = 0.004) and lower ATN-SS (0.72 ±0.12 vs 0.78±0.12, p = 0.017). In the survival analysis, a better hospital survival trend was observed in the early group, but with no statistically significant difference (p = 0.061). Use of angiotensin converting enzyme inhibitor (ACEI), 42.9% vs 13.8, p = 0.008, and longer time in MV (28.71±12.48 days vs 13.42±13.99, p = 0.001) were associated with longer mortality. In the logistic regression, use of ACEI (OR 0.007, 95% CI 0-0.29, p = 0.009), MV time (OR 0.93, 95% CI 0.88-0.99, p = 0.023) and higher APACHE II (OR 1.28, 95%CI 1.02-1.6, p = 0.03) were associated with mortality.

Conclusion: It was observed that the use of ACEI, longer ventilation time and APACHE II score were associated with mortality, while early AKRT indication had no impact in survival of patients.
Background and Aims: At least 30% of acute kidney injury (AKI) survivors lack appropriate follow up after hospital discharge. AKI survivors have highly dynamic posthospital course which warrants close monitoring to prevent adverse outcomes. Digital health solutions like remote patient monitoring (RPM) could be used to improve quality and efficiency of AKI survivor care. The purpose for this study was to assess the feasibility and effectiveness of the Mayo Clinic AKI RPM program, launched in October 2021.

Method: The Mayo Clinic AKI RPM program enrolled individuals who experienced AKI during a hospitalization and underwent nephrology consultation (Figure 1). Feasibility was assessed as the proportion of individuals approached for AKI RPM enrollment during the first year of the program who submitted at least one set of vitals after discharge. An effectiveness analysis compared stage 3 AKI survivors enrolled in AKI RPM with at least 30-days of follow-up to matched historical controls (3:1) sampled from before RPM was available (2018-2021). The primary endpoint was hospital readmission or emergency department (ED) visit within 30-days, assessed with the Chi-square test. Secondarily we explored time to first readmission or ED visit with a Kaplan-Meier survival curve with a non-parametric comparison between groups, as well as readmission length of stay with the Wilcoxon Rank Sum test due to right skewed data distribution.

Results: Of the 50 individuals approached for AKI RPM participation, 45 (90%) submitted at least one set of vitals. Among AKI RPM patients, 34 patients with stage 3 AKI were matched to 102 controls based on baseline characteristics and demographics. Dialysis during hospitalization (liberated by discharge) was used in 36 (27%) of patients. Sixty (44%) individuals required ICU level of care. Median (IQR) discharge estimated glomerular filtration rate was 15 (11, 27) mL/min/1.73m². Through matching, groups were well balanced with respect to pertinent baseline demographics. Hospital readmission or ED visit occurred in 17 (50%) of AKI RPM patients within 30-days compared to 39 (38%) of controls within 30-days ($P = .23$). The endpoint appeared driven by ED visits within 30-days, not readmissions [At least one ED visit: 13 (38%) vs 21 (21%), respectively ($P = .04$); At least one hospital readmission: 7 (21%) vs 26 (26%), respectively ($P = .56$)]. Time to first readmission or ED visit within 30-days was similar between groups ($P = .35$; Figure 2). Among the 33 patients who were readmitted to the hospital within 30-days, readmission length of stay was similar in the AKI RPM group compared to controls [Median (IQR) 76 (10.6, 121) hours vs 108 (70, 165) hours; $P = 0.33$].

Conclusion: In conclusion, AKI RPM was a feasible program when used to bridge the care continuum (hospital to home) in non-dialysis dependent AKI survivors. Incidence of at least one hospital readmission or ED visit within 30-days was statistically similar between AKI RPM patients and controls. More AKI RPM patients experienced ED encounters in the 30-days after discharge, but frequency of hospital readmission was similar. Digital health solutions such as RPM offer a unique opportunity to address the important gap in AKI care after discharging from the hospital. Additional research is needed to explore the impact of AKI RPM on patient outcomes.

Figure 1: AKI RPM algorithm for escalation of care based on laboratory and patient-provided data. RPM nurses review data daily and call patients at a minimum once weekly. If a patient has a parameter that meets emergent criteria, they are directed to the ED. Urgent criteria are referred directly to the nephrology provider. Patients who meet routine or semi-urgent criteria are monitored by RPM nurses in collaboration with specialty nurses.
Objective: To compare different vancomycin administration protocols to assess serum concentrations and area under the curve/minimum inhibitory concentration (AUC/MIC) ratio from PK/PD.

Methods Randomized, non-blind clinical trial, including critically ill adults diagnosed with septic AKI on conventional (4 hours) and prolonged HD (6 and 10 hours) and using vancomycin for at least 72 hours from May/2019 to May 2021. Sessions of patients were analyzed and randomized into three groups (G): G control (C, dose of 15 mg/kg after HD session), G intervention (I) 2 hours (dose of 7.5 mg/kg in the second hour of HD and 7.5 mg/kg after the session) and IG continuous infusion (dose of 30 mg/kg in continuous infusion pump, in 24 hours). Patients on chronic dialysis, pregnant women, and those whose session was interrupted for clinical or technical reasons were excluded.

Results Of the 316 patients recruited, 87 were randomized, and 174 HD sessions were monitored. There was a predominance of males (69.5%), age 61±11 years, APACHE II 31±6, ATN-SS 0.79±0.14. For the analysis, 28 sessions belonged to the CG, 47 sessions to the 2-hour IG, and 31 to the continuous infusion IG. The groups were similar in age, weight, comorbidities, severity scores, use of diuretics and nephrotoxic drugs, urine output, albumin, CRP, hematocrit, HD modality, recovery of renal function, and death. When HD sessions were analyzed, there was no difference between the groups regarding Kt/V, ultrafiltration, system coagulation, or hypotension. The CG had a higher frequency of subtherapeutic serum levels at the end of HD compared to the 2-hour IG and continuous infusion (86.7% vs. 42.2% vs. 3.2%, p < .0001), higher clearance dialysis (p = .04) and lower AUC/MIC (p < .0001). The IG continuous infusion had a higher frequency of supratherapeutic concentrations (71%). Logistic regression identified the initial concentration variable as a risk factor (OR 1.16, p = .001) for a non-therapeutic concentration (AUC/MIC less than 400 mg·h/L or greater than 600 mg·h/L) of vancomycin. In contrast, the 2-hour intervention group was identified as a protective factor (OR 0.24, p = .04).

Conclusion: Our results suggest that administering vancomycin during dialysis resulted in a lower proportion of supratherapeutic or subtherapeutic concentrations compared to administration in continuous infusion or after the end of the session, respectively. New studies are needed to suggest more appropriate doses and assess these findings’ impact on clinical outcomes.
DIURETIC RESISTANCE PREDICTORS IN ACUTE DECOMPENSATED HEART FAILURE ADMISSIONS: A BROADER LOOK

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Background and Aims: Failing to relieve congestion portends a rise in mortality rate and length of stay in acute decompensated heart failure (ADHF) hospitalizations. That situation corresponds to diuretic resistance (RDIUR). We sought to evaluate clinical and biochemical predictors of RDIUR, including those non-conventional ones we noticed as relevant in prognosis in our clinical practice.

Method: We conducted an observational, analytical and cross-sectional study, with prospective and consecutive patient (P) data acquisition. We included P over 18 years-old, who were admitted to the Intensive Care Telemetry Unit in our Hospital in the period between July; 2011 and May, 2022 due to ADHF diagnosis. All P received diuretic IV therapy as part of pharmacological treatment. As mentioned in earlier presentations, urine output (UO) was registered in all P and failure to achieve an UO ≥ 1.5 ml/kg/hour under a pre-established protocol that included and initial 100 mg of IV furosemide bolus followed by 2 a hours of a 3 mg/hour furosemide continuous infusion. Under failure to achieve the goal, furosemide dose was doubled for two additional hours. Failure to respond to this strategy was called “diuretic resistance”. P who received a heart transplant during index admission or those who were on chronic dialysis were excluded from this study. Clinical, epidemiological and biochemical variables were registered. Missing data was imputed by means of multiple regression with chained equations. We constructed a multivariate logistic regression, with selection of relevant predictors completed by resampling and regularization of a Lasso regression model. Statistical significance was considered with a 5% of alpha error. Analysis was conducted using R (R Core Team, 2021), with RStudio (RStudio Team, 2020) as Integrated Development Environment for R, and the tidymodels package (Silge and Kuhn, 2022).

Results: A total of 1359 P were included. RDIUR was observed in 177 P (13%). These P were younger (69 years old vs 72 p = 0.02), with a higher prevalence of diabetes (39.5% vs 28%; p = 0.002), admission creatinine levels (1.4 vs 1.1 mg/dl; p < 0.001), lower total T3 serum levels (0.56 mg/ml vs 0.7; p < 0.001), with higher incidence of cholestasis (61 vs 40%; p < 0.001), and anasarca as clinical phenotype of systemic congestion (17.5% vs 8.5% p < 0.001). In-hospital mortality was higher in P who developed RDIUR (32.8 vs 16, p < 0.001), worsening heart failure (48% vs 11; p < 0.001), and furosemide dose at 2nd admission day (175.4 vs 123.4 p < 0.001) were higher in these P. We found no differences in left ventricular ejection fraction (38 vs 41 p = 0.21), first day natriuresis (75.5 vs 78.4; p = 0.093), coronary etiology vs others (20% vs 22; p = 0.26) or one month readmission rate (33% vs 37; p = 0.27). In the adjusted model, instotropic support (OR 5.2; IC95% 3.4-8; p < 0.001), worsening heart failure (OR 3.4; IC95% 2.2-5.3; p < 0.001), furosemide dose at 2nd day (OR 1, IC95%; P 0.001), admission creatininemia (OR 2.05; IC95% 1.7-2.6; p < 0.001), anasarca phenotype (OR 2.3; IC95% 1.4-3.9; p = 0.002) and normal T3 levels (OR 0.05; IC95% 0.02-0.14; p < 0.001) were identified as independent predictors of RDIUR development. Model accuracy was 0.89 and ROC-AUC 0.87. In the same way, RDIUR (OR 2.57; IC95% 1.5-4.3; p < 0.001), worsening heart failure (OR 4.1 IC95% 2.4-7; p < 0.001), instotropic support (OR 3; IC95% 1.7-5.2; p < 0.001) and cholestasis (OR 3.1; IC95% 1.9-5.2; p < 0.001) were found as independent predictors of in-hospital mortality.

Conclusion: Diuretic resistance is a serious event in patients hospitalized for ADHF, and considerably associated with mortality. A decreased renal reserve, low T3 levels, and anasarca at admission were significantly associated with diuretic resistance development. Considering “new” biochemical predictors as admission T3 levels might add strength to this subset of patients, opposed to information displayed by “classical” event predictors in ADHF patients, as ventricular function or etiology of cardiac disease. Due to clinical potential implications these observational results should be confirmed under evidence based protocols.

Pregnancy Related Acute kidney injury (PR-AKI) is a global health problem with substantial maternal and fetal morbidity and mortality. Late referral, and late diagnosis of women with risks of PR-AKI represent the major barriers for curtailment of this ugly trend, particularly in the developing world. Our past experience per se revealed striking maternal and fetal mortality of women with PR-AKI. Great strides are strongly needed to save maternal and fetal lives. This study assessed the impact of implementing an innovative obstetric nephrology service (ONS) and healthcare program on maternal and fetal outcomes in women at risk of PR-AKI.

Method: An innovative interdisciplinary obstetric nephrology clinic was established in 2020 to improve the quality of care for pregnant women at risk of PR-AKI. The service was staffed by both nephrologists and obstetricians. Women who presented to the clinic were stratified into low, moderate, and high-risk groups. A risk stratification-based care program was adopted. Very high-risk women were admitted to the maternal care unit. The study compared the outcomes of ONS-treated women who completed their follow up (n = 43) versus two groups of conventionally treated women (n = 40) and women presented before service (n = 40).

Results: Although they had greater pre-existing risks, ONS-treated women had no reported maternal or fetal mortality compared to women in the conventionally treated group (11.8% and 51.5% respectively), and to women presented before service (22.5% and 45% respectively). Progression to end-stage renal disease was significantly less in ONS-treated women compared to both conventionally treated and those treated before service (3% versus 13.2% and 37.5% respectively).

Conclusion: Easily feasible Obstetric nephrology service implementation and adoption of early referral program and diagnosis policies were associated with better maternal and fetal survival as well as better renal outcomes. Provision of parallel services is strongly recommended to decrease the magnitude of PR-AKI.
Table 1: Sociodemographic, clinical, and laboratory characteristics of pregnant women treated versus those non treated at the Obstetric Nephrology Clinic (ONS) on presentation.

<table>
<thead>
<tr>
<th></th>
<th>ONS treated</th>
<th>Conventionally treated</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>27.66 ± 5.85</td>
<td>30.13 ± 7.29</td>
<td>0.097*</td>
</tr>
<tr>
<td>Gestational age at presentation, wk</td>
<td>25 (9-38)</td>
<td>33 (4-37)</td>
<td>0.309**</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>1 (2.4%)</td>
<td>1 (2.5%)</td>
<td>0.986***</td>
</tr>
<tr>
<td>History of HTN, n (%)</td>
<td>14 (34.1%)</td>
<td>15 (37.5%)</td>
<td>0.753***</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>120 (90-190)</td>
<td>130 (80-200)</td>
<td>0.067**</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>80 (60-110)</td>
<td>80 (50-120)</td>
<td>0.280**</td>
</tr>
<tr>
<td>Women developed PR-AKI</td>
<td>1 (2.6%)</td>
<td>23 (63.9%)</td>
<td>0.000***</td>
</tr>
<tr>
<td>Predisposing conditions</td>
<td>23 (60.5%)</td>
<td>5 (13.9%)</td>
<td>0.000***</td>
</tr>
<tr>
<td>CKD</td>
<td>8 (21.1%)</td>
<td>4 (11.1%)</td>
<td>0.010***</td>
</tr>
<tr>
<td>Hypertensive disorders of pregnancy</td>
<td>5 (13.2%)</td>
<td>1 (2.8%)</td>
<td>0.152**</td>
</tr>
<tr>
<td>obstructive kidney diseases</td>
<td>1 (2.6%)</td>
<td>3 (8.3%)</td>
<td>0.155*</td>
</tr>
<tr>
<td>Sepsis</td>
<td>10 (27.0%)</td>
<td>2 (5.3%)</td>
<td>0.099*</td>
</tr>
<tr>
<td>Nulliparous, n (%)</td>
<td>8.65 (5.3-16)</td>
<td>11.2 (2.3-36.2)</td>
<td>0.290**</td>
</tr>
<tr>
<td>WBC, (×10³/mm³)</td>
<td>10.18 ± 1.47</td>
<td>9.33 ± 2.22</td>
<td>0.000*</td>
</tr>
<tr>
<td>HB, g/dl</td>
<td>225.9 ± 87.92</td>
<td>188.11 ± 94.27</td>
<td>0.045*</td>
</tr>
<tr>
<td>PLT, (×10³/mm³)</td>
<td>1415 (0.7-1150)</td>
<td>2171 (471.2-7387)</td>
<td>0.240*</td>
</tr>
<tr>
<td>24hr.urinary protein, mg/day</td>
<td>1.18 ± 1.21</td>
<td>3.5 ± 2.86</td>
<td>0.091*</td>
</tr>
<tr>
<td>Serum creatinine, mg/dl</td>
<td>2.7 ± 0.5</td>
<td>3 ± 0.5</td>
<td>0.420*</td>
</tr>
<tr>
<td>Albumin, gm/dl</td>
<td>0.6 ± 0.16</td>
<td>4.7 ± 7.6</td>
<td>0.273*</td>
</tr>
<tr>
<td>Bilirubin, mg/dl</td>
<td>1.02 ± 0.03</td>
<td>1.27 ± 0.48</td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td>27.8 ± 11.5</td>
<td>24 ± 4.1</td>
<td></td>
</tr>
<tr>
<td>AST, U/L</td>
<td>23.12 ± 8.13</td>
<td>67.5 ± 125.1</td>
<td></td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>8.65 (5.3-16)</td>
<td>11.2 (2.3-36.2)</td>
<td>0.290**</td>
</tr>
</tbody>
</table>

* Probability of independent sample t-test. Values of its variables are expressed as mean ± standard deviation
** Probability of Mann-Whitney U test. Values of its variables are expressed as median (interquartile range).
*** Chi-square test. Values of its variables are expressed as n (%) number and (percentage).

#3056
IMPACT OF ALBUMIN BINDING FUNCTION ON PHARMACOKINETICS AND PHARMACODYNAMICS OF FUROSEMIDE

Gerd Klinkmann¹, Sebastian Klammt², Daniel Reuter¹ and Steffen Mitzner²

¹University Medical Center Rostock, Department of Anaesthesiology, Intensive Care Medicine and Pain Therapy, Rostock, Germany and ²University Medical Center Rostock, Department of Internal Medicine, Division of Nephrology, Rostock, Germany

Background and Aims: Albumin binding of furosemide forms the basis for its transport to the kidney and subsequent tubular secretion, which is a prerequisite for the effect of furosemide. Accordingly, high albumin concentrations should result in higher efficacy of furosemide. However, study results on the combination of furosemide in conjunction with albumin and on the efficacy of furosemide in hypoalbuminemia did not confirm this hypothesis. The aim of this study was to determine the efficacy of furosemide not only in relation to concentration, but also to take albumin function into account.

Method: In a prospective and non-interventional clinical observational trial, blood and urine samples from 50 intensive care patients receiving continuous intravenous furosemide therapy were evaluated. Albumin binding capacity (ABiC) determination allowed conclusions to be drawn about the binding site-specific loading state of albumin by quantifying the unbound fraction of furosemide.
the fluorescent marker dansylsarcosine. In addition, assessment of the total concentration of furosemide in plasma and urine as well as the concentration of free furosemide fraction in plasma was performed by HPLC-MS. The efficacy of furosemide was evaluated by the ratio of urine excretion to fluid intake.

**Results:** In patients with an ABiC ≥ 60% free furosemide fraction was significantly lower compared to patients with a lower ABiC (p < 0.001), urinary furosemide concentration was higher (p = 0.136), and a significantly higher proportion of infused furosemide was excreted renally (p = 0.010). ABiC was positively correlated (r = 0.908, p = 0.017) with the increase in urine excretion to fluid input ratio after initiation of furosemide therapy.

**Conclusion:** ABiC could serve as a marker for individual response to furosemide and could be used to generate patient-specific therapeutic regimens. In view of the relatively low number of patients in this study, the relationship between furosemide efficacy and albumin function should be investigated in larger studies in the future.

**Table 1: Mean values of EO at the 3 times, based on death outcome.**

<table>
<thead>
<tr>
<th>EO (pmol/L)</th>
<th>Death</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>No</td>
<td>298.34</td>
<td>85.54</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Yes</td>
<td>425.70</td>
<td>165.42</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>No</td>
<td>252.34</td>
<td>47.78</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1: Schematic overview of the ABiC determination.**

**#4720**

**SEPSIS, AKI AND MORTALITY. SEARCHING FOR NEW MARKERS: OUR EXPERIENCE WITH ENDOGENOUS OUABAIN**

Davide Raimondo, Chiara Livia Lanzani, Luca D’urbano, Lorenzo Cocchini, Marta De Filippo, Giuseppe Vezzoli, Lorena Citterio, Laura Zagato, Paolo Manunta and Marco Simonini

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**Background and Aims:** Sepsis and septic shock are quite common events in the hospital setting. The classification of these events has changed a lot over the years, to ensure better sensitivity in recognizing a situation that, if not managed properly and quickly, leads to the death of the patient. In our study we focused on the search for predictors of acute kidney injury and mortality during the evolution of this pathology, with particular attention to the role of the Endogenous Ouabain hormone.

**Method:** We enrolled 177 patients diagnosed with sepsis or septic shock, under an ordinary hospital stay. We standardized patients according to the latest classification criteria (Sepsis-III), we focused our attention specifically on SOFA score and the relationship with acute kidney injury and mortality, including its relationship with other laboratory parameters, especially lactates. In a subgroup of patients was also dosed the level of Endogenous Ouabain (EO - hormone produced by the adrenal glands but which has an important impact on renal hemodynamics), through a venous sampling in 3 different times (at the beginning of the septic state, 24 and 48 hours later). Subsequently the variation of EO and the correlation with laboratory parameters was investigated in this period, to assess its impact on the development of kidney damage and mortality.

**Results:** The 70.1% of septic patients in our study develop AKI and, of this percentage, 75% in a severe form (stage 2-3 KDIGO). Both the presence and severity of AKI are unable to predict mortality in our sample (p-value 0.13). The presence of an impaired hemodynamics status (expressed as AD MAP < 70 mmHg) has a strong impact in the severe stages of AKI but not in the mild form (p-value 0.006; ExpB 1.81 vs p-value 0.105; ExpB 1.46). The other elements related to the development of AKI were found to be the high levels of white blood cells, respiratory distress and the SOFA value at the presentation, while we found no correlation with CRP and lactate levels. Lactate levels well correlate with SOFA (p-value <0.0001 and Pearson’s index 0.407) and mortality, particularly when the initial values are > 2mg/dL (p < 0.0001; ExpB 5.31, IC95% [2.07-13.57]). In the subgroup of patients in which EO was dosed, there was a strong correlation of the basal levels of this hormone with mortality even after correction for lactate levels and SOFA (p-value 0.009) but not with the development of AKI. However, patients in AKI stage-3 show persistently higher levels of EO both at 24 and 48 h (p = 0.015).

**Conclusion:** The presence of high levels of lactates at the onset is the most important predictor of mortality, followed by EO levels at presentation and the SOFA value. Elevation of Endogenous Ouabain levels is indicative of an acute state of stress but is not a parameter influenced by the SOFA score, nor by the general condition of patient. It seems non directly related with the development of AKI, tissue hypoperfusion or activation of the inflammatory response but is associated with an inability to rapidly recover renal function. The EO could be very useful in predicting mortality in patients with sepsis and septic shock as it seems to be an earlier, more specific, and sensitive than the other laboratory parameters used so far.

**#5674**

**HYPERURICEMIA AND HIGH URINARY URIC ACID LEVELS ARE THE NEW EARLY PREDICTORS OF CONTRAST-ASSOCIATED ACUTE KIDNEY INJURY**

vilma Cadril,1 Loriana Toska1, Ariana Strakosha1, Elvana Rista2, Nevi Pasko1, Matilda Imeraj 1, Myftar Barbullushi1 and Alban Dibra3

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**Background and Aims:** Contrast associated acute kidney injury (CA-AKI) is recently evidenced with lower frequency although yet worldwide its incidence
ranges from 0-24%. Recent studies and meta-analysis have reported that hyperuricemia seem to be a useful biomarker in the early prediction of CIN incidence. The role of urine pH and spot uric acid to creatinine ratio (UACR) provide controversial evidence on the occurrence of CA-AKI. This research aims to gather evidence on the effect of uricemia, urine pH and UACR on the development of CA-AKI in acute conditions like primary percutaneous coronary interventions (PCI).

Method: A sample of 100 patients who underwent emergency coronary angiography in Cardiology Intensive Care Unit/UHCN-Tirana/Albania from October 2021- March 2022 were enrolled. Among these patients CA-AKI incidence was monitored, while CA-AKI was defined as an increased creatinine levels of more 25% of the baseline in a time window of 48-72h after the contrast. The analyses of the results were performed using ANOVA test for differences in parameters among CA-AKI/Non – CA-AKI patients. In order to understand the effect of each factor on the probability of experiencing CA-AKI a binary logistic regression model was constructed. Statistical analyses were performed using R-software.

Results: The general incidence of CA-AKI is 40%, while being different for men and women, with men incidence being 60%. The mean age for the patients observed was age 64.7 years old. The ANOVA analyses showed that incidence of patients experiencing CA-AKI is significantly different for chronic kidney disease patients (p = 0.001, OR = 32.67 (95% CI 9.65-110.55), patients with diabetes (P = 0.0033, OR = 4.64 (95%CI 1.69-12.68) and hypertension (p = 0.055, OR = 7.80 (95%CI 0.96-63.56). The binary logistic regression showed that probability to experience CIN is significantly impacted by UACR post contrast model 1:3.123 (2,385) with marginal effect 22.72, BMI index model 1: (-0.850) 0.25 with marginal effect 1.28, Uricemia model 1: (1,128) 0.52 with marginal effect 1.68 and Natremia level before contrast model 1: (-1.831) 0.0011 with marginal effect 7.81. Statistical significance for these results is 99% (as manifested by p-value).

Conclusion: CA-AKI post PCI is still the Achilles Heel of interventional cardiology. The results confirm that the increase of uricemia and BMI doubles the risk for CA-AKI. Uricemia is confirmed as an important prognostic factor for development of CA-AKI. High urinary uric acid levels post contrast define UACR independent early risk factor for CA-AKI.

INCREASING THE USE OF REGIONAL CITRATE ANTICOAGULATION FOR CKRT IN A LARGE TERTIARY CENTER: A QUALITY IMPROVEMENT PROJECT

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1Singapore General Hospital, Renal Medicine, Singapore, 2Singapore General Hospital, Respiratory & Critical Care Medicine, Singapore, 3Singapore General Hospital, Anesthesia, Singapore, 4Singapore General Hospital, Division of Nursing, Singapore and 5Singapore General Hospital, Division of Medicine, Singapore

Background and Aims: To maintain Continuous Kidney Replacement Therapy (CKRT) circuit patency, KDIGO recommends Regional Citrate Anticoagulation (RCA) as the first-line anticoagulation strategy. In a randomized controlled trial, RCA was associated with increased filter life, reduced circuit downtime, and reduced bleeding, as compared with heparin anticoagulation [1]. RCA-CKRT uptake in our institution, a 1800-bed tertiary center with seven intensive care units (ICU), was low at only 10% of all CKRT sessions. We conducted a Quality Improvement project to increase the uptake of RCA-CKRT in medical and surgical intensive care units in our institution.

Method: Following established Quality Improvement methodology, we delineated a process map and performed a root-cause analysis. Multiple plan-do-study-act (PDSA) cycles were conducted. A bespoke CKRT audit dashboard was created to automatically compile electronic CKRT prescription records and circuit monitoring data. The primary outcome measure, the percentage
Results: Problem analysis (Figure 1) identified that the top root causes contributing to low RCA-CKRT uptake rate were (1) renal physicians defaulting to ‘old habits’ of non-RCA CKRT, (2) nursing staff having inadequate experience and concerns of increased workload, (3) ICU team being uncomfortable with RCA-CKRT, especially fear of citrate toxicity. Multiple PDSA cycles were conducted. In PDSA cycle 1, inclusion and exclusion criteria for default RCA use were standardized. A poster was created to set out these criteria, along with a visual guide explaining how RCA works, and how to identify citrate toxicity. The poster was designed to be eye-catching and easy to understand for non-renal physicians, and was placed prominently in ICU and renal work areas. PDSA cycles 2-4 were educational efforts, including a peer review learning for the renal department, incorporating RCA into ICU resident didactic teaching, and an RCA refresher course for ICU nurses. Through these four PDSA cycles, all three top root causes identified were addressed in turn. Continuous feedback was sought from all stakeholders and acted on in a timely manner. For example, it was identified that some prescribers and nursing staff had the misconception that switching from non-RCA to RCA-CKRT would require changing the entire filter circuit, leading to reluctance to switch to RCA once a CKRT circuit was running. A clarification was promulgated and added to the poster. Over a 12-month period, the percentage of all CKRT sessions utilizing RCA increased from a baseline of 10.5% ± 7.7% (mean ± SD; median 9.8%) to 22.5% ± 14.6% (median 21.5%; p = 0.022) (Figure 2). This included a 3-month period after PDSA cycle 1 during which supplies of RCA-CKRT fluid were disrupted due to COVID-19 supply chain issues. Excluding the months of supply disruption, the uptake of RCA-CKRT would have been 25.3% ± 15.8% (median 25.0%).

Conclusion: A quality improvement project successfully increased the uptake of RCA-CKRT from 10.5% to 22.5% in a complex tertiary care setting. Understanding key barriers at each stage of a complex process, availability of real-time audit data, and attention to stakeholder feedback were key factors that enabled successful change. Unexpected events (in this case a supply chain disruption) may threaten a loss of momentum for change, but can be overcome with continual stakeholder engagement and additive PDSA cycles.

REFERENCE

Background and Aims: In patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), pre-existing chronic kidney disease (CKD) confers a substantial risk for poor outcomes, including the development of cardiac surgery-associated acute kidney injury (CSA-AKI). CSA-AKI occurs in $\geq 50\%$ of patients with CKD undergoing cardiac surgery with CPB vs $\sim 20\%$ of patients without CKD.$^{1,2}$ The risk of subsequent Major Adverse Kidney Events (MAKE; a composite of sustained kidney dysfunction, initiation of dialysis, and death) is also elevated in patients with CKD. Causes of CSA-AKI are multifactorial and complex, and may include inflammation, oxidative stress, renal congestion, and ischaemic injury (such as ischaemic-reperfusion injury [IRI]). IRI is a common cause of AKI and typically results from early hypoperfusion while on bypass, followed by kidney injury upon reperfusion. There are currently no approved therapies that reduce the risk of AKI and associated poor outcomes after cardiac surgery with CPB.$^{3}$ Preclinical and clinical studies suggest that damage and inflammation caused by IRI and CPB is amplified by complement activation$^{3}$; early treatment with C5 inhibitors, especially before onset of ischaemia, may lower the risk of damage.

Method: ARTEMIS is a Phase 3, randomised, double-blind, placebo-controlled, multicentre study of ravulizumab in adults with CKD and stable cardiac disease undergoing non-emergent sternotomy with CPB, to reduce the risk of post-operative AKI and subsequent MAKE 90 days post-surgery.

Key inclusion and exclusion criteria can be found in Figure 1 and a study schematic in Figure 2. Briefly, the study consists of an up to 28-day screening period, randomisation and dosing 1–7 days prior to surgery with CPB (Day 1), a 90-day primary evaluation period post-CPB, and a survival follow-up at day 365 post-CPB. Approximately 736 participants will be randomised 1:1 to receive a single weight-based dose of ravulizumab or placebo; randomisation will be based on baseline CKD stage (3A, 3B, 4) and surgery type (mitral valve replacement or combined procedures vs other single procedures). The primary objective of this study is to assess the efficacy of ravulizumab in reducing the risk of MAKE$^{90}$, defined as meeting $\geq 1$ of the following by day 90 post-CPB: $\geq 25\%$ sustained decrease from baseline in estimated glomerular filtration rate (calculated using the Chronic Kidney Disease Epidemiology Collaboration equation, based on serum Cystatin C); initiation of renal replacement therapy; death from any cause. The safety of ravulizumab in participants with CKD undergoing non-emergent CPB will also be evaluated. Other secondary objectives include assessment of ravulizumab efficacy for reducing AKI (based on serum creatinine) and MAKE risk at earlier timepoints following CPB, alongside any effects it may have on healthcare resource utilisation and health-related quality of life – as well as treatment immunogenicity – in participants with CKD undergoing non-emergent CPB.

Results: The final analysis will be conducted when all participants have completed the primary evaluation period.

Conclusion: The aim of this study is to assess whether terminal complement inhibition with ravulizumab is safe and effective in reducing kidney injury and improving outcomes in patients with CKD undergoing cardiac surgery with CPB.

REFERENCES

Figure 1: Inclusion and exclusion criteria.

Figure 2: Study design.

Abstracts
Background and Aims: Acute kidney injury (AKI) is a common clinical condition among patients who undergo cardiac surgery, significantly affecting morbidity and mortality[1]. To date, preoperative biomarkers and solid predictive models for AKI are not yet currently available in clinical practice. Recent studies reported endogenous ouabain (EO), a stress hormone secreted by the adrenal glands, as associated to worse kidney outcomes after cardiac surgery[2]. The aim was to validate the use of EO as biomarker of individual susceptibility for AKI after cardiac surgery and to create a new powerful score for postoperative AKI risk.

Method: 1174 patients undergoing elective cardiac surgery were enrolled in the study. Preoperative biological samples were collected and analysed. The primary outcome was AKI development, according to KDIGO 2012 guidelines. Results: 21.6% of patients developed AKI (9% developed severe AKI, stage ≥2). AKI confirmed strong correlation to postoperative death: all patients dead within 90 days for postsurgical complication developed AKI and each AKI stage was associated to a 10 times higher mortality risk (p < 0.001). Different preoperative clinical variables were analyzed, identifying five independent risk factors significantly correlated to AKI and severe AKI: age, FE, NYHA class, preoperative EO levels had greater incidence of AKI (p < 0.001), and reoperation and complex surgical intervention (p < 0.001 for all of them). Preoperative EO levels turned out significantly associated to the incidence of AKI (p < 0.001) and clinical complications. Specifically, patients with higher EO levels had greater incidence of AKI (p < 0.001) and worse cardiac and kidney basal function (p = 0.005 and p = 0.003, respectively). Finally, a simple score was developed based on the base of those preoperative clinical variables significantly associated to AKI (AUC for severe AKI = 0.79, p < 0.001). Adding preoperative EO to the model significantly improved the predictive capability (AUC for severe AKI = 0.82, p < 0.001; Δ-AUC +0.0229, p = 0.026).

Conclusion: We confirmed in a large population the role of preoperative plasma level of EO as an important early predictor for post-surgical AKI and we built a powerful clinical model for postoperative AKI risk, exclusively using few simple preoperative clinical factors and a single biohumoral marker.

Table 1: Preoperative characteristics of the population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62 ±13</td>
</tr>
<tr>
<td>Sex (F/M, %)</td>
<td>34.3/65.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 ± 4.1</td>
</tr>
<tr>
<td>sCr (mg/dL)</td>
<td>0.96 ± 0.46</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m²)</td>
<td>82.7 ± 20.2</td>
</tr>
<tr>
<td>CKD (%)</td>
<td>15.1</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>56.2</td>
</tr>
<tr>
<td>DM (%)</td>
<td>15.3</td>
</tr>
<tr>
<td>EF (%)</td>
<td>57 ± 10</td>
</tr>
<tr>
<td>EF class (%)</td>
<td>77.8</td>
</tr>
<tr>
<td>0 (&gt;50%)</td>
<td></td>
</tr>
<tr>
<td>1 (30-50%)</td>
<td>19.4</td>
</tr>
<tr>
<td>2 (&lt;30%)</td>
<td>2.8</td>
</tr>
<tr>
<td>NYHA class (%)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>25.0</td>
</tr>
<tr>
<td>II</td>
<td>53.9</td>
</tr>
<tr>
<td>III</td>
<td>20.1</td>
</tr>
<tr>
<td>IV</td>
<td>1.0</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>32.8</td>
</tr>
</tbody>
</table>

Dichotomous variables in % (positive)
Parametric variables as average ± standard deviation
Not parametric variables as median (interquartile range)

Table 2: Variables used in the EO-clinical model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>P-value</th>
<th>Exp(B)</th>
<th>Inf.</th>
<th>Sup.</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF</td>
<td>0.508</td>
<td>0.001</td>
<td>1.662</td>
<td>1.228</td>
<td>2.248</td>
</tr>
<tr>
<td>Complex surgical intervention</td>
<td>1.104</td>
<td>&lt;0.001</td>
<td>3.016</td>
<td>2.152</td>
<td>4.228</td>
</tr>
<tr>
<td>Reoperation</td>
<td>0.828</td>
<td>&lt;0.001</td>
<td>2.289</td>
<td>1.440</td>
<td>3.638</td>
</tr>
<tr>
<td>Age</td>
<td>0.367</td>
<td>&lt;0.001</td>
<td>1.443</td>
<td>1.243</td>
<td>1.675</td>
</tr>
<tr>
<td>NYHA class</td>
<td>0.515</td>
<td>&lt;0.001</td>
<td>1.673</td>
<td>1.298</td>
<td>2.158</td>
</tr>
<tr>
<td>EO tertiles*</td>
<td>0.374</td>
<td>&lt;0.001</td>
<td>1.454</td>
<td>1.184</td>
<td>1.786</td>
</tr>
<tr>
<td>Costant</td>
<td>-5.733</td>
<td>&lt;0.001</td>
<td>0.003</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Parameters of the ROC curves of EO, clinical model and clinical model for severe AKI onset.

<table>
<thead>
<tr>
<th>Model</th>
<th>Area</th>
<th>ES</th>
<th>P-value</th>
<th>Inf.</th>
<th>Sup.</th>
</tr>
</thead>
<tbody>
<tr>
<td>EO-clinical model</td>
<td>0.82</td>
<td>0.02</td>
<td>&lt;0.001</td>
<td>0.77</td>
<td>0.86</td>
</tr>
<tr>
<td>Clinical model</td>
<td>0.79</td>
<td>0.02</td>
<td>&lt;0.001</td>
<td>0.75</td>
<td>0.84</td>
</tr>
<tr>
<td>EO</td>
<td>0.69</td>
<td>0.03</td>
<td>&lt;0.001</td>
<td>0.63</td>
<td>0.75</td>
</tr>
</tbody>
</table>

REFERENCES
#3047
A NEW ADJUNCTIVE THERAPY WITH AVACOPAN FOR ANCA-ASSOCIATED VASCULITIS
Ryuichi Yoshii¹, Kengo Kajiwara¹, Koki Matsushita¹,
Tomohumi Nakamura¹, Masao Tomita¹ and Masashi Mukoyama²
¹National Hospital Organization Kumamoto Medical Center, Japan and
²Kumamoto University Hospital, Japan

Background and Aims: Glucocorticoids have been the standard treatment for anti-neutrophil cytoplasm autoantibody-associated vasculitis (AAV). Avacopan, a complement CsA receptor inhibitor, has been approved for the treatment of AAV in Japan, the USA, Germany, and Austria. The use of avacopan is supported by evidence from trials demonstrating disease remission with limited use of glucocorticoids [1–3]. Avacopan is a new, promising adjunctive agent for standard induction therapy for AAV and may potentially reduce steroid use.

Method: We assessed treatment responses of patients with AAV who did not require dialysis between 2018 and 2023. Group 1 consisted of six adult patients who were treated with avacopan (30 mg, twice daily) plus reduced-dose prednisone, and Group 2 consisted of 14 patients who received high-dose prednisone. We compared the mean dose of prednisone, Birmingham Vasculitis Activity Score (BVAS), creatinine, urine protein/creatinine ratio (UPCR), and C-reactive protein (CRP) at weeks 0 and 12 between the two groups.

Results: The mean total prednisone dose of oral glucocorticoids at both weeks 0 and 12 was much lower in Group 1 than in Group 2 (p < 0.05). Mean BVAS, creatinine, UPCR, and CRP in Group 1 was comparable to Group 2. Steroid-related toxicity occurred in three of six (50%) patients in Group 1, and 5 of 14 (36%) patients in Group 2. Liver damage related to avacopan occurred in two of six (33%) patients in Group 1.

Conclusion: Herein, we describe practice observations on the use of avacopan in patients with AAV. While further studies are needed to confirm the efficacy of avacopan because of the number of cases treated with avacopan is still lacking, our findings suggest that avacopan was beneficial in AAV patients because of the absence of steroid dependence.

REFERENCES
patients (17.6%) developed a thrombotic complication, whereof 13 (7.4%) were acute coronary syndrome (ACS) or ischemic stroke (IS). The Odds Ratio (OR; 95% CI) to develop any thrombosis for patients with T-TAS01 measurements below (PL-AUC) or above (AR-OT) median were 0.14 (0.05-0.40) and 0.28 (0.12-0.67), respectively. ROC analyses to predict thrombosis with T-TAS01 showed AUCs of 0.78 for all thrombosis and 0.62 for ACS/IS (PL-AUC and AR-OT data combined).

Conclusion: T-TAS01 is a promising tool to aid in the prediction of bleeding and thrombosis in HD patients.

REFERENCE


#6306 SUSTAINED LOW-EFFICIENCY DIALYSIS VERSUS CONTINUOUS VENO-VENOUS HEMODIALFILTRATION OUTCOME IN CRITICALLY ILL PATIENTS

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1Faculty of Medicine-Cairo University, Nephrology Division-Internal Medicine Department, Cairo, Egypt and 2Faculty of Medicine-Cairo University, Critical Care Department, Cairo, Egypt

Background and Aims: Acute kidney injury due to sepsis is the most common cause of AKI in critical care settings. Different modalities of renal replacement therapies (RRT) have been used to manage this condition including Continuous Renal Replacement Therapy (CRRT) and sustained low efficiency dialysis (SLED). The aim of this work was to compare the outcome of SLED and CRRT in the form of continuous veno-venous hemodiafiltration (CVVHF) as methods of dialysis in sepsis induced AKI.

Method: We retrospectively analysed data from 120 patients; 20 patients received CVVHDF to manage AKI in the context of sepsis, 47 patients received SLED to manage AKI in the context of sepsis and the third group included 53 patients who have been treated with SLED to manage AKI not due to sepsis. Age was found to be significantly higher in sepsis induced AKI patients treated with SLED than patients treated with CVVHDF (65.5±10.1 vs 59.5±9.3; p = 0.03). Sex distribution or incidences of hypertension, diabetes mellitus, malignancy or liver disease were not statistically different between groups.

Results: Unadjusted 30 day mortality was 44.7% (21pt) in the SLED group vs 50% (10pt) in the CVVHDF group; p = 0.07. Adjusted mortality was not statistically significant between SLED and CVVHDF (OR 0.97, CI = 0.95-1.06). Hypotension occurred more frequently in patients treated with SLED (24 pt = 51.1% vs 5 pt = 25%; p < 0.001).Clotting occurred more frequently in the CVVHDF group as compared to SLED group (7 pt = 35% vs 4pt = 8.5% p < 0.001).

Conclusion: Sustained low efficiency dialysis (SLED) and CVVHDF had comparable 30 day mortality as modalities of RRT in critically ill patients with sepsis induced AKI. SLED still an attractive alternative to CRRT modalities due to lower cost and lower incidence of complications. Further larger studies are recommended.

#3829 ARTERIAL STIFFNESS AND METABOLIC SYNDROME INDICES IN RENAL TRANSPLANTATION PATIENTS

Orkhan Guliyev1, Ayten Mamedzade2, Shalah Imsayilova2 and Jabrayil Jabrayilov2
1Baku Health Center, nephrology, Azerbaijan and 2Azerbaijan

Background and Aims: Although renal transplantation improves survival, cardiovascular morbidity and mortality still remain as a significant problem compared with nonrenal populations. In end stage renal disease metabolic cardiovascular risk factors such as hypertension, hyperuricemia, obesity and diabetes mellitus have been confirmed to be positively correlated with arterial stiffness. Arterial stiffness is an important characteristic of the arterial wall and can be assessed noninvasively by the measurement of carotid-femoral pulse wave velocity (PWV). The aim of this study is to evaluate the risk factors for arterial stiffness in kidney transplant recipients.

Method: One hundred and forty nine kidney transplant recipients from our renal transplant outpatient clinic were enrolled into the study. All patients were evaluated for their standard clinical (age, gender, duration of hemodialysis, post-transplant time), biochemical parameters. Anthropometric and body composition analyses were performed for all patients. Body composition were analyzed by using the Body Composition Analyzer (Tanita BC-420MA). PWV was determined from pressure tracing over carotid and femoral arteries using the SphygmoCor system.

Results: Patients were divided into two groups according to PWV levels. The frequency of patients with PWV ≥ 7 m/s was higher in patients with new onset diabetes (55.9%), hyperuricemia (uric acid level type “Periodical” type= “Periodical” type= 0.12-0.67), respectively. ROC analyses to predict thrombosis with T-TAS01 showed AUCs of 0.78 for all thrombosis and 0.62 for ACS/IS (PL-AUC and AR-OT data combined).

Conclusion: In post transplantation period, metabolic syndrome indices as high blood pressure, hyperuricemia, hyperglycemia and increased waist and hip circumferences are closely related with arterial stiffness. For cardiovascular risk reduction after renal transplantation; blood pressure, serum glucose and uric acid levels should be under strict control.

#3153 HEMOPERFUSION WITH CYTOSORB AND RENAL REPLACEMENT THERAPY IN PATIENTS WITH ACUTE KIDNEY INJURY IN THE INTENSIVE CARE UNIT

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1University of Maribor, Faculty of Medicine, Maribor, Slovenia, 2University Medical Centre Maribor, Clinic for Internal Medicine, Dept. of Nephrology, Maribor, Slovenia, 3University Medical Centre Maribor, Clinic for Internal Medicine, Dept. of Internal Intensive Medicine, Maribor, Slovenia and 4University Medical Centre Maribor, Clinic for Internal Medicine, Dept. of Dialysis, Maribor, Slovenia

Background and Aims: Severe acute kidney injury (AKI) requiring renal replacement therapy (RRT) is a serious clinical disorder in the intensive care unit (ICU), occurring in a substantial proportion of critically ill patients. The aim of our single centre retrospective observational study was to analyse the outcomes of patients admitted to a non-surgical ICU and treated with RRT and with/without continuous hemoperfusion with Cytosorb.

Method: One hundred critically ill patients (mean age, 64.3 years; 69 men) admitted to the ICU and requiring RRT for AKI were analysed. Patient demographics, comorbid diseases, type of RRT, and survival were obtained from the medical record. APACHE II and Sofa Scores on admission were calculated. 30-day mortality was assessed using Kaplan-Meyer or Cox proportional hazards models.

Results: Reasons for ICU admission were acute respiratory failure (39%), cardiopulmonary resuscitation (14%), shock (13%), acute coronary syndrome (9%), sepsis (3%), acute pancreatitis (3%), and other (19%). Prior comorbidities were hypertension (70%), diabetes (43%), heart failure (32%), chronic kidney disease (CKD) (30%), coronary artery disease (CAD) (27%), chronic obstructive pulmonary disease (COPD) (15%), malignancies (12%). Eighty-six patients were treated with continuous RRT (CRRT) and 14 with intermittent hemodialysis (HD). Twenty-four (24%) of patients treated with CRRT were also treated with hemoperfusion with Cytosorb. Using an independent-samples T test, we compared the two groups of patients with respect to the use of Cytosorb (Table 1). 30-day mortality was 82% in all patients and 87.5% in patients treated with CRRT and Cytosorb. Among concomitant diseases, only patients with previous heart failure had worse survival (p = 0.032), previous CKD, CAD, COPD, malignancy had no statistically significant impact. We found no statistically significant differences in 30-day mortality between patients treated with CRRT+Cytosorb and patients treated with CRRT or HD alone. Multivariate Cox proportional hazard regression showed that of all the variables in the statistical model (age, sex, body mass index, previous diseases, C-reactive protein, lactate, procalcitonin, serum creatinine, mean arterial pressure, APACHE II, ultrafiltration between CRRT), only lactate levels on admission (p = 0.002; 95%CI 1.08-1.38) were significant predictor of survival.

Conclusion: The use of hemoperfusion with Cytosorb in ICU patients with AKI did not reduce 30-day mortality. Patients with prior heart failure had a worse outcome. Serum lactate levels at ICU admission were an independently highly prognostic factor for death within 30 days of admission.
Abstracts

#3915

RELATIONSHIP BETWEEN URINARY DCR2/CR LEVEL AND POOR PROGNOSIS OF DIABETIC NEPHROPATHY

Weidong Wang, Jia Chen, Yani He and Kehong Chen

Daping Hospital, Army Medical University, Department of Nephrology, Chongqing, P.R. China

Background and Aims: Diabetic kidney disease (DKD) has a high prevalence rate and many complications, and it has become the main reason for the progression of chronic kidney disease to end-stage renal disease (ESRD). At present, some clinical biomarkers, such as urinary albumin/creatinine ratio (ACR), serum creatinine and cystatin C, are of positive significance in evaluating the course of DKD, but these indicators are greatly affected by the state of the body itself, which can no longer meet the clinical needs. Decoy receptor 2 (DcR2) is the transmembrane receptor of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) and is a biomarker of cell senescence and apoptosis resistance. Our previous study found that the level of urinary DcR2/CR is closely related to renal function damage and renal interstitial injury. Considering that there is still a lack of research on predicting the poor prognosis of DKD with related biomarkers, this study detected the level of DcR2/CR in the urine of patients with DKD for the first time to analyze the relationship between the poor prognosis of DKD and to determine whether urinary DcR2/CR can be used as an index to predict the poor prognosis of DKD.

Method: A total of 181 inpatients with DKD were collected from the Department of Nephrology of Daping Hospital from 2018 to 2022, of which 121 urine samples were collected. The clinical data of the patients were collected and divided into three quantiles according to the level of urinary DcR2/CR. Group 1: DcR2/CR < 321 ng/mmol, group 2: 321 ≤ DcR2/CR ≤ 505 ng/mmol, group 3: DcR2/CR > 505 ng/mmol. The adverse prognosis was based on the occurrence of end point events. Multivariate Cox regression analysis was used to evaluate the relationship between urinary DcR2/CR level and poor prognosis of DKD. ROC curve was used to analyze the value of biomarkers in predicting the poor prognosis of DKD.

Results: With the increase of urinary DcR2/CR level, the levels of urinary microalbumin, ACR, NAG, cystatin C and serum creatinine increased, while urinary creatinine and GFR decreased gradually. Correlation analysis showed that the level of DcR2/CR was positively correlated with ACR, cystatin C and NAG, and negatively correlated with eGFR, while DcR2/CR was positively correlated with IFTA score, renal artery hyaline change score and renal arteriosclerosis score. Cox regression analysis showed that there was a significant correlation between the level of DcR2/CR and the occurrence of poor prognosis (corrected by the model), and the risk of poor prognosis in the DcR2/CR group 3 was 9.903 times higher than that in the DcR2/CR1 group. Kaplan-Meier survival curve showed that the higher the level of DcR2/CR, the worse the prognosis. ROC curve analysis showed that the area under urinary DcR2 curve was the largest (AUC = 0.811), which was higher than ACR, CYC and SCR, and the best intercept value was 389.0 ng/mmol.

Conclusion: Urinary DcR2/CR is superior to ACR, Scr, CyC and other clinical indexes in predicting the poor prognosis of DKD. It is an effective biomarker for predicting poor prognosis of DKD.

#4285

CAUSES OF PEDIATRIC END STAGE KIDNEY DISEASE IN SUDAN

Rasha Hussein1, Xiaoling (Janice) Ye2, Rashid Elldiri4, Elitigani Ali1, Yassir Bakhiet1, Mohamed Karar1, Mohamed YoussiF1, Ghassan Mustafa1, Nahla Allam1, Samira Yahia1, Amna Ahmed1, Mohamed Abdelraheem1 and Peter Kotanko2

1Soba University Hospital, Department of Pediatric Nephrology, Khartoum, Sudan and 2Renal Research Institute, New York, United States of America

Background and Aims: Sudan is a large Sub-Saharan country with a population of about 48 million people, 41% of them under the age of 15 years and a median age of 18.9 years. To data, no data have been reported on the etiology of end stage kidney disease (ESKD) in children and young adults of less than 18 years of age.

Method: We conducted a chart review of all ESKD patients below the age of 18 years treated in a tertiary referral center, the Soba University Hospital (SUH) in Khartoum, the capital of Sudan. The research was approved by the SUH ethical committee. We report descriptive statics, including age, sex, ESKD causes, and kidney biopsy frequency.

Results: We included 885 patients in this analysis, their mean age (SD) was 12 (3.0) years and 57.7% were males. Glomerulonephritis, mostly post-streptococcal glomerulonephritis, was the leading cause of ESKD (36.8%), followed by unknown etiologies (25.3%) and congenital anomalies of kidney and urinary tract (CAKUT; 14.9%). In most patients with glomerulonephritis the diagnosis was based on kidney histology (96.6%). ESKD was attributed to HUS in about 7% of patients. As expected, SLE was more prevalent in females (3:1 ratio) and hereditary nephritis in males (3:1).

Conclusion: Glomerulonephritis and CAKUT account for over 50% of pediatric ESKD patients in this study from a tertiary referral center in Sudan.

Table 1:

<table>
<thead>
<tr>
<th>Variable at admission</th>
<th>Patients treated with RRT (N = 76) mean±SD</th>
<th>Patients treated with RRT and Cytosorb (N = 24) mean±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.1±10.3</td>
<td>58.4±13.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>30.5±7.4</td>
<td>29.8±4.9</td>
<td>0.57</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>22±18</td>
<td>13±9</td>
<td>0.002</td>
</tr>
<tr>
<td>Serum creatinine (umol/L)</td>
<td>311±262</td>
<td>176±112</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>111±108</td>
<td>159±163</td>
<td>0.19</td>
</tr>
<tr>
<td>Procalcitonin (mcg/L)</td>
<td>8±19</td>
<td>22±33</td>
<td>0.046</td>
</tr>
<tr>
<td>Leucocytes (10⁹/L)</td>
<td>12.9±7.8</td>
<td>20.2±20.4</td>
<td>0.098</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>115±26</td>
<td>129±37</td>
<td>0.04</td>
</tr>
<tr>
<td>Trombocytes (10⁹/L)</td>
<td>215±107</td>
<td>218±110</td>
<td>0.9</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>11±6.6</td>
<td>10.2±4.7</td>
<td>0.807</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>3.1±2.2</td>
<td>4.7±3.2</td>
<td>0.029</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>138±7.3</td>
<td>137±5.3</td>
<td>0.43</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.9±1.3</td>
<td>4.7±1.3</td>
<td>0.659</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>83±19</td>
<td>85±19</td>
<td>0.586</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>28.7±8.9</td>
<td>25.2±11.3</td>
<td>0.176</td>
</tr>
<tr>
<td>Sofa score</td>
<td>11.4±2.6</td>
<td>11.3±2.7</td>
<td>0.899</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate before RRT (ml/min)</td>
<td>12±9</td>
<td>17±12</td>
<td>0.015</td>
</tr>
<tr>
<td>Ultrafiltration during RRT (ml)</td>
<td>6031 ±8680</td>
<td>3318±3234</td>
<td>0.165</td>
</tr>
<tr>
<td>Diuresis one day before start of RRT (ml)</td>
<td>919±884</td>
<td>906±414</td>
<td>0.96</td>
</tr>
<tr>
<td>Treatment time in ICU (days)</td>
<td>15±12</td>
<td>12±9</td>
<td>0.19</td>
</tr>
</tbody>
</table>
transplantation. In the first case we observed a functional recovery from the first dose with no notable adverse effects up today, as in the post-transplant patient, maintaining a good control of TMA despite more spaced dosing (8 weeks). The inclusion of this drug in the therapeutic arsenal opens a new safe treatment route in pediatric patients with HUSAs.

**Table 1:**

<table>
<thead>
<tr>
<th>ESKD Cause</th>
<th>Number</th>
<th>Females (N; %)</th>
<th>Males (N; %)</th>
<th>Age (SD)</th>
<th>Biopsy (N; %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>885</td>
<td>389 (44.0)</td>
<td>496 (56.0)</td>
<td>12 (3.0)</td>
<td>461 (52.1)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>327</td>
<td>120 (36.7)</td>
<td>207 (63.3)</td>
<td>13.0 (2.3)</td>
<td>316 (96.6)</td>
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<td>113 (50.4)</td>
<td>1.2 (2.7)</td>
<td>4 (1.8)</td>
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<td>AKUT</td>
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<td>85 (65.4)</td>
<td>9.4 (3.2)</td>
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<td>40 (62.5)</td>
<td>24 (37.5)</td>
<td>10.1 (3.3)</td>
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<td>12 (29.3)</td>
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<td>11.6 (2.6)</td>
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<td>3 (37.5)</td>
<td>5 (62.5)</td>
<td>11.4 (2.2)</td>
<td>1 (12.5)</td>
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**RAVULIZUMAB "DE NOVO" IN PEDIATRIC PATIENTS WITH ATYPICAL HEMOLITIC UREMIC SYNDROME: FIRST WORLDWIDE CASES**

Pedro Arango Sancho 1, Osmar David Gonzalez 2, Ana Cristina Aguilar Rodriguez 1, Marta Jiménez Moreno 1, Elena Codina Sampera 1, Bernat Gómez Herrera 2, Raquel Jiménez García 1, Yolanda Calzada Baños 1, Verónica Coll Brito 3 and Álvaro Madrid Aris 4

1 Hospital Sant Joan de Déu, Pediatric Nephrolgist, Barcelona (Esplugues de Llobregat), Spain, 2 Pontificia Universidad Católica de Chile, Pediatric Nephrology, Santiago de Chile (Región Metropolitana), Chile and 3 Fundación Puigvert, Nephrology, Barcelona, Spain

**Background and Aims:** Ravalizumab is a long-acting C5 inhibitor that has recently demonstrated its effectiveness in adult and pediatric patients for the control of hemolytic uremic syndrome compared to eculizumab, allowing average annual infusion times of up to 70% less. There is still little evidence in the literature of naïve treatment with this drug in pediatrics.

**Method:** We present the first two pediatric cases worldwide with the use of de novo Ravalizumab: the first one in the onset of the disease and the second one, post-kidney transplant.

**Results:** 13-year-old girl referred from another country with 1 week history of acute gastroenteritis with bloody stools, vomitting and compromise of consciousness. Deterioration of general condition, with laboratory tests compatible with thrombotic microangiopathy (TMA), evolves to anuria and convulsive episode requiring invasive mechanical ventilation, corticosteroid boluses, 6 plasmapheresis sessions and 4 intermittent hemodialysis. One Eculizumab dose (600 mg) was administered in the center of origin and STEC was isolated. At admission presented compromised renal function (AKI III), hemolytic anemia, thrombocytopenia, normal ADAMTS-13, negative direct Coombs and decreased complement. Brain MRI study shows images compatible with multiple foci of necrosis. Due to the persistent requirement of renal replacement therapy and persistent TMA, Ravalizumab was started with a loading dose (2400 mg) and a second dose after 2 weeks. The need for renal replacement therapy ceased with improvement of hemolysis and renal function. Genetic study showed mutation of uncertain significance in heterozygosis in exon 6 (c.881_883 p.Ala292del) with risk polymorphism for HUSAs (deletion CFHR3-CFHR1).

**Case 2:** 7-year-old girl (stage 5 CKD) in chronic hemodialysis 3 times/week secondary to aHUS (CD46 mutation) was admitted for kidney transplant from a living donor (father), performing hemodialysis session before surgical intervention. Low-intermediate immunological risk (PRA 0%, 9 HLA matches) and high CMV infectious risk (valganciclovir prophylaxis). Induction treatment: Basiliximab, tacrolimus, mycophenolate and steroids. First dose of Ravalizumab was infused the day before transplantation (900mg), well tolerated. 36 hours after presented acute pulmonary edema as well as a drop in hemoglobin (4g/dL). With normal laboratory hemolysis parameters, urgent abdominal-pelvic CT was performed due to suspicion of bleeding, confirming an active bleeding. Surgical reintervention was decided due to uterine bleeding and the tunnel was redone with good results. The patient has had a favorable evolution of renal function, with a normal value of creatinine at discharge (0.43 mg/dL). Protein/Creatinine urine ratio (iPr/Cr) increases to a maximum of 8 mg/mg. Negative DSA levels but the option of renal biopsy was assessed and ruled out due to a decrease in proteinuria (iPr/Cr 0.51 mg/mg). She received second dose of ravalizumab after 2 weeks, remain stable with no data on recurrence of the underlying disease today.

**Conclusion:** In the two patients, the initial treatment with Ravalizumab was satisfactory, both in the acute phase of the disease and in the immediate post-

**ACUTE KIDNEY INJURY IN PATIENTS WITH VENTRICULAR SEPTAL RUPTURE: A SINGLE CENTER STUDY**

Rajeevalochana Parthasarathy, Anu Jacob, Deepak Selvanathan and Veena S

The Madras Medical Mission Hospital, Chennai, India

**Background and Aims:** Ventricular septal rupture (VSR) is an infrequent but dreaded complication of acute myocardial infarction (AMI). Acute kidney injury (AKI) is one of the major determinants of morbidity and mortality in these patients. Renal replacement therapy (RRT) is, in this set of patients of high-risk nature and can be prolonged. Focused data on the management of AKI in patients with VSR from developing countries is scarce. We present a large cohort of patients presenting with VSR from a tertiary care Centre in South India, evaluating the incidence of AKI, RRT and short-term outcomes in this cohort.

**Method:** Observational study of all adult patients diagnosed with VSR following AMI over 5 years in a single centre in Chennai, India. Demographic characteristics, co-morbidities, clinical and laboratory; Serial renal function tests and urine output was noted. eGFR was calculated using the CKD-EPI formula. AKI definition and staging- KDIGO clinical Practice Guidelines. Data analysis was done using the IBM SPSS version 24. P-value less than 0.05 is used to indicate statistical significance.

**Results:** During the study period, 3024 patients presented to our hospital with acute coronary syndrome (ACS) and seventy patients presented with VSR (2.3%). Of these, forty-seven (67.1%) developed AKI. A nephrology consult was obtained for thirty-three (70%) patients. Older age, higher total count and lower systolic blood pressure were significantly associated with the occurrence of AKI. The mortality in the AKI group was significantly higher (63.8%). VSR closure was done in 12.7% and 21.7% of the AKI and non-AKI groups respectively. Surgical VSR repair was done in 61.7% and 60.8% of the patients with and without AKI respectively. Most of the patients (26, 53.3%) presented with KDIGO stage 3 AKI and all were oliguric. 10 and 11 patients were staged into KDIGO stages 1 and 2 respectively. 26 patients with Stage 3 AKI, only 14 (29.7%) of them received nephrology consult. RRT was initiated in fifteen patients (31.9%). The indications for RRT were oliguria, pulmonary oedema, metabolic acidosis, and worsening electrolyte disturbance. Acute peritoneal dialysis was initiated in 11 patients (73.3%) using a 43cm swan neck double cuffed tunnelled Tenckhoff peritoneal dialysis catheter placed at the bedside. Perventricular peritoneal dialysis catheter insertion by a nephrologist was done in and the rest was inserted by open laparotomy technique by a trained general surgeon. All 11 were initiated on urgent low volume supine exchanges. Of these ten patients had manual exchanges done by a trained peritoneal dialysis nurse and one patient was put on automated peritoneal dialysis. The average volume per dwell was 500 ml±250 ml which was gradually increased if there was no leak. The total average peritoneal dialysis volume per day was 101±42 L. The strength of bags (1.36%, 2.25%, 3.86%) dextrose was determined based on volume status and patients’ hemodynamics. No patient had a leak or peritoneal dialysis-related peritonitis. All patients’ peritoneal dialysis catheter was immobilized with a tight abdominal dressing. One patient continued continuous ambulatory peritoneal dialysis at home as there was no recovery of renal function and was lost to follow up. Sustained low-efficiency
dialysis was performed on four patients. Duration of Sustained low-efficiency dialysis ranged from 6-8 hours with average blood flows of 150 ml/min and average fluid removal between 1.5-3L. Unfractionated heparin was used in three patients, and one was heparin free saline dialysis. Discharge eGFR in the AKI group was significantly lower as compared to the non-AKI group. (38 vs 104ml/min/1.73m², p<0.001). Follow up was done on 14 at 3 months. The mean eGFR was 57.8ml/min/1.73 m² when compared to 81.8 ml/min/1.73 m².

**Conclusion:** The incidence of AKI is high and is associated with a high rate of mortality in patients with VSK. Peritoneal dialysis is a safe and effective option for those patients requiring RRT. Follow up of AKI patients at three months did not show a significant decline in renal function

#6070

**PREDICTIVE MODEL OF OBSTETRIC ACUTE RENAL FAILURE IN THE INTENSIVE CARE UNIT**

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¹CHU Ibn Rochd, Anesthésie-Réanimation, Casablanca, Morocco and ²CHU Ibn Rochd, Anesthésie-Réanimation, Casablanca, Morocco

**Background and Aims:** Obstetric acute renal failure (OARF) remains a frequent and serious complication that engages the maternal and fetal prognosis. The objective of our work is to develop a predictive model of obstetric acute renal failure in the intensive care setting.

**Method:** To meet our objective we conducted a retrospective comparative and analytical study spread over a period of 7 years, from January 2014 to September 2021 within the obstetric resuscitation department of ABDERAHIM HAROUCHI hospital of CHU Ibn Rochd of Casablanca. We have thus distinguished two groups of parturients:

- Group 1 “OARF +” : parturients with ARF (n = 863)
- Group 2 “OARF -” : parturients without ARF (n = 1856)

**Results:** During this period 2719 obstetric admissions in intensive care were collected including 863 cases of ARF that we classified according to the KDIGO classification with a percentage of stages I, II and III respectively of 45.2%, 28.5% and 25.3% of cases. The average age of our OARF+ sample was 28.6±5.4 years. 40% of the parturients in this group were primiparous and 60% were multiparous, with the majority of cases occurring between 20 and 28 weeks' gestation (32%). OARF was associated with pre-eclampsia in 57% of cases, hemorrhagic shock in 37.19% of cases and severe sepsis in 31.74% of cases. Extra renal purification was necessary in 148 parturients (17.2%) and the mortality rate in the OARF+ group was 26.18%.

In univariate analysis, the clinico-biological risk factors for the occurrence of obstetric ARF were haemostasis disorders (p < 0.001), hypertension (p < 0.001), oligo-anuria (p = 0.002), severe anaemia (p < 0.001) and thrombocytopenia (p < 0.001). As for the etiological factors, our analysis allowed us to retain pre-eclampsia (p < 0.001), hemorrhagic shock (p < 0.001), sepsis (p < 0.001),HELLP Syndrome (p = 0.002) and DIC (p = 0.002).

**Conclusion:** Pre-eclampsia, pre- and postpartum hemorrhage, and sepsis represent the main etiologies of obstetric ARF, which is a frequent obstetric complication in the ICU setting and responsible for significant maternal morbidity and mortality. The determination of the risk factors for the occurrence of such a complication allowed us to detect and prevent the patients at risk.

#3644

**CLINICAL VALUE OF SOLUBLE UROKINASE-TYPE PLASMINOGEN ACTIVATOR RECEPTOR IN DIAGNOSIS AND PROGNOSIS OF SEPSIS-ASSOCIATED ACUTE KIDNEY INJURY**

Yue Gu, Wenwen Zhang and Jing Zhou

Henan Provincial People's Hospital;Zhengzhou University People's Hospital; Henan University People's Hospital, Department of Nephrology; Henan Provincial Clinical Research Center for Kidney Disease, Henan Provincial Key Laboratory of Kidney Disease and Immunology, Zhengzhou, P.R. China

**Background and Aims:** Acute kidney injury (AKI) is a common complication of hospitalized adults with increased risk of chronic kidney disease and end-stage kidney disease. Sepsis is the most common reason of AKI in patients admitted in intensive care unit(ICU) with the incidence over 50%. Soluble urokinase-type plasminogen activator receptor (suPAR) is an important immune mediator involved in kidney injury. Numerous studies have shown that the suPAR is associated with a variety of kidney diseases.However, it remains unknown on the diagnosis and prognosis value of suPAR in sepsis-associated acute kidney injury (S-AKI). Hence, this study aimed to explore the diagnostic value for the prediction of S-AKI courses and 28-day death.

**Method:** In this prospective study, adult patients with sepsis admitted to the ICU of Henan people's Hospital from December 2020 to February 2022 were enrolled. Plasma suPAR levels at 0, 12, 24 and 48 hours after admission to ICU were measured by enzyme-linked immunosorbent assay. We assessed the development of S-AKI as the primary outcome and the occurrence of death within 28 days in patients who had S-AKI as a secondary outcome. The prediction of the suPAR level on S-AKI and death was tested using receiver operating characteristic curve (ROC) analysis, by calculating the area under the curve (AUC), and 95% confidence interval (CI).

**Results:** Of the 182 sepsis patients, 66 (36.3%) developed AKI during hospitalization, of whom 31 (46.9%) died. At 12, 24 and 48 hours after admission to ICU, the plasma suPAR level was significantly higher in patients with S-AKI than in patients without AKI (P<0.05). (Figure 1) In sepsis patients dead with 28 days after admission in ICU, the plasma suPAR level was significantly higher at 0 and 48 hours after admission in ICU compared to the survival patients (P<0.05). (Figure 1) Diagnostic performance of plasma suPAR level improved over time with the highest area under the receiver operating characteristic curve of 0.701 (95% CI, 0.623–0.779) 24 hours after study inclusion. Additionally, plasma suPAR levels at 0h have the highest area under the receiver operating characteristic curve of 0.647 (95% CI, 0.512–0.782) in predicting 28-day death. The best discrimination ability for the S-AKI was achieved for suPAR 24 hours after inclusion by applying a cutoff value of greater than or equal to 3.11 ng/mL (sensitivity 62.1, specificity 71.6). The suPAR at 0h after inclusion performed best in discriminating 28-day death by using a cutoff value of greater than or equal to 4.57 ng/mL (sensitivity 87.1, specificity 51.4).

**Conclusion:** Plasma suPAR level can be a potential biomarker for early diagnosis of S-AKI and has a certain clinical value in predicting the short-term death of S-AKI. However, further clinical studies with larger sample size is needed.
Figure 1: Comparison of suPAR levels between the S-AKI vs non-AKI groups and the survival vs death groups at 0, 12, 24 and 48 hours after admission to ICU.

Table 1: The receiver operating characteristic analysis for predicting S-AKI and death based on the suPAR level.

<table>
<thead>
<tr>
<th>Time after admission to the ICU</th>
<th>Predict S-AKI</th>
<th>Predict death</th>
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<tr>
<td></td>
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<td>Death</td>
</tr>
<tr>
<td></td>
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<td>66</td>
</tr>
<tr>
<td></td>
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#5001
AKI AND AKD AFTER RADICAL CYSTECTOMY FOR MUSCLE INVASIVE BLADDER CANCER: AN UNEXPECTED NEPHROLOGICAL AFFAIR

Francesco Trevisani¹, Mattia Longoni¹, Alessandra Cinque², Giuseppe Rosiello³, Marco Malvestiti³, Andrea Salonia¹, Alberto Briganti¹, Francesco Montorsi¹, Marco Moschini¹ and Matteo Floris³

¹IRCCS San Raffaele Scientific Institute, Department of Urology and Division of Experimental Oncology, Milan, Italy, ²Bièrek srl, Milan, Italy and ³San Michele Hospital, ARNAS G. Brotsu, Department of Medical Science and Public Health, Cagliari, Italy

Background and Aims: Radical cystectomy (RC) represents the first line surgical treatment for muscle-invasive bladder cancer (MIBC). RC is a complex surgical procedure characterized by significant morbidity and mortality. The incidence of significant complications following RC is a well-recognized issue however still paucity of data exists regarding postoperative renal function. Aim of the study was to evaluate the incidence of acute kidney injury (AKI) and Acute kidney disease (AKD) after RC, evaluating the impact of surgery (open or robotic one), comorbidities (hypertension, diabetes, CAD) and previous oncological treatments (chemotherapy, immunotherapy and radiotherapy).

Method: We collected a consecutive cohort of 839 patients who underwent RC for MIBC in a single tertiary institution between 2010 and 2022. All clinical variables and comorbidities were reported pre and after surgery. Serum creatinine with subsequently eGFR using CKD-EPI formula were collected at baseline pre-operative and in the acute setting at 24h, 48, 72h, 6 days for the AKI onset, and after 9, 12, 15, 18, 21, 24, 27, 30, 45, 60, 75, 90 days for the AKD establishment. We compared the incidence of AKI and AKD upon the two different surgical approaches for RC: the open and robotic one. Fisher’s exact test; Wilcoxon rank sum test; Pearson’s Chi-squared test were used for the statistical analyses.

Results: General characteristics of patients included in the study are summarized in Table 1. Surprisingly, a very high rate of both AKI (30%) and AKD (50%) was reported in the total cohort of patients, with an augmented incidence in the robotic surgery (p < 0.001). Moreover, stage II and III of both AKI and AKD affected a non-negligible percentage of patients, requiring advanced nephrological medical treatments and prolonged hospitalization (Table 1). The multivariate analysis showed that age, blood hypertension and BMI represent the major risk factors to develop both AKI and AKD (Table 3 and Figure 1).

Conclusion: AKI and AKD are very frequent and insidious side effects in the RC for MIBC. Therefore, a personalized nephrological counseling both in the pre and post -surgery asset is mandatory to reduce morbidity and mortality.
URINARY DCR2/Cr LEVEL PREDICTS RENAL OUTCOME IN PATIENTS WITH ACUTE KIDNEY INJURY
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Background and Aims: Acute kidney injury (AKI) is a well-recognized complication of critical illness which increases the risk of morbidity and mortality. It has been reported that about 30% of AKI patients developed to chronic kidney disease (CKD), and even to end-stage renal disease (ESRD). It is urgent to explore novel biomarkers to evaluation the renal outcome of AKI. Decoy receptor 2 (Dcr2), a senescent marker, is expressed specifically in senescent tubular epithelia. And urinary Dcr2 (uDcr2) is associated with renal fibrosis in chronic kidney disease. The aim of study is to investigate the association of urine Dcr2 with renal outcome of AKI.

Method: 153 biopsy-proven AKI patients were included from Daping Hospital, Army Medical University from January 2018 to October 2022. A composite renal endpoint included creatinine more than 50% higher than the baseline or ESRD after 90 days. All patients were divided into positive endpoints (n = 75) and negative endpoints (n = 78). The clinical characteristics were collected, and the pathological injury was scored. uDcr2 levels were measured using enzyme-linked immunosorbent assay and normalized to urinary cre (uDcr2/Cr). The correlation of uDcr2/Cr levels with renal function and renal pathological scores were analyzed. The logistic regression analysis was used to investigate the association of uDcr2/Cr with renal outcome of AKI.

Results: The level of uDcr2/Cr was positively correlated with cystatin C, and negatively correlated with estimated glomerular filtration rate (eGFR). And uDcr2/Cr was positively associated with renal pathological acute scores. Univariate logistic regression results increase the risk factors for poor kidney prognosis are age, female, with hypertension or (and) CKD, eGFR, Cystine C and uDcr2/Cr. Multivariate logistic regression analysis showed that the effect of uDcr2/Cr on renal outcome was statistically significant. After a median follow-up of 16 months, 75 participants achieve endpoint and there were 16 patients with end-stage renal disease. The ROC curve was used to analyze the value of uDcr2/Cr for predicting kidney prognosis in AKI with an area under the curve of 0.72 and the cut-off value of 365ng/g Cr. The median time from at the time of AKI to endpoint in the uDcr2/Cr ≥ 365ng/g Cr group (7.6 months) was significantly shorter compared to the uDcr2/Cr < 365ng/g Cr group (36.6 months).

Conclusion: Urinary Dcr2/Cr is closely associated to kidney injury and renal prognosis of AKI, suggesting that uDcr2/Cr could sever as a novel biomarker for predicting adverse outcomes in patients with AKI.

ROLE OF STATINS IN THE CONTRAST-INDUCED ACUTE KIDNEY INJURY PREVENTION AFTER COMPUTED TOMOGRAPHY WITH CONTRAST MEDIA
Andrey Vasin, Elham Pahlevani, Valentina Biryukova, Olga Mironova and Victor Fomin
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Background and Aims: Contrast-induced acute kidney injury (CI-AKI) is a serious complication of the use of iodinated contrast media (CM). A number of researches have shown that statins have a protective role in the prevention of CI-AKI due to their pleiotropic effects. The aim of the study was to assess the influence of statins on the incidence of CI-AKI after intravenous CM administration.

Method: A randomized controlled open-label prospective study was conducted. Statin naive patients with cardiovascular diseases referred for contrast-enhanced computed tomography (CT) were included. Exclusion criteria were the use of statins and chronic kidney disease (CKD) stages 4-5. Acute kidney injury was defined as an increase in serum creatinine level by more than 44 μmol/L (0.5 mg/dL) or 25% from baseline within 48 hours after CM administration according to KDIGO guidelines. Glomerular filtration rate was calculated using the CKD-EPI formula. Overall, 181 patients were included in the study and divided into two groups. The first group (120 people) received high doses of atorvastatin (80mg or 40mg) 24 hours after and before the CM administration, while the second group (61 people), the control group, did not receive any statin therapy. Low-osmolar solutions in an amount of 100 ml were used. All patients were given intravenous hydration with saline before the study and 24 hours later. The statistical analysis was done using IBM SPSS Statistics v26.0.
Results: The patients in both groups did not significantly differ in age, BMI, coexisting conditions, and medications taken (Table 1). Both groups showed an increase in average creatinine levels after CT with intravenous contrast media. Table 2 shows an increase in average creatinine levels after CT with intravenous contrast media. In 12 individuals (6.7%), 9 of them were in the control group, and 3 were in the Statin group. The average level increased less, p = 0.06. The chances of AKI development in the group receiving high doses of statins were 6.95 times higher compared to the control group (OR = 6.95, 95% CI: 1.7-21.5). Most of the patients with preserved kidney function in the Statin group did not suffer from diabetes mellitus. There were statistically more significantly patients with preserved kidney function in the Statin group, p = 0.007, OR: 2.374 (CI 95% 1.258 - 4.479), and fewer patients with CKD 3a stage, p = 0.05, OR: 0.406 (CI 95% 0.195 – 0.844).

Conclusion: Despite the presence of patients at risk, the incidence of CI-AKI was 6.7%, possibly due to additional prevention of this complication with intravenous saline before and after administration of the CM. In this trial, we observed that periprocedural administration of atorvastatin in high doses for a short duration, reduced the incidence of CI-AKI.

#3436

Efficacy of Adjunct Hemoperfusion Versus Standard Medical Therapy on 28-Day Mortality in Leptospirosis Patients with Renal Failure and Shock

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National Kidney and Transplant Institute, Adult Nephrology, Quezon City, The Philippines

Background and Aims: Leptospirosis, a ubiquitous zoonotic infection in the Philippines, is a classic representation of sepsis-induced multi-organ dysfunction with its life-threatening complications: pulmonary hemorrhage, renal and liver failure. Despite pre-established treatment guidelines, leptospirosis-induced morbidity and mortality continue to rise. Hemoperfusion with HA 330 is a promising adjunct therapy as it removes rogue cytokines responsible for the dysregulated inflammatory response in severe sepsis. However, studies on its survival benefit have yielded conflicting results, so far. This study was designed to assess the efficacy and safety of hemoperfusion among leptospirosis patients in septic shock and renal failure, in terms of improvement in 28-day mortality, SOFA score, level of inflammatory markers, hemodynamics, renal and pulmonary function.

Method: This is an open-label randomized controlled trial which enrolled a total of 37 adult presumptive leptospirosis patients with early signs of septic shock and acute renal failure. The study participants were randomized into either of the two treatment arms: 1. standard medical therapy (SMT) alone or 2. SMT + HA330 Hemoperfusion (HP). All patients were managed based on the NKT Leptospirosis treatment protocol (hydration, antibiotics, three-day steroid pulsing, single cyclophosphamide dose and respective organ support) and were placed on daily intermittent hemodialysis. Subjects randomized to the HP group received three hemoperfusion sessions (on top of SMT). Vital signs, urine output, vasopressor dose, P/F ratio and biochemical parameters (including level of inflammatory markers) of patients from each treatment arm were measured at baseline, day 3 and day 7 and compared subsequently. Monitoring of participants continued until 28 days post-randomization. Descriptive statistics was used to summarize the general and clinical characteristics of the participants. Independent Sample T-test, Mann-Whitney U test, and Fisher's Exact/Chi-square test was used to determine the difference of mean, median and frequency between hemoperfusion group and control group, respectively. Mean, median, or risk difference and their corresponding 95% confidence intervals were calculated. Friedman test or Kruskal-Wallis test was used to determine whether differences between groups were significant over time. Intention to treat and per protocol analyses were performed. Null hypothesis was rejected at 0.05alpha-level of significance. Stata 15.0 (StataCorp LLC, TX) was used for data analysis.

Results: Hemoperfusion conferred a 36.84% (p = 0.017) risk reduction in 28-day mortality. Serial monitoring of inflammatory markers and SOFA score of patients showed significant improvement in sepsis score (p = 0.018 HP, 0.002 SMT) and levels of procalcitonin (p = 0.013 HP, 0.003 SMT), IL6 (p = 0.033 HP, 0.020 SMT) and lactate (p < 0.001 HP, 0.021 SMT) in both treatment arms, from baseline to Day 7. There is, however, no statistically significant difference in the change in SOFA (p = 0.965) and inflammatory marker levels if we compare HP versus SMT (p = 0.997, 0.451, 0.858, 0.052 for hsCRP, procalcitonin, IL6 and lactate, respectively). Statistically significant improvement in serum creatinine (p = 0.04) and PF ratio (p = 0.045) were observed in the hemoperfusion cohort as early as Day 3. Vasopressor dose did not differ significantly between two groups (p = 0.792). No adverse events were observed in both treatment arms.

Conclusion: Hemoperfusion is a safe and effective adjunct therapy in managing severe sepsis. It promotes earlier renal and pulmonary function recovery and, in doing so, improves survival of septic shock patients.
#3652

ACUTE KIDNEY INJURY (AKI) IN CANCER PATIENTS TREATED WITH COMBO THERAPIES: CHEMOTHERAPY, OR IMMUNOTHERAPY, THAT IS THE QUESTION

Marta Pirovano1, Giulia Vanessa Re Sarto1, Nico La Verde2, Annalisa Bramati2, Laura Cosmai1 and Maurizio Gallieni1,3

1 ASST Fatebenefratelli Sacco, Nephrology and Dialysis, Milan, Italy, 2 ASST Fatebenefratelli Sacco, Clinical Oncology, Milan, Italy and 3 University of Milan, Department of Biomedical and Clinical Sciences, Milan, Italy

Background and Aims: Lung cancer is the second most common malignancy in men and the third in women and approximately 85% of all cases are constituted by non-small cell carcinoma (NSCLC). In recent years, the introduction of immune checkpoint inhibitors and molecular targeted therapies, as monotherapy or in association with chemotherapy, has revolutionized the treatment of NSCLC. Pembrolizumab in association with pemetrexed and carboplatin, for instance, has been approved as first-line treatment for non-squamous NSCLC. Nephrotoxic side effects of both old and new therapies continue to be a substantial adverse event (AE) and could preclude effective oncological treatment. When a patient in combined oncological therapy develops AKI it is not always easy to establish which drug is responsible of the AE. The objective of our study was to develop a diagnostic algorithm to help the clinician to diagnose and manage AKI in patients treated with pembrolizumab + pemetrexed +/- carboplatin.

Method: We performed a retrospective multicentric data collection. We analyzed data about all the patients referred to the onconephrology outpatient clinic due to AKI (Stage 2 or higher) during oncological treatment with pembrolizumab + pemetrexed +/- carboplatin, from 2020 to 2022.

AKI stages were identified according to KDIGO guidelines and CTCAE 5.0. We focused on the following data: chemical-physical urinalysis, urinary electrolytes, serum electrolytes, kidney function (AKI progression and trend of renal function after oncological drug discontinuation).

Results: A cohort of 89 patients was analyzed: 54 males (61%) and 35 females (39%), with an average age of 69 years (51-76). The main comorbidities were hypertension (76%), diabetes mellitus (36%), CKD (64%) and cardiovascular diseases (26%). Overall, 11 patients (12%) had a non drug-related AKI, 90% of which due to pre-renal causes. 43 patients developed immune-related AKI; among these 23 pts had sterile pyuria and/or WBC casts, 35 pts had other organ IrAEs, 32 pts had AKI progression upon discontinuation of oncological therapy, and 37 pts had an increase in serum creatinine ≥ 1 mg/dl between two consecutive pretherapy blood tests.Chemotherapy-induced nephrotoxicity occurred in 35 patients and had the following features: hypo K or hypo Mg in 9 pts, increased urinary electrolytes in 16 pts, stable renal function after oncological drugs discontinuation in 32 pts and an increase in serum creatinine ≤ 0,5 mg/dl between two consecutive pretherapy blood tests in 27 pts. Characteristics of drug-related AKI are summarized in Table 1.

Conclusion: One of the main challenges with patients on multiple cancer therapies who develop AKI is to identify the possible drug responsible for the nephrotoxicity to avoid unnecessary suspension of one or more oncological drugs. Although the most frequently suggested approach is the execution of the renal biopsy, it is not always possible to perform it in a short time due to difficulties in organizing the diagnostic procedure and the time necessary for the histological analysis. Furthermore, Oncological Guideline recommend starting steroid therapy as soon as the Grade ≥2 immune related AEs develop. The above retrospective results shed light on the main characteristic of AKI due to immunotherapy or chemotherapy; the information obtained helped us to develop a diagnostic algorithm that addresses the clinician in identifying with reasonable certainty the cause of AKI without the need to perform a renal biopsy (Figure 1).

<table>
<thead>
<tr>
<th>Immune-related AKI</th>
<th>Chemotherapy related AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients 43 (48%)</td>
<td>35 (40%)</td>
</tr>
<tr>
<td>Sterile pyuria and/or WBC casts 23 (53%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other IrAEs 35 (82%)</td>
<td>10 (30%)</td>
</tr>
<tr>
<td>Worsening of renal function upon discontinuation of oncological therapy 32 (74%)</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Increase in serum creatinine ≥ 1 mg/dl between two consecutive pretherapy blood tests 37 (86%)</td>
<td>6 (17%)</td>
</tr>
<tr>
<td>Hypo K or Hypo Mg 1 (2%)</td>
<td>9 (25%)</td>
</tr>
<tr>
<td>Increased urinary electrolytes 0 (0%)</td>
<td>16 (46%)</td>
</tr>
<tr>
<td>Not worsening of renal function after oncological drugs discontinuation 11 (26%)</td>
<td>32 (91%)</td>
</tr>
<tr>
<td>Increase in serum creatinine ≤ 0,5 mg/dl between two consecutive pretherapy blood tests 0 (0%)</td>
<td>27 (77%)</td>
</tr>
</tbody>
</table>
Figure 1: Algorithm for AKI.

KIM-1, IL-18 AND NGAL IN MACHINE LEARNING PREDICTION OF KIDNEY INJURY AMONG CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background and Aims: Children undergoing allogeneic hematopoietic stem cell transplantation (alloHSCT) are particularly vulnerable to acute kidney injury (AKI), especially in the early post-transplantation period. The major risk factors of AKI development are aggressive immunosuppression and infectious complications. In the meantime, malnutrition and hypermetabolic state of the patient, together with the routine intensive hydration during first 3 weeks after HSCT and subsequent forced diuresis, alter the serum creatinine concentration, modifying the estimated glomerular filtration rate (eGFR) value too. Therefore, the risk of underrating serum creatinine and overrating eGFR values is high, making the assessment of the degree of kidney damage during the first month after HSCT a challenge. Therefore, markers of tubular dysfunction and damage, like kidney injury molecule (KIM)-1, neutrophil gelatinase-associated lipocalin (NGAL) or interleukin (IL)-18, may be of added value while assessing renal function and analyzing the risk of AKI in this population. The aim of study was to assess the serum concentrations of damage biomarkers (KIM-1, NGAL, IL-18) in children undergoing alloHSCT, in relation to another surrogate marker of renal dysfunction, hyperfiltration. Another aim was to analyze the potential value of KIM-1, NGAL, and IL-18 as predictors of kidney damage in children after alloHSCT, with the use of artificial intelligence tools.

Method: The study group contained 22 children undergoing alloHSCT, followed up for 4 weeks after transplantation. Serum concentrations of KIM-1, NGAL, and IL-18 were assessed by ELISA in fixed time points (before HSCT, 1 day after HSCT, 1, 2, 3, 4 weeks after transplantation). eGFR values (counted based on Schwartz formula) and the rate of hyperfiltration (eGFR > 140ml/min/1.73sq.m.) were evaluated at the beginning (before HSCT) and at the end (4 weeks after HSCT) of observation, when neither hydration nor diuretics were used. Statistical analysis was performed with the use of package Statistica, the comparisons between paired data were evaluated by using nonparametric tests (Friedman, Wilcoxon). Additionally, the patients within the database were randomly divided into two groups. The training group allowed to build a Random Forest Classifier (RFC) with the highest possible predictive power, while the testing group allowed to assess the effectiveness of prediction on new data and the clinical utility. Moreover, the contribution of individual variables was evaluated by GINI importance.

Results: KIM-1, NGAL, and IL-18 serum concentrations increased systematically until the 3rd week after HSCT, with statistically significant differences between subsequent observation points, then remained elevated until the 4th week after HSCT. Median eGFR values before transplantation and 4 weeks after HSCT were comparable, although the rate of patients with hyperfiltration increased. The RFC model built on the basis of 3 input variables, KIM-1, NGAL, and IL-18 concentrations in serum of children before HSCT, was able to effectively assess the rate of patients with hyperfiltration 4 weeks after the procedure. RF Classifier achieved AUROC of 0.8333, accuracy of 80.00%, positive predictive value of 0.8667, and sensitivity of 0.8000. The contribution of KIM-1, IL-18 and NGAL to the prediction in this model was comparable (33.73%, 32.77%, and 33.5%, respectively).

Conclusion: KIM-1, NGAL, and IL-18 are useful in assessing acute tubular damage in children after HSCT. Their values before HSCT may also serve as markers of incipient renal dysfunction 4 weeks after alloHSCT. The developed model seems a clinically useful tool to target patients who are at risk of kidney injury after HSCT. The Random Forest Classifier seems a promising tool for such analysis, that should be tested on a larger group of patients.

EXTRACORPOREAL BLOOD PURIFICATION DURING OPEN HEART SURGERY WITH PROLONGED CPB: CYTOSORB 300 VS JAFRON HA330

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National Research Cardiac Surgery Center, Astana, Kazakhstan

Background and Aims: Cardiac surgery is maintained by various complications. Major contribution associated with cardiopulmonary bypass (CPB).
Cardiac surgery with CPB provokes activation of the cascade mechanism of inflammation with releasing of cytokines and a systemic inflammatory response syndrome (SIRS). Activation of the contact system due to exposure of artificial surface of the bypass circuit to blood cells, endotoxemia, ischemia and reperfusion injury and surgical trauma are all potential triggers of inflammation following CPB. This inflammatory reaction may lead to the development of postoperative complications, including vasoplegia, cytokine storm, myocardial dysfunction, respiratory failure, acute kidney injury, and reperfusion injury and surgical trauma are all potential triggers of inflammation following CPB. This inflammatory reaction may lead to the development of postoperative complications, including vasoplegia, cytokine storm, myocardial dysfunction, respiratory failure, acute kidney injury, coagulopathy bleeding, and multiple organ dysfunction syndrome (MODS).

A number of different strategies, including new pharmacologic agents, CPB circuits and components, and surgical techniques, have been employed during the last few years in attempts to minimize the impact of SIRS on the outcome of cardiac surgical patients. However, the complex pathophysiology of this problem has not allowed, until now, the use of a single strategy. The aim of our study is assessment of early application of extracorporeal cytokine adsorbers to the inflammation system during open-heart surgery with prolonged cardiopulmonary bypass.

Method: This prospective randomized single-center controlled trial observed this prospective randomized single-center controlled trial observed this prospective randomized single-center controlled trial observed this prospective randomized single-center controlled trial observed this prospective randomized single-center controlled trial observed this prospective randomized single-center controlled trial observed this prospective randomized single-center controlled trial observed.

Results: The data of the HA 330 (n = 22) and CytoSorb300 (n = 22) groups were compared with the data of the control group (n = 22). The primary results and details of the work are given in Tables 1-3.

Conclusion: Intraoperative hemadsorption may be beneficial for patients who underwent open-heart surgery with prolonged CPB. The early hemadsorption has positive impact to postoperative period after cardiac surgery and may reduce requirement of renal replacement therapy.
of selective extracorporeal elimination can prevent the development of irreversible renal failure and make it possible to carry out adequate antitumor therapy.

#6030 CARDIAC ULTRASOUND ASSESSMENT AND THE NOVEL INFLAMMATION, FIBROSIS AND CALCIFICATION BIOMARKERS IN ESKD PATIENTS ON HD THERAPY: A PILOT STUDY

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Background and Aims: Novel biomarkers for inflammation, fibrosis, and vascular calcification have been recently used for further assessment of cardiovascular risk. The aim of our prospective study is to assess the relation between the novel cardiovascular biomarkers and biomarkers for vascular calcification with cardiac ultrasound function/morphology alteration in high cardiovascular risk patients with end stage kidney disease (ESKD) on haemodialysis (HD) therapy. Baseline findings are discussed in this pilot paper.

Method: The study included 58 ESKD patients [55% men, mean age of 60.3 ± 11.7 years, and median hemodialysis therapy duration of 6.2 years (1.2 - 25.7)], treated with HD (3 sessions of 4 hours /week with high flux dialyzers). Personal and laboratory data have been retrieved from the patients HD files. Cardiac ultrasound assessment was performed during the second HD session of the week, after 2 hours of HD therapy. Blood samples have been taken before the same HD session in order to determine FGF 23, BMP 2, IL 1 beta, Galectin 3 and soluble ST 2 levels. All patients signed an informed consent for the study participation and the use of personal and laboratory data for scientific purposes. The study was approved by the medical ethics committee of the "Victor Babes" University of medicine and pharmacy and of the ethics committee of the HD center.

Results: On cardiac ultrasound assessment the patients presented aorta atheroma in 74.1%, aorta valve fibrosis in 74.1%, mitral valve fibrosis in 74.1% of the cases. Calcifications have been evidenced at aorta valve level in 58.6%, mitral valve level in 75.8% and endocardial valve level in 67.2% of the cases. Increased left ventricular mass was present in 82.7%, enlarged interventricular septum in 74.1% of the cases. Decreased left ventricle diastolic filling (Appleton pattern - E/A) was evidenced in 55.1% of the cases and decreased left ventricular ejection fraction in 37.9%. Right ventricle enlargement was detected in 24.1% of the patients. At baseline, FGF 23 was inversely correlated with serum albumin levels and inversely with left ventricle diastolic filling (E/A) (p < 0.05). IL1 levels were inversely correlated with iPTH (p = 0.046), calcium (p = 0.046 and phosphate (p = 0.030) levels but not with the ultrasound findings. BMP 2 levels correlated directly with serum albumin levels and inversely with left ventricle diastolic filling (E/A) (p < 0.05). IL1 levels were inversely correlated with iPTH (p = 0.046), calcium (p = 0.046 and phosphate (p = 0.030) levels but not with the ultrasound findings. Galectin 3 inversely correlated with cu Hb (p = 0.002), Urea (p = 0.036) and K levels (p = 0.001) and directly with bicarbonate (p = 0.035), FGF 23 (p < 0.05) and CRP levels (p<0.0001), ST2 inversely correlated with ESA dose (p = 0.009) and decreased left ventricle diastolic filling (E/A) (p < 0.05). At one year follow-up 12% of the patients died and mortality was significantly influenced by inter ventricle sept and right ventricle enlargement.

Conclusion: At baseline, though the investigated ESKD patients on HD therapy presented extensive cardiac valve fibrosis and heart valve and endomyocardial calcifications the investigated biomarker changes were not significantly supporting the ultrasound findings. One- and two-years follow-up results may reveal the utility of biomarker assessment for cardiovascular outcomes in HD treated ESKD patients.

#2634 ROLE OF LIGHT CHAIN CLEARANCE IN THE RECOVERY OF RENAL FUNCTION IN MULTIPLE MYELOMA: ANOTHER POINT OF VIEW

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Background and Aims: Acute Kidney Injury (AKI) in patients with multiple myeloma (MM) requiring renal replacement treatment (RRT) is associated with high morbidity and mortality. Early reduction of serum free light chains (FLC) using both targeted therapy against MM and intensive hemodialysis (IHD) may improve renal outcomes. We evaluated the effectiveness of two different RRT techniques on renal recovery in a MM patient population: standard dialysis procedure versus IHD with either PMMA or hemodiafiltration with endogenous reinfiltration (HFR).

Method: Multicentric retrospective study with severe AKI related to MM, between 2011 and 2018. Twenty-five consecutive patients with AKI secondary of MM requiring RRT were included. Patients that underwent IHD received 6 dialysis sessions per week during the first 14 days (PMMA vs HFR). All patients were diagnosed with de novo MM or first relapsed MM. Primary outcome was renal recovery defined as dialysis-free at six months follow-up.

Results: A total of 25 patients were included. Seventeen patients received IHD and standard dialysis. All patients were treated with targeted therapy. 84% bortezomib-based. Of the 25 patients included, fourteen (56%) became dialysis independent. We observed a higher proportion of patients who received IHD in the group who recovered kidney function compared to those who remained in HD (92.9% vs 36.4%, p=0.007). In our study, the use of IHD to remove FLC had a statistically significant association with renal recovery compared to standard dialysis group (p = 0.024).

Conclusion: Early reduction of FLC with IHD as an adjuvant treatment along with MM targeted therapy may exert a positive impact on renal recovery.

#4733 NEFROTOXICITY CAUSED BY COLISTIN USE: A SINGLE CENTER EXPERIENCE

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Background and Aims: In resistant infections and septic patients, the choice of colistin in the selection of antibiotic therapy is important in the treatment response. Kidney damage is common after antibiotic use. In our study, we evaluated the clinical and laboratory data of the patients who developed nephrotoxicity after the use of colistin, followed in the intensive care unit of our hospital.

Method: The clinical and laboratory characteristics and treatment results of 148 patients (54 nephrotoxic patients) with infection who were followed up in the intensive care unit (ICU) of our hospital evaluated.

Results: The group that developed nephrotoxicity was older [70.5 (40-91), p<0.001]. The APACHE II score was higher in the nephrotoxicity group [20.5 (5-49), p = 0.004]. Positive inotrope use and mortality were higher in the nephrotoxicity group [32 (59.3%), p<0.001 and 30 (55.6%), p = 0.004]. The duration of colistin use was longer in the nephrotoxicity group [13.5 (3-36), p = 0.045]. In the group that developed nephrotoxicity, the highest growth was detected in the tracheal aspirate (TAS) [49 (90.7%), p = 0.045]. Positive inotrope use and growth in TAS culture predisposed the development of nephrotoxicity in multivariate analysis [3.12 (1.38-7.02), CI 95%, p = 0.006, 5.70 (1.64-19.79), CI 95%, p = 0.006].
Background and Aims: This difference can be expressed in absolute terms (mL/min) or relative terms between the stimulated glomerular filtration rate (GFR) and the baseline GFR.

Conclusion: Consideration should be given to the use of colistin in resistant infections and septic patients in terms of nephrotoxicity and mortality. Antibiotic selection should be considered in critically ill patients, and patients should be closely monitored.

Table 1: Distribution of Demographic and Clinical Findings of the Patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (N = 148)</th>
<th>Nephrotoxicity (+) (n = 94)</th>
<th>Nephrotoxicity (-) (n = 54)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>38 (25.7)</td>
<td>24 (25.5)</td>
<td>14 (25.9)</td>
<td>1.000</td>
</tr>
<tr>
<td>Male</td>
<td>110 (74.3)</td>
<td>70 (74.5)</td>
<td>40 (74.1)</td>
<td></td>
</tr>
<tr>
<td>Age, year, median (min-max)</td>
<td>65 (21-91)</td>
<td>61 (21-89)</td>
<td>70.5 (40-91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR, median (min-max)</td>
<td>104 (70-176)</td>
<td>109 (70-176)</td>
<td>90.5 (70-168)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>APACHE-II score, median (min-max)</td>
<td>17 (2-49)</td>
<td>16 (2-43)</td>
<td>20.5 (5-49)</td>
<td>0.004</td>
</tr>
<tr>
<td>Stage-I</td>
<td>10 (18.9)</td>
<td>NA</td>
<td>10 (18.9)</td>
<td></td>
</tr>
<tr>
<td>Stage-II</td>
<td>15 (28.3)</td>
<td>NA</td>
<td>15 (28.3)</td>
<td></td>
</tr>
<tr>
<td>Stage-III</td>
<td>28 (52.8)</td>
<td>NA</td>
<td>28 (52.8)</td>
<td></td>
</tr>
<tr>
<td>Use of positive inotropes, n (%)</td>
<td>60 (40.5)</td>
<td>28 (29.8)</td>
<td>32 (59.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Alive</td>
<td>90 (60.8)</td>
<td>66 (70.2)</td>
<td>24 (44.4)</td>
<td></td>
</tr>
<tr>
<td>Exit</td>
<td>58 (39.2)</td>
<td>28 (29.8)</td>
<td>30 (55.6)</td>
<td></td>
</tr>
</tbody>
</table>


Table 2: Evaluation of Risk Factors Affecting the Development of Nephrotoxicity.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate OR (95% CI) p-value</th>
<th>Multivariate OR (95% CI) p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04 (1.02-1.07) 0.001</td>
<td>1.04 (1.01-1.07) 0.004</td>
</tr>
<tr>
<td>APACHE II</td>
<td>1.05 (1.02-1.09) 0.003</td>
<td>1.03 (0.98-1.07) 0.227</td>
</tr>
<tr>
<td>Nephrotoxic Agent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>2.26 (1.12-4.54) 0.023</td>
<td>1.97 (0.85-4.57) 0.115</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>0.58 (0.20-1.72) 0.328</td>
<td></td>
</tr>
<tr>
<td>Amphotericin</td>
<td>1.17 (0.19-7.21) 0.868</td>
<td></td>
</tr>
<tr>
<td>Use of positive inotropes</td>
<td>3.43 (1.70-6.91) &lt;0.001</td>
<td>3.12 (1.38-7.02) 0.006</td>
</tr>
<tr>
<td>Basal serum creatinine level</td>
<td>4.81 (1.22-18.99) 0.254</td>
<td>3.78 (0.76-18.89) 0.105</td>
</tr>
<tr>
<td>Usage period of colistin, day</td>
<td>1.06 (1.01-1.11) 0.046</td>
<td>1.05 (0.98-1.13) 0.148</td>
</tr>
<tr>
<td>Reproduction in TAS</td>
<td>3.00 (1.06-8.44) 0.038</td>
<td>5.70 (1.64-19.79) 0.006</td>
</tr>
</tbody>
</table>

TAS: Tracheal aspirate.

Conclusion: Consideration should be given to the use of colistin in resistant infections and septic patients in terms of nephrotoxicity and mortality. Antibiotic selection should be considered in critically ill patients, and patients should be closely monitored.

#5079
THE EVALUATION OF RENAL FUNCTIONAL RESERVE WITH ORAL PROTEIN LOAD OR ULTRASOUND TEST: A REAL-LIFE PERSPECTIVE

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Background and Aims: The RFR (renal functional reserve) is the difference between the stimulated glomerular filtration rate (GFR) and the baseline GFR. This difference can be expressed in absolute terms (mL/min) or relative terms (percentage of increment relative to the baseline GFR). This index makes it possible to highlight a subclinical renal functional deterioration when the laboratory values of creatinine are still within the normal range. Measurement of RFR by protein load (1 g/kg of oral protein) (RFR-T) is now considered the gold standard for RFR assessment. RFR measured with protein load (RFR-T) predicts the risk of acute kidney injury (AKI) or chronic kidney disease (CKD) in both healthy and diseased patients and is particularly useful in patients with apparently normal renal function before stress candidate for interventions at real risk of renal failure (kidney donors, cardiac surgery, bone marrow transplants). However, the protein load test has a long duration (about 5 hours), requires numerous blood and urine samples, and is challenging to use on a large scale. Recent studies have proposed another method based on the variation of the renal intraparenchymal resistance index (IRRIV-T). In this case, the stress to which the kidney is mechanical. That is a weight (saline bag, representing 10% of the body weight) placed on the abdomen of the supine patient, which induces maximal renal vasodilation. The sampling of the intraparenchymal resistance doppler indices before and after the weight application would correlate, in preliminary studies, with the RFR tested with the protein load. Thus, offering a fast and non-invasive method. Eventually, comparing these divergent diagnostic procedures can guide us in choosing the most cost-effective approach to gain deeper insight into renal health. (Fig. 1)
Exclusion criteria were: (i) non-steroidal inflammatory drugs (NSAIDs), (ii) ultrasound evidence of renal morphological changes or artery stenosis. Each patient underwent oral protein load testing (RFR-T) and an ultrasound test (IRRIV-T). Pearson’s correlation index analyzed the comparison between the 2 tests.

**Results:** There was no statistically significant correlation between RFR-T and IRRIV-T in terms of the RFR either in absolute numbers ($R = 0.14$, $p = 0.37$) or in percentage values ($R = 0.15$, $p = 0.33$). (Fig. 2) Based on our experience, the IRRIV test proved unreliable in evaluating RFR compared with the gold standard (RFR-T). Therefore, not suitable to be used as a possible alternative to the oral protein load test.

**Conclusion:** Unlike previous studies, our survey is a real-life study. Many of our patients have pathologies or take drugs that could alter the hemodynamic and the renal vascular response, consequently changing the outcome of the IRRIV test. However, it is a real-life experience that aims to offer a practical point of view, bringing to light the possible limitations of the ultrasound test when applied to a standard evaluation population and not to a healthy or highly selected population as in the only three previous works published in the literature up to now. Our work is the first original real-life study in this field.

#5781

**DRUG-INDUCED ACUTE INTERSTITIAL NEPHRITIS (D-AIN): HOW TO IDENTIFY THE RESPONSIBLE DRUG?**

Javier Azores Moreno1, Begoña Rivas1, Cristina Vega Cabrera1, Rosario Cabañas2, Eugenia García Fernández3, Laura Yébenes1, Sara Aldana Barceló1, Irene Vázquez Raso1 and Gema Maria Fernandez Juárez1

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**Background and Aims:** The mainstay of D-AIN treatment is the removal of the responsible drug. However, it is not always easy to identify the culprit drug as this entity mainly affects elderly patients on multiple medications, they rarely associate systemic symptoms (rash, fever), and the timeline regarding the diagnosis and the associated drug is not always clear. Therefore, the diagnosis and treatment are delayed, making full renal function recovery less likely. The lymphocyte transformation test (LTT) has demonstrated to be useful in the identification of the involved drug in other hypersensitivity-mediated lymphocyte T diseases such as Stevens-Johnson Syndrome or Dress Syndrome. For this reason, we wonder if this test could be relevant in identifying the responsible drug in D-AIN. The aim of this study is to test LTT in patients with clinical and histological diagnosis of D-AIN.

**Method:** We have conducted a retrospective observational study in which we have collected data from 2019 to 2022 from our electronic databases.

**Results:** We have registered 9 cases of D-AIN diagnosed with histological confirmation in whom the LTT had been performed. 22.2% of these patients were men. The mean age was 48.1 years (standard deviation of 15.8). None of them had previous chronic kidney disease (CKD). Mean peak creatinine at diagnosis was 4.66 mg/dl (standard deviation of 1.95). Regarding the typical symptoms of the D-AIN, three patients (33%) presented with fever and none of them suffered from rash. 6 patients had sterile pyuria (66%). All of them received steroid treatment. Concerning the LTT results, 7 cases were positive for one of the drugs the patient was taking, and 2 were negative. Among the positive cases, the identified drugs were 1 case of beta lactams (piperacillin), 1 case of PPIs (omeprazole), 1 case of metamizole, 1 case of paracetamol, 1 case of eslicarbazepine and 2 cases of NSAIDs (dextropropofen), while the negative cases have not been suspected of taking any culprit drug.

**Conclusion:** LTT may be a useful test to identify the responsible drug for D-AIN, especially in patients taking multiple medications in which may be included some of great importance like immunotherapy (typical cause of D-AIN) in oncological treatments. In negative cases, it could be expected that the patient had taken medications difficult to be identified in the clinical history or, in some situations, the drug hapten responsible for kidney damage might be a drug metabolite and not the drug itself, which cannot be detected by the test.
#4810

### DIAGNOSTIC AND THERAPEUTIC IMPACTS OF AIM ON END-STAGE KIDNEY DISEASE

Toru Miyazaki and Satoko Arai

The Institute for AIM Medicine, Tokyo, Japan

**Background and Aims:** End-stage kidney disease (ESKD) is life-threatening, and indispensably requires dialysis which however imposes huge burdens on patients’ QOL and medical expense. No therapies to prevent CKD progression to the end-stage have reached clinic to date. Patients undergoing dialysis exhibit a high mortality mainly due to cardiovascular diseases (CVDs), but no biomarkers are available to predict the patients’ death and the incidence of cardiovascular disease (CVD), the major cause of death, before initiation of dialysis. AIM is a macrophage-derived circulating protein present in blood at relatively high levels (~5 μg/mL). We initially identified AIM as a supporter of macrophage survival, and it is now known as a facilitator of repair in many diseases. In healthy state, AIM associates with IgM pentamer through disulfide-bond formation and charge-based interaction with IgM-Fc, using the solitary cysteine residue and the positively charged-amino acid cluster present at the carboxyl-terminal. During various diseases including acute kidney injury, hepatocellular carcinoma and peritonitis, AIM dissociates from IgM and binds to the body-derived types of inflammatory elements using the identical sites necessary for binding to IgM, thereby promoting their phagocytic removal by phagocytes.

**Method:** In 561 CKD patients of all stages and 310 dialysis patients, we analyzed the serum AIM and the serum solute profiles, and thereby assessed their efficacy in predicting survival and CVD risk after dialysis induction. Additionally, a therapeutic efficacy of recombinant AIM (rAIM) in preventing CKD progression to end-stage was addressed in house cats, that are highly susceptible to CKD and show a similar disease course to humans.

**Results:** AIM dissociated from IgM pentamer along CKD progression. Dialytic patients showing low levels of AIM dissociation before initiation of dialysis harbored less serum detrimental solutes, exhibited lower risk of CVD and had better survival than those with high grades of AIM dissociation, suggesting that the IgM-free AIM represents the state of serum toxic solutes, and predicts patients’ prognosis before initiation of dialysis. In addition, treatment of pre-uremic (late IRIS stage 3) cats, 50% of which died of severe uremia within 196 days after diagnosis, with recombinant AIM prevented aggravation of renal function and inflammation, as well as serum toxic solute profile, thereby improving the cats’ survival dramatically. Importantly, the same serum toxin/inflammatory solutes regulatable by rAIM in cats influenced dialysis patients’ prognosis.

**Conclusion:** There results promise the effects of AIM treatment in humans, reducing the need for dialysis. Our findings could be a platform for new CKD therapies and predictive diagnoses to improve the prognosis of patients with ESKD.

#2608

### IV IRON IN CKD AND HF: IMPROVING CLINICAL OUTCOMES WITH HIGH-DOSE IV IRON IN PATIENTS WITH IRON DEFICIENCY, HEART FAILURE AND CKD

Philip A. Kalra and Foizia Ahmed

NHS Nightingale Hospital Exeter, United Kingdom

**Background and Aims:** The emerging role of IV iron to reduce cardiovascular risk, particularly risk of hospitalisation for heart failure. Cardiovascular diseases are a common comorbidity in patients with chronic kidney disease. There is emerging evidence that treating with IV iron may not only correct for iron deficiency and anaemia but also have positive effect on hard clinical endpoints.

**Method:** The most recent RCT trial published is the IRONMAN trial, which was a prospective, randomised, open-label, blinded-endpoint trial done at 70 hospitals in the UK. 1137 patients with heart failure, a reduced left ventricular ejection fraction and iron deficiency were randomised to receive either ferric derisomaltose (FDI) on top of usual care or usual care alone. A large proportion of the patients (64%) had an eGFR < 60 mL/min/1.73 m².

**Results:** Compared to usual care, FDI was associated with a 18% lower risk of recurrent heart failure hospitalisations and CVD death, which approached statistical significance (p = 0.07). In the prespecified COVID-19 sensitivity analysis, the primary endpoint was nominally statistically significant with a relative risk reduction of 24% (p = 0.047). Between Aug 25, 2016, and Oct 15, 2021, 1869 patients were screened for eligibility, of whom 1137 were randomly assigned to receive intravenous ferric derisomaltose (n = 569) or usual care (n = 568). Median follow-up was 2.7 years (IQR 1.8–3.6). 336 primary endpoints (22.4 per 100 patient-years) occurred in the ferric derisomaltose group and 411 (27.5 per 100 patient-years) occurred in the usual care group (rate ratio [RR] 0.82 [95% CI 0.66 to 1.02]; p = 0.070). In the COVID-19 analysis, 210 primary endpoints (22.3 per 100 patient-years) occurred in the ferric derisomaltose group compared with 280 (29.3 per 100 patient-years) in the usual care group (RR 0.76 [95% CI 0.58 to 1.00]; p = 0.047). No between-group differences in deaths or hospitalisations due to infections were observed. Fewer patients in the ferric derisomaltose group had cardiac serious adverse events (200 [36%]) than in the usual care group (243 [43%]; difference −7.00% [95% CI −12.69 to −1.32]; p = 0.016).

**Conclusion:** For a broad range of patients with heart failure, reduced left ventricular ejection fraction and iron deficiency, intravenous ferric derisomaltose administration was associated with a lower risk of hospital admissions for heart failure and cardiovascular death, further supporting the benefit of iron repletion in this population.

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Table 1: Main characteristics of patients.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>History of chronic kidney disease (CKD)</th>
<th>Peak creatinine value (mg/dl)</th>
<th>Proteinuria on debut (mg/g)</th>
<th>Sterile leukocyturia</th>
<th>Fever/Skin rash/Eosinophilia</th>
<th>Creatinine value at 6 months (mg/dl)</th>
<th>Lymphocyte transformation test</th>
<th>drug involved</th>
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<td>1</td>
<td>50</td>
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<td>No</td>
<td>2.68</td>
<td>309</td>
<td>Negative</td>
<td>Negative</td>
<td>1.05</td>
<td>Negative</td>
<td></td>
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<td>2</td>
<td>37</td>
<td>Female</td>
<td>No</td>
<td>7.7</td>
<td>1390</td>
<td>Positive</td>
<td>Fever</td>
<td>0.65</td>
<td>Amoxicillin, Piperacillin and Penicillin</td>
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<tr>
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<td>42</td>
<td>Female</td>
<td>No</td>
<td>1.76</td>
<td>837</td>
<td>Positive</td>
<td>Fever + eosinophilia</td>
<td>1.02</td>
<td>Metamizole</td>
<td></td>
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<tr>
<td>4</td>
<td>65</td>
<td>Female</td>
<td>No</td>
<td>5.16</td>
<td>2185</td>
<td>Negative</td>
<td>Fever</td>
<td>1.04</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>25</td>
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<td>No</td>
<td>7.14</td>
<td>284</td>
<td>Positive</td>
<td>Negative</td>
<td>0.83</td>
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<td>3.75</td>
<td>869</td>
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<td>Dextropropofen, Ibuprofen</td>
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<td>3.70</td>
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<td>Fever + eosinophilia</td>
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<td>4.55</td>
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<td>0.72</td>
<td>Eslicarbazepine</td>
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Figure 1:
Upar Activation by Uparan Induced Functional and Structural Recovery of Podocytes After FSGS-Serum Damage

Deborah Mattinzoli, Silvia Armelloni, Min Li, Daniele Dalonzo, Maria Defenza, Masami Ikehata, Carlo Maria Alfieri, Vincenzo Pavone and Giuseppe Castellano

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Background and Aims: Idiopathic focal segmental glomerular sclerosis (FSGS) is characterized by progressive damage to the renal parenchyma leading to end-stage renal disease, frequent recurrence after kidney transplantation and no specific therapeutic intervention. Since the podocytes (PODO) are the principal target of FSGS injury, their protection could be an efficient, targeted therapy. In this context, we investigated a potential therapeutic approach based on a new peptide, UPARANT, capable of modulating the Urokinase-type plasminogen activator receptor (uPAR) on PODO.

Method: PODO were activated with 4% sera of 5 patients with recurrent FSGS for 48 h and then treated with 100 nM of UPARANT for 48 h. Proteins were then extracted for TMT proteomics. The Gene Ontology system database, valid for large-scale analysis, was used to identify the significantly enriched biological pathways and molecular functions. An in vitro model of a glomerular filtration barrier composed of PODO-endothelial co-culture was used to assess the change in filtration capacity by albumin (BSA) permeability test. The difference from baseline BSA percentage was measured after damage induced with sera from three FSGS patients and after 48 h of treatment with UPARANT.

Figure 1: Overall distribution of differentially expressed proteins Volcano plot in FSGS-sera PODO injury versus the same condition followed by UPARANT addition (A). Gene ontology analysis of all overexpressed proteins ranked by fold enrichment for biological process (B) and molecular function (C). n=4/group.

Figure 2: Albumin filtration capacity evaluation in the PODO-ENDO co-culture system after FSGS sera patient sera, and after sera followed by UPARANT treatment *=p<0.05, by Student’s t-test. n=3/group.
#6773

PROTECTIVE POTENTIAL OF 17-β-ESTRADIOL ON OXIDATIVE STRESS AND RENAL METABOLISM IN AGED FEMALE RATS

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Background and Aims: The objective of this study was to observe the changes in activity of antioxidant enzymes, hepatic glucose homeostasis, lipogenic enzymes and lipid metabolism, serum lipid profile and liver function occurring in livers of female rats of 3, 12 and 24 months age groups, and to see whether these changes are restored to 3 months control levels rats after exogenous administration of steroid hormone estrogens (17-β-estradiol, E2).

Methods: The aged rats (12 and 24 months old) (n= 8 for each group) were given subcutaneous injection of 17beta estradiol (0.1 ug/g body weight) daily for one month. After 30 days of hormone treatment, experimental animals of all the groups were sacrificed and livers were isolated for further study. A detailed study was carried on non-enzymatic glutathione (GSH) and enzymatic antioxidants [superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT)], hepatic glucose homeostasis, lipogenic enzymes, lipid metabolism, serum aspartate aminotransferase (GOT), alanine aminotransferase (GPT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), phosphatase alkaline (PAL) as well as bilirubin level.

Results: The results obtained in the present work revealed that normal aging was associated with significant decrease in the activities of antioxidant enzymes, serum expression and an increase in hepatic glucose homeostasis, lipogenic enzymes and lipid profile and GGT, PAL, GOT, ALP as well as bilirubin level increased significantly in livers of aging female rats. Our data showed that exogenous administration of E2 brought these changes to near normalcy in aging female rats.

Conclusions: The present study showed that E2 treatment reversed the changes to normal levels. E2 treatment may be beneficial in preventing some of the age related changes in the liver by increasing antioxidant defences and decrease oxidative stress. E2 plays important role in the progression of chronic hepatic diseases.

#3276

LUPUS NEPHRITIS: THE INTERPLAY BETWEEN SENESCENT B AND NAÏVE T LYMPHOCYTES

Eleni Moysidou1, Georgios Lioulous1, Michalis Christodoulou1, Aliki Xochelli2, Vasiliki Nikolaidou1, Stamatis Stai1, Asimina Fylaktou2, Aikaterini Papagianni1 and Maria Stangou1
1Aristotle University of Thessaloniki, Greece, Department of Nephrology, Hippokration Hospital of Thessaloniki, Greece, Thessaloniki, Greece and 2Hippokration Hospital of Thessaloniki, Department of Immunology, National Peripheral Histocompatibility Center, Greece, Thessaloniki, Greece

Background and Aims: Systemic Lupus Erythematosus (SLE) is characterized by a shift to senescent B cells, namely, switched memory (SM) (CD19+IgD-CD27+) and exhausted-double negative (DN) (CD19+IgD-CD27-) subtypes. The aim of this study was to evaluate the impact of T cell immunity in the distinct B cell - senescent pattern of SLE.

Method: A wide range of senescent and exhaustion related lymphocyte surface molecules, including CD45RA, CCR7, CD31, CD28, CD57, on T cells and CD27 and IgD on B cells, was analyzed by flowcytometry and distinct naïve, active and senescent B and T lymphocyte subtypes were determined in 31 patients with inactive Lupus Nephritis (LP).

Results: Comparison of SM and DN B cells with T cell subpopulations revealed significant correlation of naïve and “unexperienced” CD4 and CD8 compartment with SM and DN B cells. Indeed, the correlation appeared even stronger regarding SM B cells and Recent thymic emigrants (RTE) CD4CD31+ (r=0.575), CD4+ Central Memory (CM) (CD45RA-CCR7+) (r=0.546), CD4CD45RA+CD28+(r=0.556), CD4CD28+CD57- (r=0.621), CD4CD45+CD57- (r=0.544), CD4CD45+CD57- (r=0.65), CD8CD28+CD57- (r=0.596), CD8CD45+CD57- (r=0.556) while weak yet significant was their correlation with CD4 Naïve (CD45RA+CCR7+) (r=0.432), CD8CM (CD45RA+CCR7+) (r=0.474), RTE CD8CD31+ (r=0.461), CD8CD28+CD57- (r=0.442), Less apparent was this phenomenon between DN B cells and CD4 CM (CD45RA-CCR7+) (r=0.381), CD4CD45RA+CD28+ (r=0.504), RTE CD4CD31+ (r=0.587), CD8CD28+CD57- (r=0.487), CD8CD28+CD57+ (r=0.491), CD4CD45+CD57- (r=0.419), CD4CD45-CD57- (r=0.397), CD8 Naïve (CD45RA+CCR7+) (r=0.432), RTE CD8CD31+ (r=0.366), CD8CD28+CD57- (r=0.363), CD8CD28+CD57+ (r=0.483), CD8CD45+CD57- (r=0.444), CD8CD45-CD57- (r=0.384).

Conclusion: The predominant shift to senescent/exhausted B lymphocytes in SLE and LN may have a direct impact on naïve CD4 and CD8 T lymphocyte subpopulations.

A2 - RENAL DEVELOPMENT & MOLECULAR GENETICS

#5276

DEVELOPMENT OF A MULTIMODAL "KIDNEY AGE" PREDICTION BASED ON AUTOMATIC SEGMENTATION CT IMAGE IN PATIENTS WITH NORMAL RENAL FUNCTION

Zuxian Hou1, Gu-Mu-Yang Zhang2, Yixin MA1, Peng Xia1, Xiaoxiao Shi1, Hao Sun3, Zhengguang Chen1 and Limeng Chen1
1Peking Union Medical College Hospital, Department of Nephrology, Beijing, P.R. China, 2Dongzhimen Hospital, Beijing University of Chinese Medicine, Department of Radiology, Beijing, P.R. China and 3Peking Union Medical College, Department of Radiology, Beijing, P.R. China

Background and Aims: Renal function, for decades, has been of interest to clinicians and researchers to describe. For example, serum creatinine (Scr) and estimated glomerulus filtration rate (eGFR) is familiar but also limited in many circumstances. Meanwhile, the physiological volumes of the kidney cortex and medulla are presumed to change with age and have been proven to change with decreasing kidney function.

Method: We recruited 182 patients with normal Scr levels and contrasted CT images between Oct. 2021 and Feb 2022 in Peking Union Medical College Hospital (PUMCH) with their demographic and clinical data. The automatic segmentation method was modified from U-NET and used for both cortex and medullary separation and their volumecalculation, respectively. We combined the kidney volume and clinical data as multimodal features of the machine learning model. All the data were separated into a training dataset (PUMCH training set, 80%) and a test dataset (PUMCH test set, 20%). Besides, we included patients with the same inclusion criteria but with diabetes (PUMCH-DM test set) and diabetic nephropathy (PUMCH-DN test set) for internal comparison to verify the possible clinical value of “KIDNEY AGE” (K-AGE).

Data from DongZhiMen Hospital (DZMH test set) was used as separate external validation sets to evaluate model generalizability.

Results: The PUMCH training set included 146 participants with a mean age of 47.5±7.4 years. 58.9% were female, and the mean Scr is 63.5±12.3 μmol/L. The PUMCH test set included 36 participants with a mean age of 47.1±7.9 years, 52.7% were female, and the mean Scr was 66.9±13.0 μmol/L. For segmented kidneys, volume differences between non-contrast-enhanced CT and non-contrast-enhanced CT in the left and right kidneys were not evident. The multimodal network predicted: K-AGE approximately close to the patient’s actual physiological age, with 92% prediction within the 95% confidence interval (Figure 1). We also compared the K-AGE prediction in PUMCH, PUMCH-DM, and PUMCH-DN test sets by applying U-NET-nonCon segmentation algorithm in non-contrast CT images. The mean absolute error increases along with the disease process (control group 5.00, diabetes group 6.99, diabetic nephropathy group 9.32) (Figure 2).

Conclusion: We established a machine learning model for predicting the K-AGE of normal Scr patients.
A3 - GENETIC DISEASES (INCLUDING CYSTIC DISEASES)

#5124

GENETIC GLOMERULAR DISEASES IN THE ADULT PATIENT: A WORK IN PROGRESS – SINGLE CENTRE COHORT

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1Centro Hospitalar Universitário Lisboa Norte, Nephrology and Renal Transplantation, Lisboa, Portugal, 2Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal and 3Centro Hospitalar Universitário Lisboa Norte, Genetics, Lisboa, Portugal

Background and Aims: Recent advances in genetic molecular techniques have allowed the expansion of knowledge in glomerular diseases of genetic cause, including the identification of genes involved in focal and segmental glomerular sclerosis (FSGS). The prevalence of adult-onset genetic FSGS varies widely depending on the population studied. In central Europe, NPHS2 and COL4A3, COL4A4 e COL4A5 genes are postulated to be the most frequent genes implicated in genetic causes of adult FSGS. This study aims to characterize patients submitted to genetic study of glomerular diseases in the Nephrogenetics Clinic of our centre.

Method: We conducted a single-centre retrospective analysis of the patients submitted to genetic study of glomerular diseases in the Nephrogenetics Clinic of our centre from 2016 to 2022. Adult patients with a glomerular disease phenotype suggestive of a genetic cause were studied, using a predetermined phenotype-targeted panel of genes, through massive parallel sequencing. The number of genes included in this panel has increased (from 21 genes in 2016 to 49 genes since 2018); given this change, patients with a negative result on the first approach repeated screening with the broader panel. Additionally, patients presenting with advanced chronic kidney disease (CKD) without an identifiable phenotype, studied with a larger panel for CKD causing genes, are reported. In patients with a negative result but highly suggestive presentation, whole exome sequencing (WES) was considered, after multidisciplinary discussion with a Geneticist’s evaluation. Patients with variants of unknown significance (VUS) were referred to a Genetics’ consultation for genetic counselling and segregation studies.

Results: Of the 80 patients studied (comprising 74 families), 52.5% were female (n=42) and 79% (n=63) of Caucasian ascent. Mean age was 45.4 ± 16.0 years. Nine patients were studied with the larger gene panel for CKD. 85% (n=68) had CKD (all stages) at presentation, with proteinuria (ranging from sub-nephrotic to nephrotic range) and 15% had asymptomatic urinary changes. 50% (n=40) of patients had positive family history, and 31% (n=25) had a syndromic presentation and/or extra renal manifestations. 27.5% (n=22) had a renal biopsy, and the most prevalent result was FSGS (11%; n=9). Genetic variants were identified in 70% (n=56) of the patients; but pathogenicity is not fully established in all: genotype-phenotype correlations, including inheritance pattern and histological correlation, and segregation studies (when indicated and possible) are ongoing. In 5 patients results are pending. Pathogenic / likely pathogenic variants were identified in at least 47.5% (n=38) patients. The most frequently implicated genes were: COLA3, COL4A4 e COL4A5 (n=21), high risk APOL1 (n=8); NPSH2 (n=5), IFN2 (n=6, 3 pathogenic, 1 variant of unknown significance (VUS), 2 under segregation studies) and MYH9 (n=3). COL4A3, COL4A4 e COL4A5 mutations occur with Alport syndrome, but also with histologically documented FSGS, sub-nephrotic and nephrotic proteinuria, nephrotic syndrome and asymptomatic urinary changes. In our
cohort, NPHS2 p.R229Q was identified in 5 patients (6%), but only with pathogenic significance in 3 patients, and APO1 high risk haplotype was co-identified with COL1 variants in 3 patients.

**Conclusion:** The genetic study of a cohort of patients suspected of genetic FSGS allowed the identification of genetic variants in the genes of interest in a high percentage of cases. The most frequently implicated genes were COL4A3, COL4A4 e COL4A5, NPHS2, INF2 and APO1 high risk haplotype. The high percentage of gene variants identified in our cohort is probably due to the selection of a population with a high likelihood of genetic FSGS. Further studies will clarify the causal and/or modifier effect of some genes, namely COL4A3, COL4A4 e COL4A5. The future use of WES in cases of high likelihood of genetic cause will probably allow the identification on novel candidate genes and increase the clinical benefits of a genetic diagnosis of FSGS.

**#4485**

**CLINICAL CASE OF MOSAICISM IN ADPKD PATIENT**

Nenzi Marzano1, Valentina Corradi2, Carlotta Caprara3, Matteo Rigato3, Anna Giuliani2, Fiorella Gastaldon2, Claudio Ronco1 and Monica Zanella2

1International Renal Research Foundation (IRRIV), Vicenza, Italy and 2AUSS 8 Berica, San Bartolo Hospital, Department of Nephrology, Dialysis and Transplantation and International Renal Research Foundation (IRRIV), Vicenza, Italy

**Background and Aims:** Autosomal Dominant Polycystic Kidney Disease (ADPKD) is mainly characterized by renal involvement with progressive bilateral development of renal cysts and volumetric increase of the kidneys, responsible for the progressive loss of renal function that leads to chronic kidney disease (CKD) and the need of renal replacement therapy. There are some cases (doubtful, uncertain) in which it is necessary to perform genetic testing to achieve a definitive diagnosis. It looks like in ADPKD patients, mosaicism could modulate the clinical course of the disease. Mosaicism is characterized by few cell populations with different genomes. In these special cases the diagnosis is very difficult and the genetic analysis could be an important and helpful tool. With this report, we want to highlight the importance of the use of several diagnostic methods in those ‘atypical’ cases where otherwise the analysis would have been negative from a first molecular approach.

**Method:** A 47 years old woman came to our attention with typical picture of ADPKD, arterial hypertension and chronic kidney disease CKD (3b). She had no ADPKD family history, but since she had a son, genetic testing was performed. According to our workflow, first level analysis includes Next Generation Sequencing (NGS). Second level analysis, performed to investigate other genes and large rearrangement, was based on Multiplex Ligation-dependent Probe Amplification (MLPA) analysis of PKD1 and PKD2 genes, using Salsa MLPA ProbeMix P352 PKD1PKD2 kit and ProbeMix P351 PKD1 kit ©MRCHolland. Results: NGS did not detect the presence of any genomic variants. Therefore, second-level genetic analysis (several approaches), showed a large deletion in heterozygosis of the portion comprising the 3-33 exons of PKD1 gene in mosaic in percentage close to the resolution limits of the used technique (25-30%). The same analysis was confirmed in another laboratory.

**Conclusion:** We concluded that the identified large deletion, without establishing the real borders due to MLPA technical restrictions, was present as mosaicism. The variant is not reported, but due to the type of mutation and the clinical picture of the patient, it is to be considered as likely pathogenic. A stepwise genetic approach might be useful in those cases where standard methods do not allow to reach a definitive diagnosis.

**Abstract**

For clinical FD phenotype a 60-year-old woman (index case) with cadaveric donor renal transplantation and unknown cause of renal disease was undergoing genetic investigation. She reported D313Y as single variant in the GLA gene. A prospective analysis of clinical manifestation, genetic and biochemical (lyso-GB3 and enzyme activity) data was performed in all her brothers, sisters and sons. Data were assessed as part of routine follow-up visits.

**Results:** Genotype information of our index case was: nucleotide change c.937G>T, exon 6 involved, amino acid change p.Asp313Tyr, HGMD accession CM930335, mutation type missense. In our cohort comprising n.9 family members: n.5 (55%), n.3 females, n.3 males age range 45-60) had the p.D313Y mutation. In nobody the biomarker lyso-GB3 was elevated. Two brothers (age range of 40-50 y) died for acute cardiovascular attack before genetic investigation was performed. The 5 family members showed the following clinical features: 2 hypertension and cardiac hypertrophy (2M, 44/61y); our index case renal failure, LVH and bruning pains; 2F with burning pains (49/46y). Enzyme replacement therapy (ERT) was started in our index case. Annual routine visits are performed in the others.

**Conclusion:** D313Y mutation seems to correlate with clinically relevant symptoms (mainly cardiovascular and renal) compatible with FD, also without lyso-GB3 elevation. ERT might be considered as therapeutic option not only in patients with already organ involvement, but also in paucisymptomatic to prevent disease progression.

**#4973**

**PATHOGENIC ROLE OF D313Y MUTATION IN FABRY DISEASE**

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**Background and Aims:** Fabry disease (FD) is a multisystem lysosomal storage disorder caused by mutations in the GLA gene. The significance of the mutation p.D313Y in the GLA gene is under debate. Our aim is to evaluated the pathogenic role of the D313Y mutation.

**Method:** For clinical FD phenotype a 60-year-old woman (index case) with cadaveric donor renal transplantation and unknown cause of renal disease was undergoing genetic investigation. She reported D313Y as single variant in the GLA gene. A prospective analysis of clinical manifestation, genetic and biochemical (lyso-GB3 and enzyme activity) data was performed in all her brothers, sisters and sons. Data were assessed as part of routine follow-up visits.

**Results:** Genotype information of our index case was: nucleotide change c.937G>T, exon 6 involved, amino acid change p.Asp313Tyr, HGMD accession CM930335, mutation type missense. In our cohort comprising n.9 family members: n.5 (55%), n.3 females, n.3 males age range 45-60) had the p.D313Y mutation. In nobody the biomarker lyso-GB3 was elevated. Two brothers (age range of 40-50 y) died for acute cardiovascular attack before genetic investigation was performed. The 5 family members showed the following clinical features: 2 hypertension and cardiac hypertrophy (2M, 44/61y); our index case renal failure, LVH and bruning pains; 2F with burning pains (49/46y). Enzyme replacement therapy (ERT) was started in our index case. Annual routine visits are performed in the others.

**Conclusion:** D313Y mutation seems to correlate with clinically relevant symptoms (mainly cardiovascular and renal) compatible with FD, also without lyso-GB3 elevation. ERT might be considered as therapeutic option not only in patients with already organ involvement, but also in paucisymptomatic to prevent disease progression.
A SCREENING AND CLINICAL MANIFESTATIONS OF FABRY DISEASE IN PATIENTS ATTENDING DIALYSIS AND NEPHROLOGY CLINICS IN DURBAN, SOUTH AFRICA

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Background and Aims: Fabry disease is inherited in an X-linked manner in which the mutated gene inhibits the functioning of the alpha-Galacosidase-A enzyme causing a deficiency or absence of the enzyme, characterizing it as a progressive, lysosomal storage disorder. Subsequently, the accumulation of globotriaosylceramide (Gb3) in the lysosomes causes damage to tissues and major organs. Fabry nephropathy is one of the major organ complications caused by Fabry disease resulting in end-stage kidney disease. The aim of our study is to determine the prevalence of Fabry disease in our patients.

Method: This study was a prospective, quantitative study. A cohort of 200 male patients with chronic kidney disease (CKD stage 2-5D) was enrolled. A control group of 14 healthy males was also enrolled for this study. The ELISA technique was employed to determine the alpha Gal-A enzyme concentration levels in plasma. A questionnaire using the MSSI scoring system was presented to the participants to identify clinical manifestations. The SPSS Version 27 (IBM, New York, USA) was used to analyse the data.

Results: A cut-off value for the alpha Gal-A enzyme concentration levels of <500 pg/ml was calculated. A total of 17 participants from the patient group (n=11) and the control group (n=6) displayed alpha-Gal-A enzyme levels <500 pg/ml. Using the univariate regression analysis, statistically significant results were revealed between alpha-Gal levels <500 pg/ml and age (P = .007), heat or cold intolerance (P = .049), hypertension (p < .001) and eGFR (p < .001). MSSI scores displayed a negative association (P = .001). The multivariate regression analysis showed that age and MSSI scores retained their significance when eGFR was excluded as a variable, however, with the inclusion of eGFR as a variable, none of the variables retained their significance.

Conclusion: Fabry disease is suspected in 17 participants with alpha-Gal levels of <500 pg/ml. The cause of CKD nephropathy raises interest as conditions such as FSGS have been associated with FD. The low levels of the alpha-Gal enzyme and presentation of the clinical manifestations can be utilized as preliminary findings. Confirmatory tests such as DNA analysis or Gb3 and GL3 analysis are warranted.

Table 1: Demographic and clinical and laboratory data of the study participants.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fabry (n=76)</th>
<th>CKD (n=46)</th>
<th>Healthy controls (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>37 (26.3–48)</td>
<td>49 (34.8–56.3)</td>
<td>36 (30 – 45)</td>
<td>0.0061,3</td>
</tr>
<tr>
<td>Gender, Male, n(%)</td>
<td>26 (34.2)</td>
<td>15 (32.6)</td>
<td>24 (58.5)</td>
<td>0.0181,2</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.7 (20.4 – 28.3)</td>
<td>29.9 (24.7 – 33.6)</td>
<td>24.8 (21.8 – 27.6)</td>
<td>&lt;0.0011,3</td>
</tr>
<tr>
<td>Smoking, n(%)</td>
<td>27 (38.6)</td>
<td>9 (21.4)</td>
<td>10 (25.6)</td>
<td>0.121</td>
</tr>
<tr>
<td>Diabetes mellitus, n(%)</td>
<td>7 (9.3)</td>
<td>14 (30.4)</td>
<td>0</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19 (22.1)</td>
<td>29 (63)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1 (1.3)</td>
<td>2 (4.3)</td>
<td>0</td>
<td>0.557</td>
</tr>
<tr>
<td>Urea, mg/dl</td>
<td>23 (18.2 – 29)</td>
<td>34 (26.7 – 42.6)</td>
<td>25 (19 – 30.5)</td>
<td>&lt;0.0011,3</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>0.65 (0.39 – 0.82)</td>
<td>0.95 (0.71 – 1.15)</td>
<td>0.78 (0.67 – 0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR(cr), mL/min/1.73 m2</td>
<td>114.86 (97.27 – 126.65)</td>
<td>88 (63.5 – 109)</td>
<td>111 (100.5 – 117.5)</td>
<td>0.0011,3</td>
</tr>
<tr>
<td>eGFR(cr-cys), mL/min/1.73 m2</td>
<td>86 (54.3 – 117.5)</td>
<td>63 (36.8 – 97.3)</td>
<td>111 (97 – 125.5)</td>
<td>&lt;0.0011,2</td>
</tr>
<tr>
<td>UPCR (mg/g)</td>
<td>163.3 (118 – 591.8)</td>
<td>413.5 (121.5 – 1007)</td>
<td>NA</td>
<td>0.240</td>
</tr>
<tr>
<td>UACR (mg/g)</td>
<td>29 (12 – 352)</td>
<td>141 (30.2 – 335.5)</td>
<td>NA</td>
<td>0.113</td>
</tr>
</tbody>
</table>

eGFR: Estimated glomerular filtration rate, UPCR: Urine protein creatinine ratio, UACR: Urine albumin creatinine ratio 1Healthy control-Fabry patients, 2Healthy control-CKD patients, 3Healthy control-CKD patients

#5718

ASSOCIATION OF MULTIPLE PLASMA BIOMARKER LEVELS WITH KIDNEY DISEASE ACTIVITY IN FABRY DISEASE

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Background and Aims: Fabry disease is a rare, systemic, genetic, and metabolic lysosomal storage disease. Phenotypic heterogeneity prevents accurate predictions for the disease progression. We aimed to evaluate the association of multiple plasma biomarkers with disease severity in Fabry disease.

Method: In a cross-sectional study, we examined 76 Fabry, 46 CKD patients and 41 healthy controls. We studied KIM-1, MCP-1, YKL-40, TNFR-1, TNFR-2, cystatin-C with enzyme linked immunoassay. Fabry patients on renal replacement therapy were excluded from the analysis.

Results: Demographic, clinical and laboratory data of the study participants are shown in Table 1. eGFR was calculated with creatinine and creatinine-cystatin C using CKD-EPI formula. While there was no difference between Fabry patients and healthy controls regarding eGFR(cr); eGFR(cr-cys) was significantly lower in Fabry patients. Biomarker levels in three groups were shown in Table 2. After performing age, sex and BMI adjusted analysis, MCP-1 was significantly lower in Fabry patients compared to CKD group (p<0.011). MCP-1 was significantly higher in Fabry patients with cardiac involvement than in those without cardiac involvement (p<0.039). KIM-1 was significantly higher in Fabry patients compared to healthy controls (p<0.011). There was no significant difference regarding biomarker levels between Fabry patients with and without kidney involvement. YKL-40 was significantly lower in Fabry patients without kidney involvement compared to both control groups (p<0.025), probably reflecting the effect of ERT.

Conclusion: MCP-1, KIM-1, YKL-40 and Cystatin C seems to be useful markers for the management of Fabry patients. Each biomarker is associated with different aspect of the disease. MCP-1 might be a useful regarding Fabry disease activity especially in patients with cardiac involvement. KIM-1 might be an early sign in Fabry disease. Cystatin-C should be used for...
better management of patients since it shows renal involvement better than creatinine.

#4043
FABRY DISEASE: A RARE ENTITY IN THE NEPHROLOGY SETTING
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Background and Aims: Fabry disease is a rare genetic disorder that affects multiple organs, including the kidneys. It is characterized by the accumulation of globotriaosylceramide (Gb3) in various tissues and organs, leading to progressive interstitial fibrosis and renal dysfunction. We aim to determine the renal manifestations of Fabry disease in particular the histological aspects.

Method: This study analyzed 9 patients with Fabry disease and renal involvement in a retrospective, single-center analysis. Clinical and biological data, as well as histologic findings, were collected based on patients' observations.

Results: Data was collected from 9 patients, including 7 males and 2 females, with an average age at diagnosis of 25.2 years (ranging from 17 to 32 years). All patients showed depleted activity of alpha 1 lysocidase, confirming the diagnosis. Acrocyrosis and vascular cutaneous lesions (angiokeratomas) were the dominant signs at admission with respectively (n=7; n=4), with only 3 patients being identified through familial screening without symptoms. Uncontrolled Hypertension was noted in 2 patients. Renal manifestations included renal hyperfiltration in 2 cases, isolated proteinuria in 4 patients, and renal failure in 3 others with a mean serum creatinine levels of 240 ± 36 μmol/l. Four patients underwent renal biopsy, which showed characteristic lesions of Fabry disease with sphingolipid accumulation and tubular cell vacuolization. Thickening of the glomerular capillary walls was observed in one patient. Interstitial fibrosis and tubular atrophy were noted in 3 patients. All patients received enzyme replacement therapy. Angiotensin-converting enzyme inhibitors (ACEi) and/or angiotensin II receptor blockers (ARB) were used in 6 patients. Five patients progressed to terminal stage of renal failure requiring dialysis after an average follow-up period of 13±2.7 years. Four patients died from cardiovascular complications.

Conclusion: Early recognition and diagnosis of Fabry disease from the onset of glomerular hyperfiltration and albuminuria are crucial for the initiation of appropriate treatment and management, which can help to delay the progression of renal and other organ damage.

#4061
PHARMACOKINETICS OF SETMELANOTIDE IN INDIVIDUALS WITH RENAL IMPAIRMENT: RESULTS FROM A PHASE 1, OPEN-LABEL, SINGLE-DOSE STUDY
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Background and Aims: Setmelanotide is an approved treatment for chronic weight management and control of hunger in patients aged ≥6 years with specific forms of obesity including Bardet-Biedl syndrome (BBS). Setmelanotide may be considered for patients with renal impairment, including those with BBS, who often experience impaired renal function as a primary feature of the syndrome. This study evaluated the pharmacokinetics (PK) and safety of a single dose of setmelanotide in individuals without BBS who have renal impairment.

Method: This Phase 1, open-label study (NCT04348175) was conducted in 3 centers in the United States. Eligible individuals were aged 18-83 years and had general obesity with a body mass index (BMI) of 24-40 kg/m². Individuals were assigned to a study cohort according to renal function, determined by estimated glomerular filtration rate (normal renal function [healthy volunteers]: ≥90 mL/min/1.73 m²; mild renal impairment: 60-89 mL/min/1.73 m²; moderate renal impairment: 30-59 mL/min/1.73 m²; severe renal impairment: 15-29 mL/min/1.73 m²). A single dose of 2.0 mg of setmelanotide was administered subcutaneously; however, 1.0 or 0.5 mg was administered to most patients with severe renal impairment following safety review of the patient cohorts with mild and moderate renal impairment because of the potential impacts of nausea and vomiting, and consequential dehydration, on renal function. Blood samples were collected for PK analysis from hour 0 up to hour 96 after setmelanotide administration. Patients with renal impairment and healthy volunteers were matched according to sex, age, and BMI. PK parameters in individuals who received <2.0 mg setmelanotide were dose normalized for comparisons across renal function groups. Safety and tolerability were monitored and evaluated.

Results: In total, 32 individuals were included. Age, sex, and BMI were generally similar across cohorts. Setmelanotide PK parameters were comparable regardless of renal function (Table 1). Mean area under the concentration-time curve was higher in individuals with renal impairment compared with healthy volunteers and increased with worsening renal function. Mean clearance was lower in individuals with renal impairment compared with healthy volunteers and decreased with worsening renal function. Thirty individuals (94%) experienced a treatment-emergent adverse event (TEAE), with gastrointestinal disorders (n=22; 69%) having the highest incidence. There were no severe, serious, or fatal TEAEs and no TEAEs leading to withdrawal. There were no meaningful differences in incidence of the most common TEAEs across cohorts.

Conclusion: Minimal differences in PK parameters were observed in individuals with mild and moderate renal impairment compared with healthy volunteers. Findings from this study are consistent with current setmelanotide dosing recommendations, which suggest a modified dosing regimen in patients with severe renal impairment.

#3697
FAMILIAR PAPILLARY RENAL CELL CARCINOMA: A CASE REPORT
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1 Beaumont Hospital, Nephrology, Dublin, Ireland, 2 CHI at Temple Street, Ireland and 3Belfast City Hospital, United Kingdom

Background and Aims: The incidence of Renal Cell Carcinoma (RCC) is the 9th commonest cancer worldwide. It originates from the renal tubular epithelium and to date has been subclassified into five different categories. Of which, papillary carcinoma is one subclassification and it includes two variants: sporadic and hereditary. This case report aims to outline a rare case of hereditary papillary RCC and the implications for the family involved.

Table 1: Setmelanotide Pharmacokinetics Parameters by Renal Function Following a Single Subcutaneous Dose of Setmelanotide.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal renal function (n=7)</th>
<th>Mild renal impairment (n=8)</th>
<th>Moderate renal impairment (n=9)</th>
<th>Severe renal impairment (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>tmax, h</td>
<td>6.0 (3.0-8.0)</td>
<td>7.0 (5.0-8.0)</td>
<td>6.0 (3.0-12.0)</td>
<td>5.5 (4.0-8.0)</td>
</tr>
<tr>
<td>Cmax, ng/mL</td>
<td>260 (3.9)</td>
<td>27.8 (7.7)</td>
<td>25.9 (7.3)</td>
<td>29.8 (7.3)</td>
</tr>
<tr>
<td>AUGc, hng/mL</td>
<td>360 (34)</td>
<td>420 (92)</td>
<td>501 (133)</td>
<td>673 (97)</td>
</tr>
<tr>
<td>AUC∞, h·ng/mL</td>
<td>379 (34)</td>
<td>439 (94)</td>
<td>524 (134)</td>
<td>751 (129)</td>
</tr>
<tr>
<td>CL/F, L/h</td>
<td>5.3 (1.2)</td>
<td>4.8 (1.2)</td>
<td>4.1 (1.2)</td>
<td>2.7 (0.4)</td>
</tr>
<tr>
<td>Vz/F, L</td>
<td>96.9 (12.5)</td>
<td>96.5 (23.5)</td>
<td>113 (26.6)</td>
<td>89.6 (19.5)</td>
</tr>
<tr>
<td>t1/2, h</td>
<td>12.8 (2.2)</td>
<td>14.6 (4.8)</td>
<td>19.6 (2.9)</td>
<td>23.5 (7.3)</td>
</tr>
<tr>
<td>Unbound fraction</td>
<td>0.21 (0.02)</td>
<td>0.22 (0.02)</td>
<td>0.21 (0.02)</td>
<td>0.19 (0.04)</td>
</tr>
</tbody>
</table>

1Data are the mean (standard deviation) unless otherwise indicated. 2Dose normalized to 2.0 mg; tmax is the median (range). 3Unbound fraction is the average of the data obtained at 5 and 6 hours after dose. AUCc, area under the curve; AUC∞, AUC from time 0 extrapolated to infinity; AUGc, AUG from hour 0 to last measured concentration; CL/F, clearance; Cmax, maximum plasma concentration; F, bioavailability; t1/2, apparent terminal elimination half-life; tmax, time to maximum plasma concentration; Vz/F, volume of distribution.

Abstract
Method: We performed a retrospective assessment of clinical and radiological characteristics of the index patient and affected relatives. Genetic diagnosis and management have been summarised.

Results: A 62-year-old male (II.1) was diagnosed with RCC after presenting with right-sided flank pain and multiple complex cystic lesions within both kidneys. A kidney biopsy revealed a papillary structure with foamy histocytes and clear cell-type epithelium clusters. Immunostaining of tumour cells demonstrated CK7 and P504S positivity consistent with RCC. Subsequently, he underwent bilateral nephrectomies and was rendered anephric, was commenced on haemodialysis. He underwent deceased donor renal transplantation four years later at the age of 66 (HLA 1:2:1, CMV -/-, cRF 35%).

Conclusion: The case outlines a rare form of hereditary RCC and the implications that detection of the genetic variant has meant in terms of early diagnosis of disease. Incidence of RCC is increasing worldwide. Hereditary papillary RCC is rare, it is typically inherited in an autosomal dominant pattern. Germline mutations in the MET proto-oncogene are located at 7q31, which encodes for the tyrosine kinase signaling pathway. Variants lead to uncontrolled activation of MET protein and aberrant cell growth.

Discussion: Hereditary papillary RCC has an estimated incidence of <1:1500000, its rarity highlighted by the fact that only ~35 families have been reported worldwide in literature. In these cases it exhibits 100% penetrance, with patients developing renal cell carcinoma typically between their fifth and sixth decade.

We would like to acknowledge the family involved in this case report. As with many cancers, early diagnosis is helped by detection of a genetic variant, leading to improved long-term disease-free survival. In the case of metastatic papillary RCC 2-year survival is still estimated at 18% (3).

REFERENCES
Background and Aims: Fabry Disease (FD) is a multisystemic disorder that affects the function of major organs, such as the kidneys, the heart, and the central nervous system, reducing the quality of life and leading ultimately to premature death. Early diagnosis and timely treatment are the cornerstones to change the natural history of this disorder.

Method: To evaluate clinical, laboratory and renal histological profiles of FD patients with a classic pathogenic variant (p.G35V), identified by targeted screening in hemodialysis patients followed by family screening, who were under enzyme replacement therapy (ERT), alglucosidase-beta (0.1 mg/kg/e.o.w), for at least 48 months. Kidney biopsy was performed at baseline. Glomerular filtration rate, estimated according to the CKD-Epi equation, 24-h urinary protein and albumin were measured annually. Cardiac manifestations were evaluated by electrocardiogram, transthoracic echocardiography (TTE) or magnetic resonance imaging (cMRI) at baseline and at the end of the study. cMRI was not performed in the index patient, due to CKD 5D, and in a pregnant female patient.

Results: Nine patients (age: 33.8±12.3 years) were followed-up for 80.67±4.43 months. Their main clinical manifestations were hypohidrosis (67%) gastrointestinal symptoms (56%), cornea verticilata and acroparesthesia (100%). In 2 patients (index case and a 46-years old female) entrapment of NO in the abundant stagnant mucus. Were recruited 27 patients with ADPKD and 25 randomly selected controls. We compared nNO measurements between the two groups, stratifying for truncated mutations and eGFR. After stratification according to ADPKD phenotype of the disease is the formation of multiple cysts in the kidneys but in many cases it also involves other organs like heart, brain and lungs. The latters are not yet well studied; some papers report a higher prevalence of bronchiectasis in ADPKD patients compared to the general population; moreover, one work describes the absence of PC-1 in motile cilia of ADPKD pts compared to controls, who actually do express the protein. Based on available literature, we hypothesized that the PC-1 and PC-2 could have a role also in motile cilia. Exhaled nasal nitric oxide (nNO) is an indirect marker of cilia dysfunction, standardized for the screening of primary ciliary dyskinesia, a motile ciliopathy, in which very low levels of nNO are found because of the entrapment of NO in the abundant stagnant mucus.

Method: We recruited 27 patients with ADPKD and 25 randomly selected controls. We compared nNO measurements between the two groups, stratifying for truncated mutations and eGFR. After stratification according to ADPKD genetic mutation, we analyzed separately each of the two subgroups with the control group.

Results: nNO levels were no different in ADPKD patients compared with healthy controls (mean ± standard deviation: 850±240 vs 923±290, \( P = .05 \)), given the entrapment of NO in the abundant stagnant mucus.

Discussion: nNO levels did not differ in ADPKD individuals compared to controls, although lower nNO measurements were observed in ADPKD patients exhibiting a truncated mutation.

Conclusion: Even at the edge of the statistical significance (\( P = .05 \)), given it's confirmed in a wider population, this finding could signify that pts who
carry a more aggressive genotype (PKD-1 truncated mutation) may not express polycystins in motile cilia; this aspect is in line with the verified knowledge that this kind of mutation ends up in the total absence of the protein. On the other hand, pts with a missense mutation may still express the protein in motile cilia, therefore without any functional impairment.

#6931
TWO CASES OF PREGNANCY IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX
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Background and Aims: Tuberous sclerosis complex (TSC) is a rare autosomal dominant genetic disorder that is characterized by formation of benign tumors of the brain, kidney, eyes, heart, lung, liver and skin. The disease is frequently associated with adverse pregnancy outcomes. Our aim is to present two cases of Tuberous sclerosis complex in pregnancy which might be illustrative in the management of these patients.

Method: The first patient was a 32-year-old woman with a history of renal angiomyolipoma (AML) and pulmonic lymphangiomylomatosis (LAM) due to Tuberous sclerosis complex diagnosed at a young age. In the 35th gestational week she had an emergency Cesarean section due to acute retroperitoneal bleeding from angiomyolipoma of the right kidney and gave birth to a preterm male infant (birth mass 2077 g, Apgar 4/6). The patient did not take any medications during the course of pregnancy. Since 2015 she is being treated with everolimus (5 mg/day) due to complications for pulmonic lymphangiomylomatosis, subependymomas and epilepsy and AMLs. After being treated with everolimus (5 mg/day) due to complications for pulmonic lymphangiomylomatosis, subependymomas and epilepsy and AMLs. After the course of the pregnancy she was treated with phenobarbital, folic acid and iron supplementation. Her epilepsy is well-controlled and AMLs show no dynamic in size or number. The second patient was a 29-year-old nulliparous woman who has presented with seizures at the age of 2 and was diagnosed with TSC. At 37th gestational week of a twin pregnancy she gave birth to one male neonate (birth mass 2660 g, Apgar 8/9), while the other fetus died in utero. The neonate (birth mass 2660 g, Apgar 8/9), while the other fetus died in utero. The patient did not take any medications during the course of pregnancy. Since 2015 she is being treated with everolimus (5 mg/day) due to complications for pulmonic lymphangiomylomatosis, subependymomas and epilepsy and AMLs. After being treated with everolimus (5 mg/day) due to complications for pulmonic lymphangiomylomatosis, subependymomas and epilepsy and AMLs. The first patient was a 32-year-old woman with a history of renal angiomyolipoma (AML) and pulmonic lymphangiomylomatosis (LAM) due to Tuberous sclerosis complex diagnosed at a young age. In the 35th gestational week she had an emergency Cesarean section due to acute retroperitoneal bleeding from angiomyolipoma of the right kidney and gave birth to a preterm male infant (birth mass 2077 g, Apgar 4/6). The patient did not take any medications during the course of pregnancy. Since 2015 she is being treated with everolimus (5 mg/day) due to complications for pulmonic lymphangiomylomatosis, subependymomas and epilepsy and AMLs. After being treated with everolimus (5 mg/day) due to complications for pulmonic lymphangiomylomatosis, subependymomas and epilepsy and AMLs.

Results: Conclusion: We have showed two cases with relatively good outcomes which have long-term stable disease. Female patients with TSC have increased risk of hemorrhagic complications of AMLs during pregnancy and it can be complicated by intrauterine growth restriction. A multidisciplinary approach is needed in the planning and monitoring pregnancies in these patients to achieve optimal outcomes.

#3314
DIURETIC AND RENOPROTECTIVE EFFECTS OF GOREISAN IN A RAT MODEL OF NEPHROTIC SYNDROME
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Background and Aims: Goreisan, a traditional Chinese medicine composed of five herbs, is commonly used for the purpose of control of edema and gastrointestinal symptoms. However, the detailed mechanisms have not been fully elucidated. In clinical settings, nephrotic syndrome often causes edema, mainly due to hypoalbuminemia and sodium retention. Thus, we investigated the effects of Goreisan on the kidney using a rat model of nephrotic syndrome.

Method: A model of nephrotic syndrome was created by a right nephrectomy and subsequent administration of adriamycin using Sprague Dawley rats. Nephrotic rats were randomly divided into three groups at 10 weeks of age as follows: control (control), Goreisan (0.5 g/kg (GL), and Goreisan 1.0 g/kg (GH) groups. Goreisan was administered once a day for 4 weeks. At 14 weeks of age, the rats were sacrificed for the evaluation of blood, urine, mRNA expressions, and kidney histopathology.

Results: Urine volume was significantly increased in the GL and GH groups than in the control group (Δurine volume: control; −1.25±2.48 mL, GL group; 9.83±4.16 mL, GH group; 10.00±2.62 mL). The GH group showed significantly lower urine osmotic pressure compared to the control group. There were no significant differences in urinary sodium excretion and serum arginine-vasopressin levels among the three groups. Subsequently, we assessed the expression of aquaporin (AQP) in kidney tissue using real-time PCR and immunohistochemical staining. The mRNA expression of AQP1, AQP2, AQP3, and AQP4 did not differ among the three groups. However, immunohistochemical staining showed that the localization of AQP2 at the apical plasma membrane of the collecting ducts was decreased by treatment with Goreisan. Furthermore, deterioration of kidney function was prevented by treatment with Goreisan. Histological analysis revealed that glomerular and tubulointerstitial damages were ameliorated in the GL and GH groups compared to the control group (glomerular damage score: control; 2.19±0.05, GL group; 1.71±0.05, GH group; 1.10±0.05, tubulointerstitial damage score: control; 2.55±0.09, GL group; 2.28±0.10, GH group; 2.12±0.10). In addition, urinary 8-OHdG, which is an oxidative stress marker, was significantly lower in the GL and GH groups than in the control group.

Conclusion: Our results suggested that Goreisan may have diuretic and renoprotective effects by suppressing the trafficking of AQP2 to the apical plasma membrane of the collecting ducts and possibly reducing systemic oxidative stress.

#5511
EXPLORING THE IMPACT OF POTENTIAL UREMIC TOXINS IN CHRONIC KIDNEY DISEASE BY PROTEOMICS: POTENTIAL BENEFITS OR ADVERSE EFFECTS?
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Background and Aims: Chronic kidney disease (CKD) is a progressive disorder characterized by a gradual reduction in kidney function. Proteomics, a large-scale analysis of protein modifications, has been used to study CKD and identify potential therapeutic targets. Studies have found that CKD is associated with changes in the expression of numerous proteins, including
those involved in inflammation, cell adhesion, and metabolism. Additionally, proteomic studies have been used to identify potentially novel uremic toxins, which are compounds that accumulate in the body due to impaired kidney function.

**Method:** We performed a cross-sectional shotgun-proteomic study of pooled plasma across CKD stages and compared them to healthy controls. After sample pooling and heparin-column purification we analysed proteomes from healthy to CKD stage 1 through 5 participants’ plasma by liquid-chromatography/mass-spectrometry.

**Results:** Our results of proteomic profiling of the plasma of the patients with CKD1-5, including those after kidney transplantation, unequivocally showed that the key processing of the disease, regardless of the type and function of the observed protein groups, occurs in stage 2 of CKD, which we could call the stage - a tipping point. Through the analysis of 453 proteins, 7 established uremic toxins of “middle molecular mass” were identified. Further analysis was conducted to identify potential candidates for new uremic toxins, resulting in the identification of 15 novel proteins that may have a systemic inflammatory effect, atherogenic potential, or increase the risk of cardiovascular diseases.

**Conclusion:** These findings suggest that proteomics can be used to identify novel uremic toxins and provide new insights into the pathophysiology of CKD and selected toxins arrange by toxic, beneficial effect or both. Further research is needed to validate these findings and explore the potential therapeutic implications of targeting these uremic toxins.

### #5219

**PeroxiRedoxins Are Related to eGFR Decline in IGA Nephropathy, Membranous Nephropathy and Lupus Nephritis: A 5-Year Follow-up**

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**Background and Aims:** Oxidative stress (OS) is known as a disturbance between pro- and antioxidant factors, that may lead to DNA or protein oxidation, resulting in cellular damage. PeroxiRedoxins (PRDXs) are enzymes with an antioxidant properties. They play dominant role in regulation of cellular peroxide levels, which is crucial in maintaining organisms’ oxidative balance. PRDXs types 1-5 are involved in the pathophysiology of various diseases (e.g. cancer, inflammatory, or renal). We aim to study their role as a prognostic marker of eGFR changes in IgA nephropathy (IgAN), lupus nephritis (LN) and membranous nephropathy (MN) patients.

**Method:** This is a retrospective 5-year-follow-up study of 108 IgAN, MN and LN patients, in whom PRDX 1-5 serum levels were assessed with ELISA in 2017. In 2022, we were able to collect the data out of 80 patients: IgAN (n=36); MN (n=22) and LN (n=22). The remaining 28 were considered as lost-to-follow-up, namely: lack of any medical results within last 2 years (n=23); on dialysis (n=2); after renal transplantation (n=2); deceased (n=1). We classified patients depending on the changes of eGFR (decline/stable/increase; Fig. 1) between baseline and after 5 year follow-up and the PRDX levels (high/medium/low; Table 1). The Mann Whitney-U, Kruskal-Wallis and Chi-Square Test were used for statistical analysis, the p-values <0.05 were considered significant.

**Results:** Baseline PRDX measurements indicated, that the mean concentrations of serum PRDX 1-5 differ between the glomerulonephropathies (GN). In 2022, we observed significantly different (P=.012) change of eGFR depending on the GN type. 16/80 individuals had eGFR decline and 75% of them were diagnosed with IgAN. The MN and LN groups had increase of eGFR in the last 5 years in most cases, probably as a result of the treatment. We verified if follow-up eGFR was associated with baseline PRDX levels. The 2022 eGFR differed significantly between the GNs depending on the level of serum PRDX 2, 4 and 5 at baseline (P=.002; P=.009; P=.006, respectively, Table 1).

**Conclusion:** Our results showed the link between serum PRDXs concentration and IgAN, MN and LN follow-up. Importantly, selected PRDXs might be used to predict eGFR decline, particularly in IgAN and LN.

### #6156

**Tubular Changes in Patients with Autosomal Dominant Polycystic Kidney Disease**

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**Background and Aims:** Autosomal dominant polycystic kidney disease (ADPKD) is characterized by the presence of multiple cysts, leading to progressive reduction in renal function and systemic involvement. The possible presence of tubular alterations has been suggested, but the mechanisms involved have not yet been fully identified. The study aims to highlight possible tubular alterations in ADPKD patients compared to patients with chronic kidney disease (CKD).
Method: A total of 145 patients were enrolled, including 37 with ADPKD and CKD, while 108 had CKD with the same clinical characteristics, and a comparative analysis of urinary and serum parameters were performed. A venous blood gas analysis was performed on each patient to assess serum pH, lactate concentration, and base excess, and a spot urine test was performed to evaluate urinary pH using a pH meter and specific gravity (SG).

Results: The comparative analysis of serum parameters showed a significant reduction in serum pH (spH) in ADPKD patients (p < 0.001), with a significant increase in lactates (1.3 vs 0.9 mmol/L, p < 0.001) and a significant reduction in base excess (BE) (p < 0.001). The evaluation of urinary parameters in ADPKD patients showed a urinary pH (upH) that was on average more acidic compared to patients with CKD (p < 0.001) with a reduction in the capacity to concentrate urine (p < 0.001). No statistically significant differences were found in terms of glomerular filtration rate between the two groups.

Conclusion: The collected data showed some alterations in the serum and urinary metabolic profile of ADPKD patients compared to the CKD group. The alterations in upH are consistent with those of recent studies in the literature, where it is hypothesized that a urinary concentration defect, already present in early stages, may cause a reduction in upH due to a reduced medullary trapping of ammonium and a reduced presence of bicarbonates. The hypothesis of a preferentially anaerobic metabolism in ADPKD patients is also in line with the increased levels of serum lactates.

Figure 1: Comparative Analysis of urinary parameters in ADPKD patients (n=37) and CKD patients (n=108). (a) Median values of urinary pH. (b) Median values of urinary specific gravity.

Figure 2: Comparative analysis of EGA parameters in ADPKD patients (n=37) and CKD patients (n=108). (A) Median pH values. (B) Median values of HCO₃⁻. (C) Median values of BE. (D) Median lactate values. The circles are the outliers.
Table 1: Comparative analysis between ADPKD patients and CKD patients.

<table>
<thead>
<tr>
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<th>ADPKD (n=37)</th>
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<td>57 (52.8) / 51 (47.2)</td>
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<td>Diabete, n (%)</td>
<td>3 (8.1)</td>
<td>5 (4.6)</td>
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<td>IVU in atto, n (%)</td>
<td>3 (8.1)</td>
<td>9 (8.3)</td>
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**B2 - GLOMERULONEPHRITIS & SYSTEMIC DISEASES (AAV, SLE, ETC.)**

#2907

ASYMPTOMATIC NEPHROTIC SYNDROME: AN INTERESTING PRESENTATION OF ADULT ONSET MINIMAL CHANGE DISEASE

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**Background and Aims:** Minimal change disease (MCD), a predominantly pediatric disease, is less common in adults. Patients often present with florid hypervolemia, manifested by significant lower extremity edema, anasarca, pericardial effusion or pleural effusion. Herein, we present a case of newly diagnosed MCD in an elderly gentleman with an atypical presentation.

**Method:** A 69 year old male with hypertension and benign prostate hypertrophy presented to the emergency department (ED). He was noted to have abnormal labs at an outside clinic on routine testing and was directed to the ED. In the ED, he was found to have a serum creatinine (SCr) of 10.89 mg/dL. Initial urine studies also revealed proteinuria of 11g/g with 6.5 g/g of albuminuria. Other initial labs were significant for a potassium of 4.5 mEq/L, BUN 126 mg/dL and albumin 2.2 g/dL with normal liver enzymes. Renal ultrasound was unremarkable. Upon further discussion with the patient, he endorsed long term daily use of diclofenac for many months. He denied any proton pump inhibitor or recent antibiotic use. He denied any fevers, nights sweats or weight loss to suggest Type B symptoms. There was no personal kidney disease history nor family history of kidney disease. He was a non-alcoholic and non-smoker. We continued to hold further non-steroidal anti-inflammatory medications as well as other nephrotoxic medications. Although patient had elevated SCr and azotemia, he did not meet any acute indications for dialysis and we continued to manage the patient conservatively. Serologies were negative for ANA, ANCA, Anti-GBM, HIV, hepatitis B and C, as well as antiPLA2R. Serum protein electrophoresis, kappa to lambda ratio, complements 3 and 4 were all within normal values. A kidney biopsy was revealing for patchy interstitial inflammatory infiltrate containing mononuclear cells admixed with few eosinophils on light microscopy as well as diffuse foot process effacement on electron microscopy (Figure 2). The patient had a one-week hospital stay with improvement of SCr to 2.29 mg/dL without any prednisone or treatment for MCD. Spot urine protein improved to 7.4 g/g by time of discharge. At clinic follow up 2 weeks later his creatinine had improved to 1.1 mg/dL with UPCR of 0.4 g/g.

**Results:** MCD is a podocytopathy that can occur in up to 10% of adults with nephrotic syndrome [1]. Secondary MCD has been reported with NSAIDs. Steroids are the first line therapy for MCD and can lead to remission in the majority of the cases. In patients who do not respond to steroids, calcineurin inhibitors or mycophenolate can be used. Our patient presented with biopsy proven-MCD that was presumed to be secondary to diclofenac. His clinical presentation was not characteristic of nephrotic syndrome with no edema. Few reports exist of spontaneous remission in these patients with most of the patient requiring steroids. While it is uncommon for patients with MCD to spontaneously resolve, not all patients with NSAID-induced MCD require treatment and these patients could be monitored conservatively.

**REFERENCE**

PROGNOSIS OF CRESCENTIC GLOMERULONEPHRITIS IN ADULTS

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Background and Aims: Crescentic glomerulonephritis (C-GN) is characterized by severe glomerular inflammation and injury that leads to crescent formation, rapid loss of kidney function and severe prognosis in absence of prompt immunosuppressive therapy. Depending on the histological findings, there are three main types of C-GN: anti-glomerular basement membrane antibody GN (anti-GBM GN), immune complex GN, and pauci-immune GN. This study aims to assess whether the kidney and vital outcome are different among the three histologic types of crescentic GN.

Method: This unicentric, retrospective study included seventy-six subjects [50% males, 55 (95%CI 52 to 60) years; eGFR 9.6 (95%CI 7.8-13.7) mL/min and proteinuria 1.9 (95%CI 1.5 to 2.6) g/g] that had undergone a kidney biopsy between 1st January 2008 and 31st December 2017 and had a histologic diagnosis of crescentic glomerulonephritis (crescent formation in more than 50% of the glomeruli). The subjects were followed for a mean of 47.6 (95%CI 33.5 to 61.6) months. Primary endpoints were the need of renal replacement therapy initiation (RRT) and all cause death. Kaplan-Meier method was used to evaluate kidney and patients’ survival and variables related to kidney and vital outcome were evaluated by multivariate Cox proportional hazard modelling. Patients were stratified in three groups according to the type of C-GN: pauci-immune GN (n=58 pts.), anti-GBM GN (n=9 pts.) and immune-complex GN (n=9 pts.).

Results: No demographic differences were found among the three groups. Except for a higher frequency of solid neoplasia in immune-complex GN group (2.7% vs 1.3% in pauci-immune GN vs. 0% in anti-GBM GN; P = .001), no other differences regarding the clinical or laboratory data were identified. Immunosuppressive treatment was very frequent, in more than 80% of subjects, regardless of the group, corticotherapy and cyclophosphamide being the most common immunosuppressive agents. During the follow-up period, 54% of subjects needed RRT and 19.2% died. The frequency of RRT initiation or death was not different among the three groups (P = .9 and P = .4). The univariate time-dependent analysis showed similar survival times among the analysed groups (log rank =0.9) (Figure 1). In the multivariate analysis, the only independent predictor of RRT was lower baseline eGFR (OR 0.49 (95%CI 0.31 to 0.78), P = .03). Time to death did not differ among groups (log rank P = .4) (Figure 2). The only independent predictor of death was higher Charlson comorbidity score (OR 56.8 (95%CI 6.3 to 512), p<0.001) in the Cox analysis.

Conclusion: In this cohort of subjects with crescentic glomerulonephritis, although limited by the low number of subjects, the kidney and vital prognosis seem to be similar indifferent of the histologic type of crescentic glomerulonephritis.
syndromewas positive in 61 cases (41%). The histopathological study showed positive anti-ds-DNA, mean C3 was 29 (84-122 mg/dL), and mean C4 was 0.6 g/24 h. ANA was positive in a diffuse pattern in all cases, ± proteinuria of 2.4 in 28.1%, hypertension in 24.3%, and renal failure in 17.5% with a mean creatinine of 1.75 mg/dL with de novo hematuria, a protein to creatinine ratio (RPC) 1.1 mg/g and candesartan (4 mg twice daily) was started. The patient received the second dose of COVID-19 vaccine 21 days after the first injection. Two weeks later he developed anorexia, nausea and de novo hematuria. He was admitted at the emergency department with deteriorating renal function with a sCr of 5.5 mg/dL, worsening hematuria with dysmorphic red blood cells and proteinuria (RPC 2.9 mg/g). Renal ultrasound was normal. Immunological studies revealed an elevated ANCA-MPO titer of 561. A kidney biopsy was performed and showed a crescentic necrotizing glomerulonephritis. Immunofluorescence confirmed paucimune glomerulonephritis. He was diagnosed with renal limited myeloperoxidase (MPO) ANCA AAV. He started 3 pulses of 500 mg I.V methylprednisolone followed by prednisolone 1 mg/kg/day after that. He also started rituximab (4 doses of 500 mg I.V once week apart). Despite the immunosuppression, the patient never recovered renal function and remained dialysis dependent.

Conclusion: Whether autoimmune diseases can be triggered after vaccination remains a matter of discussion among experts. ANCA associated vasculitis and autoimmune reactions have been reported with COVID-19 infection and following vaccination.

ANCA-ASSOCIATED VASCULITIS FOLLOWING PFIZER-BIONTECH COVID-19 VACCINE: TRUE ASSOCIATION OR CIRCUMSTANTIAL?

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Background and Aims: Antineutrophil cytoplasmatic antibody (ANCA)- associated vasculitis (AAV) is a small vessel vasculitis hallmarked by the presence of antibodies against antigens in cytoplasmic granules of neutrophils. Vaccines per se stimulate the immune system, including the innate and the adaptive immune response. Therefore, it is possible that an excess of autoimmunity is observed after vaccine administration. Vaccination (notably influenza) is a recognized trigger for the relapse of ANCA-associated vasculitis. ANCA associated vasculitis and autoimmune reactions have been reported with COVID-19 infection and following vaccination.

Results: We report the case of a Caucasian, 62 year-old-man, with a previous history of type 2 diabetes mellitus, hypertension and atrial fibrillation. Blood analysis one year before presentation showed preserved renal function and normal urinalysis. He received the first dose of Pfizer-BioNTech COVID-19 vaccine and two weeks later routine blood analysis showed acute kidney injury with serum Creatinine 1.75 mg/dL with de novo hematuria, a protein to creatinine ratio (RPC) 1.1 mg/g and candesartan (4 mg twice daily) was started. The patient received the second dose of COVID-19 vaccine 21 days after the first injection. Two weeks later he developed anorexia, nausea and de novo hematuria. He was admitted at the emergency department with deteriorating renal function with a sCr of 5.5 mg/dL, worsening hematuria with dysmorphic red blood cells and proteinuria (RPC 2.9 mg/g). Renal ultrasound was normal. Immunological studies revealed an elevated ANCA-MPO titer of 561. A kidney biopsy was performed and showed a crescentic necrotizing glomerulonephritis. Immunofluorescence confirmed paucimmune glomerulonephritis. He was diagnosed with renal limited myeloperoxidase (MPO) ANCA AAV. He started 3 pulses of 500 mg I.V methylprednisolone followed by prednisolone 1 mg/kg/day after that. He also started rituximab (4 doses of 500 mg I.V once week apart). Despite the immunosuppression, the patient never recovered renal function and remained dialysis dependent.

Conclusion: The findings of this study suggest that IFTA is a significant prognostic factor for the progression of renal failure in lupus nephritis, regardless of the class of the disease. The pathogenesis of tubulointerstitial lesions seems to be the result of circulating immune complexes specifically interacting with tubulointerstitial autoantigens.

THE INTERSTITIAL TUBULAR INJURY IN THE COURSE OF LUPUS NEPHRITIS

Najjar Mariem1, Rania Dridi1, Hana Ben Braie1, Hayet Kaaroud1, Fethi Ben Hamida1, Amel Harzallah1 and Ezzeddine Abderrahim1
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Background and Aims: Tubulo-interstitial involvement in lupus nephritis (LN) refers to the presence of interstitial fibrosis and tubular atrophy (IFTA) in the renal biopsies of patients with lupus. The impact of these features on patient outcomes has not been fully established. The aim of this study was to determine the correlation between IFTA and patient outcomes in LN.

Method: A retrospective descriptive study was conducted on 160 patients with systemic lupus erythematosus who underwent renal biopsy between 2020 and 2022. Clinical and biological data, as well as histologic findings, were analyzed to determine the outcomes associated with IFTA in LN. Other causes of tubulointerstitial nephritis like drugs and toxins were excluded.

Results: The study population consisted of 148 females and 12 males, with a mean age of 37.2 years (ranging from 18 to 62 years) at the time of renal biopsy. Hematuria was observed in 62.5% of patients, nephrotic syndrome in 28.1%, hypertension in 24.3%, and renal failure in 17.5% with a mean proteinuria of 2.4±0.6 g/24 h. ANA was positive in a diffuse pattern in all cases, positive anti-ds-DNA, mean C3 was 29 (84-122 mg/dL), and mean C4 was 16.2 (20-40 mg/dL). Other serology - ANCA and P-ANCA were all negative as well as negative HBV and HCV serology. However serology for Sjögren's syndrome was positive in 61 cases (41%). The histopathological study showed mild mononuclear and plasma cell infiltration of the interstitium, and tubular hyaline casts in 87% of cases. Examination of renal vessels was unremarkable in 94.5% of cases. IFTA was present in 72 patients (45%), with the most frequent glomerular involvement being LN class IV (55.5%) followed by LN class III (32.4%) with respectively (P = .09, P = .2) and was associated significantly with the anti-DNA antibody titer (P = .003). The severity of these lesions was found to be independently correlated with worsening of renal failure at 6 months follow-up (P = .02).

Conclusion: The findings of this study suggest that IFTA is a significant prognostic factor for the progression of renal failure in lupus nephritis, regardless of the class of the disease. The pathogenesis of tubulointerstitial lesions seems to be the result of circulating immune complexes specifically interacting with tubulointerstitial autoantigens.

#6178

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Results: We report the case of a Caucasian, 62 year-old-man, with a previous history of type 2 diabetes mellitus, hypertension and atrial fibrillation. Blood analysis one year before presentation showed preserved renal function and normal urinalysis. He received the first dose of Pfizer-BioNTech COVID-19 vaccine and two weeks later routine blood analysis showed acute kidney injury with serum Creatinine 1.75 mg/dL with de novo hematuria, a protein to creatinine ratio (RPC) 1.1 mg/g and candesartan (4 mg twice daily) was started. The patient received the second dose of COVID-19 vaccine 21 days after the first injection. Two weeks later he developed anorexia, nausea and de novo hematuria. He was admitted at the emergency department with deteriorating renal function with a sCr of 5.5 mg/dL, worsening hematuria with dysmorphic red blood cells and proteinuria (RPC 2.9 mg/g). Renal ultrasound was normal. Immunological studies revealed an elevated ANCA-MPO titer of 561. A kidney biopsy was performed and showed a crescentic necrotizing glomerulonephritis. Immunofluorescence confirmed paucimmune glomerulonephritis. He was diagnosed with renal limited myeloperoxidase (MPO) ANCA AAV. He started 3 pulses of 500 mg I.V methylprednisolone followed by prednisolone 1 mg/kg/day after that. He also started rituximab (4 doses of 500 mg I.V once week apart). Despite the immunosuppression, the patient never recovered renal function and remained dialysis dependent.

Conclusion: Whether autoimmune diseases can be triggered after vaccination remains a matter of discussion among experts. ANCA associated vasculitis and autoimmune reactions have been reported with COVID-19 infection and following vaccination, which prompts the question whether this response could be a direct reaction to the RNA present in the vaccine. While an association with de novo ANCA vasculitis and COVID-19 vaccine may be possible, further investigation is necessary.

RENA L LIMITED VASCULITIS: DATA FROM A CROATION REFERR AL CENTER

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1Dubrava Clinical Hospital, Department of Nephrology and Dialysis, Zagreb, Croatia, 2Galway University Hospital, Department of Internal Medicine, Galway, Ireland and 3Dubrava Clinical Hospital, Department of Clinical Pathology, Zagreb, Croatia

Background and Aims: Small vessel vasculitis and in particular ANCA associated vasculitis (AAV) are diseases with variable clinical presentation. Renal limited vasculitis (RLV) can vary in presentation and characteristics compared to systemic disease. There is a tendency to categorise RLV as a part of microscopic polyangiitis (MPA) spectrum though there seem to be differences in terms of both histology and serology between RLV and MPA. We present data on patients with renal limited vasculitis from our referral center.
Method: This study included 106 consecutive AAV patients with biopsy proven renal involvement in the period from 2007-2017. Category variables were analysed with Fisher Exact testom and continuous with Kruskal-Wallis testom. Statistical difference was then analysed posthoc with Chi-square test. Kaplan Meyer survival analysis and multivariate Cox proportional hazard regression analysis were used to explore difference between clinical phenotypes and finding significant predictors regarding outcomes which were defined as combined outcome end-stage renal disease and death (ESRD), ESRD alone, the death alone and relapse rate.

Results: Out of 106 AAV patients with renal involvement in our database: 66 (61.1%) MPA, 20 (18.5%) GPA (granulomatosis with polyangitis), 20 (18.5%) RLV. In RLV group 14 (70%) were female and average age was 55 (IQR 47-60). Average Scr in RLV group was 234 μmol/l (IQR 168-376,5) and median proteinuria was 3.3g/24h (IQR 0,9-3,8) and most of these patients were treated with either nephrotic syndrome (30%) or RPGN (30%). Serologically 90% of RLV patients were ANCA negative and 10% were MPO-ANCA positive. Histologically (Berden classification) 60% had mixed class, 25% crescentic, 10% focal and 1% sclerotic. Average BVAS score was 14 (IQR 12-17). Compared to MPA and GPA, RLV patients were younger (p=0,058), had less expressed constitutional symptoms (p=0,013) with lower average BVAS (p=0,0001) and lower CRP levels (p=0,001). Though there was no significant difference of average Scr level RLV patients presented more often with nephrotic syndrome (p=0,014), had histological predominantly mixed class (p=0,006) and higher interstitial fibrosis and tubular atrophy (IFTA) percentage (p=0,086). Interestingly, compared to MPA and GPA majority of RLV patients were ANCA negative (p=0,001). There were no statistically significant differences in treatment used both in induction (including need for dialysis and/or PLEX) or remission maintenance treatment between RLV, MPA and GPA group. In survival analysis there was no statistical differences for all of the outcomes between RLV group, MPA and GPA group.

Conclusion: RLV can be challenging disease considering its clinical presentation but also characteristics of renal involvement in terms of more often nephrotic proteinuria and higher IFTA percentage. This might suggest that these patients could have slower disease course (so called slower progressors). Also interestingly in our cohort most of these patients were ANCA negative which also makes diagnosis predominantly a combination of clinical presentation and histology thus prompting a question of how should we classify RLV within a spectrum of small vessel vasculitis. More research is needed to better understand the RLV.

#2598
KLOTHO DEFICIENCY INDUCES REGULATORY T CELLS IN MURINE LUPUS NEPHRITIS
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1International University of Health and Welfare, Nephrology, Tokyo, Japan, 2Kitsato University, Biochemistry, Kanagawa, Japan, 3Saitama Medical University, Nephrology, Saitama, Japan, 4Kagawa University, Pharmacology, Kagawa, Japan and 5Keio University, Nephrology, Tokyo, Japan

Background and Aims: Recent studies demonstrate that klotho deficiency participate in various chronic kidney disease. However, it has not been fully assessed the influence of klotho in autoimmune kidney diseases. On the one hand, klotho is known but rare entity, where calcineurin inhibitor treatment may be required to generate and maintain regulatory T cells with inducing FOXP3, an important cell population for immunological tolerance.

Method: NZBW1F mice were used as a model of lupus nephritis. NZBW1F mice were housed separately in metabolic cage, and divided into two groups (n=10 for each): one group was treated with daily subcutaneous injection of klotho protein (20 μg/kg/day), and the other received vehicle alone. Systolic blood pressure was measured by tail-cuff method. Glomerular filtration rate was assessed using FITC-inulin. Four weeks later, the animals were killed to harvest the spleen and kidneys for analyses.

Results: Klotho supplementation suppressed blood pressure, 8-epi-prostaglandin F2α excretion and renal angiotensin II levels (p<0.05 for all) without changes in albuminuria and glomerular filtration rate in NZBW1F mice. Exogenous klotho protein supplementation increased serum klotho levels, urine klotho excretion, and endogenous renal expression of klotho in NZBW1F mice (p<0.05 for all). Surprisingly, anti-double strand DNA antibody was slightly elevated in klotho-treated NZBW1F mice (p<0.05). Glomerular pathology and interstitial cell infiltration were similar between 2 groups. The spleen tended to be greater in klotho-treated group, but statistical significance was not observed. In concisely, CD4+FOXP3+ T cells were unaltered between 2 groups. However, klotho supplementation reduced CD4+FOXP3+ T cells in spleen of NZBW1F mice (p<0.05).

Conclusion: The present data indicated that klotho protein supplementation suppressed blood pressure, 8-epi-prostaglandin F2α excretion and renal angiotensin system, ameliorating blood pressure and oxidative stress. Our results suggest that klotho supplementation worsened auto-antibody, possibly by inhibiting TGFβ with resultant deterioration in regulatory T cells. The present findings implicate that although klotho may not be suitable for the management of autoimmune kidney diseases, such as lupus and ANCA-related nephritis, klotho supplementation for dialysis patients could mitigate against the defect in cellular immunity and susceptibility to infections including tuberculosis and COVID-19.

#3928
NEPHROTIC SYNDROME IN LIVER DISEASES: PRESENTATION OF TWO UNUSUAL AND INSTRUCTIVE CASES
Nóra Lédi1, Deján Dobizi2 and Anikó Folhofer3
1Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary and 2Semmelweis University, Department of Pathology, Forensic and Insurance Medicine, Budapest, Hungary

Background and Aims: However, there are known associations between chronic liver diseases and glomerulopathies, here we report two rare cases, where diagnostic and therapeutic challenges influenced the patients’ care.

Method: The patients’ medical parameters were obtained from the electronical charts of the hospital. Kidney biopsy samples were examined with immunofluorescence (frozen samples), light microscopy (paraffin embedded tissue, 2-3 μm sections) and electron microscopy (1 μm, toluidine blue). The follow-up time was 24 months for case 1 and 23 months for case 2. Both patients gave written consent to the presentation of the reports.

Results: Case 1: A 42-year-old man with recent pulmonary embolism was presented in our hospital with nephrotic syndrome and reduced kidney function (estimated glomerular filtration rate (eGFR): 43 ml/min/1.73 m², urinary protein/creatinine ratio (UPCR): 2124 mg/mmol, serum albumin: 24 g/L). Kidney biopsy confirmed primary membranous nephropathy (MN). The anti-phospholipase-A-2 receptor (aPLA2R) was positive in high titer, and PLA2R positivity was also seen in the renal sample. Additionally, an active hepatitis C (HCV) infection with viremia was confirmed. The nephrotic syndrome was worsened with severe edema requiring ultrafiltration; therefore, after one-week direct anti-HCV therapy, mephyblendesilone was started. Immunosuppressive therapy had to be determined soon due to severe infections. With combined direct antiviral treatment, HCV PCR test became negative, which was followed by the disappearance of the aPLA2R antibodies. The patient’s kidney function stabilized and there are no symptoms of nephrotic syndrome (eGFR: 52 ml/min/1.73 m², serum albumin: 37 g/L, UPCR: 321 mg/mmol).

Case 2: A 66-year-old woman was admitted to the hospital with coronavirus disease (COVID)- associated pneumonia. At admission, nephrotic syndrome was diagnosed (eGFR: 29 ml/min/1.73 m², serum albumin: 22 g/L, proteinuria: 8 g/day). Additionally, elevated gamma glutamyl transferase was registered. Immune serology was negative for aPLA2R, but antinuclear antibodies (anti-cytoplasm, chromatin, Ro), and anti-mitochondrial antibodies (AMA-M2) were positive. Biopsies were performed after the COVID infection. Liver biopsy confirmed primary biliary cholangitis (stage 1-2), while the kidney biopsy showed secondary membranous nephropathy with signs of potential monoclonal gammopathy (monoclonal immunoglobulin-G1-kappa deposits). After the exclusion of malignancies, monoclonal gammopathy, and other causes of the secondary MN, PBC-associated MN was diagnosed. Based on case reports in the literature, cyclosporine A treatment was started. The patient reached complete remission in 5 months (no significant proteinuria, stable eGFR around 34 ml/min/1.73 m²).

Conclusion: The association of an active HCV infection and an aPLA2R positive MN has not been reported in the literature. Nephrotic syndrome and the aPLA2R positivity disappeared related to the direct antiviral treatment, which may indicate a diagnosis of secondary MN. PBC-associated secondary MN is a known but rare entity, where calcineurin inhibitor treatment may reduce the symptoms of nephrotic syndrome.
## Abstract

### #5132

**POST-COVID-19 ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE: TWO CLINICAL CASES**

Carolina Branco, Joana Gameiro, João Oliveira, Bernardo Marques Da Silva, Nadiesda Peres, José Agapito Fonseca, Paulo Fernandes, Iolanda Godinho, Cristina Outerelo, Sofia Jorge, José António Lopes and Estela Nogueira

Centro Hospitalar Universitário Lisboa Norte, Nephrology and Renal Transplantation, Lisboa, Portugal

**Background and Aims:** Acute kidney injury is a common complication in patients hospitalized with COVID-19, has multiple aetiologies, and is usually multifactorial. We present two cases of anti-glomerular basement membrane (anti-GBM) disease diagnosed after SARS-CoV-2 infection, suggesting a causal correlation.

**Case Reports:** A 76-year-old female, with chronic kidney disease (serum creatinine 1.5mg/dL), hypertension, weight loss (16 Kg/6 months) and a pancreatic nodule under surveillance, presented to the emergency department with 1 week of nausea, vomits, diarrhoea and oliguria, as well as a history of mild SARS-CoV-2 infection 2 weeks before presentation. Lab work revealed severe anaemia (7.4 g/dL), inflammatory markers elevation, nephrotic proteinuria (proteinuria/creatininuria ratio 30 g/g), leucoerythrocyturia, serum creatinine of 19.3 mg/dL, hyperkalaemia and metabolic acidosis requiring dialysis induction. Renal ultrasound showed signs of chronicity and several cysts. Aetiological study disclosed positive anti-GBM antibody (1800 U/L) and negative ANCA. Complementary study failed to identify pulmonary involvement or neoplasms. Given the severity of the renal dysfunction along with the absence of alveolar haemorrhage, immunosuppression and plasmapheresis were not initiated. Patient was discharged and remains dialysis dependent.

A 65-year-old male smoker with type 2 diabetes and hypertension, weight loss (16 Kg/6 months) and a history of dyspnoea and haemoptysis in the past 3 days. Lab work exposed moderate anaemia (9.7 g/dL), elevated inflammatory markers, serum creatinine of 1.18 mg/dL (previously 0.8 mg/dL), leucoerythrocyturia and positive SARS-CoV-2 test. Angio-Computed Tomography exhibited known pulmonary fibrosis and possible bacterial superinfection. Despite antibiotic therapy (10 days of levofloxacin), haemoptysis remained and kidney function continuously worsened (serum creatinine 2.1 mg/dL). Complementary study showed positive ANCA-MPO (1125.4 U/L) and anti-GBM antibody (460.8U/L). Renal ultrasound was innocent. Kidney biopsy revealed: 6 glomeruli with cellular crescents with segmental necrosis, 3 with focal Bowman's capsule rupture; erythrocyte casts; intimal arterial fibrosis; moderate tubular atrophy; diffuse linear deposits of IgG. Immunosuppression was initiated with prednisolone (1 mg/Kg/day), cyclophosphamide (3x 12.5mg/Kg;750 mg, 2x 500 mg), rituximab (2x 1g), immunoglobulin (1x 2 g/Kg) and plasmapheresis (15 sessions). Kidney function continued to deteriorate (maximum serum urea 306 mg/dL, maximum serum creatinine 6.92 mg/dL) requiring dialysis induction 3 weeks after the beginning of immunosuppression. Even though haemoptysis ceased, the patient remains dialysis dependent 8 months after.

**Conclusion:** Literature reports an increase of Anti-GBM disease since the beginning of the pandemic. The presented cases support the apparent correlation, suggesting SARS-CoV-2 as a precipitant of this disease by endothelial injury with basal membrane exposure and autoantibody development. In the second case, the authors assume a subacute ANCA-MPO vasculitis with superimposed anti-GBM (eventually precipitated by COVID-19). Even though the causal association is not established, we highlight the importance of clinical suspicion of this rare aetiology in cases of acute kidney injury after SARS-CoV-2 infection.

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### #3081

**ASSOCIATION OF URINE PROTEIN EXCRETION LEVELS, AS A MEASURE OF DISEASE ACTIVITY, AND QUALITY OF LIFE IN IGA NEPHROPATHY PATIENTS**

Jonathan Barratt1, Sarah Clayton2, Mollie Lowe1, James Jackson2, Adam Roughley3 and Wan Tsong3

1 University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom, 2 Adelphi Real World, Bollington, United Kingdom and 3 Omeros Corporation, Health Economics & Outcomes Research (Medical Affairs), Seattle, United States of America

**Background and Aims:** Little is known about the quality of life (QoL) of patients with IgA nephropathy (IgAN). Understanding the relationship between disease activity (as measured by urine protein excretion [UPE]) and QoL could allow decision-makers to understand how treatments that improve UPE might improve patient QoL.

**Methods:** The 2021 United States subset of the Adelphi IgAN Disease Specific Programme™ was a point-in-time survey of 43 nephrologists (who completed structured forms for 305 IgAN patients) and 70 patients (who elected to complete patient surveys of the 305). This analysis utilised physician-reported data (patient demographics, disease characteristics, and current 24-hour UPE levels [categories: <0.5, >0.5 to ≤1, >1 to ≤2, >2 to ≤3.5, >3.5 grams/day]) and patient-reported data (symptoms, Kidney Disease Quality of Life [KDQOL] scores, and EQ-5D scores). The association between UPE and patient-reported symptoms was evaluated using chi-squared and Fisher’s exact tests. The association between UPE and QoL (KDQOL, EQ-5D) was evaluated using generalized linear regression to adjust for age, sex, chronic kidney disease stage, corticosteroid use, and non-steroidal immunosuppressant use.

**Results:** The analytical dataset included 69 patients with UPE data (reported by 8 physicians) out of the 70 patients who completed the patient survey. Of these 69, data were complete for the symptoms (n=63), KDQOL (n=60), and EQ-5D (n=67). Patients were an average age of 43 years, an average BMI of 26.3, 49% male, 55% White, 23% Asian, 64% never smokers, 78% in full-time occupation, and 74% with commercial health insurance. The most prevalent comorbidities were hypertension (33%), hyperlipidaemia (30%), and diabetes (11%). UPE was not associated with any demographic characteristics, regular dialysis, or kidney transplants. Among comorbidities, higher UPE was associated with a higher percentage of hyperlipidaemia (P = .03). Among medications for IgAN, higher UPE was associated with a higher percent use of diuretics (P = .046), sodium-glucose co-transporter 2 inhibitors (P = .002), corticosteroids (P = .0009), non-steroidal immunosuppressants (P<.0001), and anti-depressants.

**Conclusion:** Increased UPE is associated with worse QoL in IgAN. Further studies are needed to determine the most effective treatments to improve UPE and QoL in IgAN patients.
Table 1: Association of urine protein excretion and KDQOL.

<table>
<thead>
<tr>
<th>KDQOL means (range 0-100)*</th>
<th>Urine protein excretion levels**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 0.5 g/d</td>
</tr>
<tr>
<td>n</td>
<td>15</td>
</tr>
<tr>
<td>Burden</td>
<td>71.9</td>
</tr>
<tr>
<td>Symptoms</td>
<td>86.3</td>
</tr>
<tr>
<td>Effects</td>
<td>81.5</td>
</tr>
<tr>
<td>Physical Health</td>
<td>49.1</td>
</tr>
<tr>
<td>Mental Health</td>
<td>51.1</td>
</tr>
</tbody>
</table>

* Higher scores indicate better quality of life.
** Adjusted for sex, age, CKD stage, corticosteroid use, non-steroidal immunosuppressant use.

Table 2: Association of urine protein excretion and EQ-5D.

<table>
<thead>
<tr>
<th>EQ-5D means (range 0-1)*</th>
<th>Urine protein excretion levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 0.5 g/d</td>
</tr>
<tr>
<td>N</td>
<td>15</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.960</td>
</tr>
<tr>
<td>Adjusted **</td>
<td>0.943</td>
</tr>
</tbody>
</table>

* Higher scores indicate better quality of life.
** Adjusted for age, sex, CKD stage, corticosteroid use, non-steroidal immunosuppressant use.

**References**


**Abstract**

Background and Aims: Crescentic glomerulonephritis (CrGN) is a disease presented as nephritic syndrome with hypocomplementemia usually secondary to a skin or throat infection by beta hemolytic Streptococcus and with histopathological findings of endocapillary proliferation. C3 deposits along the capillary wall and mesangium, subepithelial immune complex deposits and IF positive for IgG. There are other unusual presentations of PIGN with IgA dominance or C3-IgA codominance.

Method: A 58-year-old Guatemalan male, with history of one-week duration pain in the right upper quadrant associated with jaundice, diagnosed with cholangitis and intravenous antibiotics use. History of consumption of 10 beers a month for 40 years. No other medical history. During hospitalization, presented a lower-limb cellulitis, for which clindamycin was started. Blood cultures were taken and were positive for S. epidermidis and AKI (Cr 2.84 mg/dl) was observed, associated with de novo appearance of hematuria (80% acanthocytes), proteinuria (580mg/day) and hypertension. Diagnostic approach for nephritic syndrome was performed obtaining: C3 0.592 (low) ANA, ANCA, HIV-HCV-HBV negative, total cholesterol 184 mg/dl, albumin 2.78 g/dl.

Results: Renal biopsy was performed and reported: PIGN with IgA dominance with extra capillary proliferation. Reason why pulses of methylprednisolone were given for 3 days and then oral prednisone (1 mg/kg/day), progressively decreasing it until it was discontinued. Resolved the soft tissue infection and was discharged. At 1-month follow-up as outpatient, was evidence of a 50% decrease in proteinuria compared to baseline, disappearance of hematuria but with persistent of high Cr (2.09 mg/dl).

Conclusion: IgA-dominant PIGN is characterized by usually presenting in patients >60 years with DM, alcohol consumption and staphylococcal skin infections. It can present hypocomplementemia and histopathological findings are characterized by IgA dominance over C3 and no IgG in IF. Elevated serum IgA levels may be involved in the pathogenesis. Treatment is based on eradication of the infection with antibiotics and in some cases the use of steroids is suggested depending on the aggressiveness of the lesion and the presence of crescents in the renal biopsy. It has worse prognosis than the traditional PIGN.

**#5035**

**CRESCENTIC GLOMERULONEPHRITIS IN A PAEDIATRIC POPULATION: A SINGLE-CENTRE EXPERIENCE FROM SOUTH ASIA**

Basavaraj Sajjan¹, Dharmandr Bhadouria¹, Narayan Prasad¹, Anupama Kaul¹ and Manoj Jain²

¹Sanjay Gandhi Postgraduate Institute of Medical Sciences, Nephrology, Lucknow, India and ²Sanjay Gandhi Postgraduate Institute of Medical Sciences, Pathology, Lucknow, India

**Background and Aims:** Crescentic glomerulonephritis (CrGN) is defined clinically by Rapidly progressive renal failure due to crescent formation in ≥ 50% of glomeruli. Most of these patients have a relatively poor prognosis. Therefore, early diagnosis and treatment of these patients may help to prevent renal complications. There is a scarce data on pediatric CrGN. We aim to study the etiopathogenesis and outcome of CrGN in children and adolescents.

**Method:** Retrospective observational study of pediatric patients of age ≤ 18 years with biopsy-proven CrGN from January 2010 to December 2021. Clinical and laboratory data with validated renal biopsy report were obtained from the hospital information system. CrGN was defined as crescents in ≥ 50% glomeruli. Rapidly Progressive Glomerulonephritis (RPGN) is the clinical presentation of CrGN, which is classified based on immunofluorescence findings and serology. Risk factors predicting poor renal outcome were determined.

**Results:** Of 47 patients (13.8% of total biopsy proven CrGN) patients, 30 were male patients (M:F ratio 1.7:1) and median age of 14 (range 7–18) years. 32 (68%) were ANCAnegative (71%). Poor renal outcome is related to severity of initial presentation and extent of IFTA, and serum creatinine at presentation.

**Conclusion:** Immune complex GN is the most common etiology, that constitutes 68% of patients with crescentic GN. Majority of pauci-immune GN were ANCA negative (71%). Poor renal outcome is related to severity of initial presentation and extent of IFTA.

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**#2627**

**IGA-DOMINANT POSTINFECTIOUS GLOMERULONEPHRITIS, “THE OTHER SIDE OF THE COIN”: A CASE REPORT**

Rodolfo Moreno¹, Guillermo Navarro Blackaller³, Jonathan S. Chávez-Iniguez² and Werner De Leon³

¹Military Medical Center, Ciudad de Guatemala, Guatemala, ²Mariano Gálvez University of Guatemala, Ciudad de Guatemala, Guatemala, ³Hospital Civil de Guadalajara Fray Antonio Alcalde, Guadalajara, Mexico and ⁴San Carlos University, Ciudad de Guatemala, Guatemala

**Background and Aims:** Postinfectious glomerulonephritis (PIGN) is a disease presented as nephritic syndrome with hypocomplementemia usually secondary to a skin or throat infection by beta hemolytic Streptococcus and with histopathological findings of endocapillary proliferation, C3 deposits along the capillary wall and mesangium, subepithelial immune complex deposits and IF positive for IgG. There are other unusual presentations of PIGN with IgA dominance or C3-IgA codominance.

**Method:** A 58-year-old Guatemalan male, with history of one-week duration pain in the right upper quadrant associated with jaundice, diagnosed with cholangitis and intravenous antibiotics use. History of consumption of 10 beers a month for 40 years. No other medical history. During hospitalization, presented a lower-limb cellulitis, for which clindamycin was started. Blood cultures were taken and were positive for S. epidermidis and AKI (Cr 2.84 mg/dl) was observed, associated with de novo appearance of hematuria (80% acanthocytes), proteinuria (580mg/day) and hypertension. Diagnostic approach for nephritic syndrome was performed obtaining: C3 0.592 (low) ANA, ANCA, HIV-HCV-HBV negative, total cholesterol 184 mg/dl, albumin 2.78 g/dl.

**Results:** Renal biopsy was performed and reported: PIGN with IgA dominance with extra capillary proliferation. Reason why pulses of methylprednisolone were given for 3 days and then oral prednisone (1 mg/kg/day), progressively decreasing it until it was discontinued. Resolved the soft tissue infection and was discharged. At 1-month follow-up as outpatient, was evidence of a 50% decrease in proteinuria compared to baseline, disappearance of hematuria but with persistent of high Cr (2.09 mg/dl).

**Conclusion:** IgA-dominant PIGN is characterized by usually presenting in patients >60 years with DM, alcohol consumption and staphylococcal skin infections. It can present hypocomplementemia and histopathological findings are characterized by IgA dominance over C3 and no IgG in IF. Elevated serum IgA levels may be involved in the pathogenesis. Treatment is based on eradication of the infection with antibiotics and in some cases the use of steroids is suggested depending on the aggressiveness of the lesion and the presence of crescents in the renal biopsy. It has worse prognosis than the traditional PIGN.

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**#6843**

**CITATION CLASSICS IN LUPUS NEPHRITIS: A BIBLIOMETRIC ANALYSIS**

Arunkumar Subbiah¹ and Sudarshan K²

¹AIIMS, New Delhi, Nephrology, New Delhi, India and ²JIPMER, Pediatrics, Puducherry, India

**Background and Aims:** Lupus nephritis is an important risk factor for morbidity and mortality in systemic lupus erythematosus. During the past three decades, extensive research has been done to address this important complication and devise better management strategies. In this article we aimed to perform a thorough assessment of the research productivity in lupus nephritis by identifying the 100 most-cited articles in lupus nephritis.

**Methods:** The top 100 most-cited English language articles on lupus nephritis from 1990 were examined by bibliometric analysis from the Google Scholar

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**Table 1: Breakdown of Berden classification by renal biopsy and corresponding serological ANCA subtype.**

<table>
<thead>
<tr>
<th>MPO/pANCA (n=53)</th>
<th>PR3/cANCA (n=21)</th>
<th>ANCA negative (n=5)</th>
<th>p-value between MPO/PR3 groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerotic 23%</td>
<td>14%</td>
<td>20%</td>
<td>0.53</td>
</tr>
<tr>
<td>Crescentic 19%</td>
<td>28%</td>
<td>20%</td>
<td>0.37</td>
</tr>
<tr>
<td>Mixed 19%</td>
<td>10%</td>
<td>0%</td>
<td>0.49</td>
</tr>
<tr>
<td>Focal 39%</td>
<td>48%</td>
<td>60%</td>
<td>0.61</td>
</tr>
</tbody>
</table>
ANCA AND IGA NEPHROPATHY: ASSOCIATION OR PROGNOSTIC FACTOR

Nouha Ben Mahmud, Meriem Ben Salem, Manel Ben Salah, Ahmed Letaief, Mouna Hammouda, Aloui Sabra and Habib Skhiri

Monastir, Tunisia

Background and Aims: Immunoglobulin A (IgA) nephropathy (IgAN), the most prevalent form of primary glomerulonephritis worldwide, is characterized by mesangial cell proliferation, matrix expansion, and mainly mesangial IgA deposition, often in conjunction with C3 and IgG and/or IgM. Its pathogenesis is enigmatic. It is reported that approximately 35-42% of IgAN patients have a history of macrohaematuria before kidney biopsy. Its a benign pathology which sometimes could be associated with crescentic proliferation and more rarely by the presence of ANCA antibodies.

Method: We retrospectively analyzed the epidemiologic, clinical and histological data of 27 patients with IgA nephropathy proven by biopsy and we compared 2 groups ANCA positive and ANCA negative patients.

Results: The present study involved 27 patients, 18 men and 9 women, the average age was 27.9 years 3 patients were ANCA positive compared to 24 ANCA negative; (2 were MPO-ANCA and 1 PR3-ANCA). ANCA positive patients were older, with more severe initial renal function, lower hemoglobin, and a higher percentage of general symptoms than the ANCA negative ones. Patients were older, with more severe initial renal function, lower hemoglobin, and a higher percentage of general symptoms than the ANCA negative ones. ANCA positive patients with IgA nephropathy had a higher percentage of crescentic glomeruli (54.5%) compared with ANCA-negative patients with crescentic IgA nephropathy (26%). The ANCA positive patients were all treated by solumedrol bolus and oral corticosteroid and showed more severe prognosis, the 3 patients progressed to ESKD. 4 ANCA-negative patients were treated with oral corticosteroid, some from the other 20 patients have been put on renin angiotensin system blockers treatment and thy showed a better renal prognosis.

Conclusion: ANCA patients with ANCA positivity showed more severe clinical and histological features when compared with ANCA-negative IgAN patients and lower renal prognosis. The ANCA antibodies should be screened in patients with severe forms of IgAN.

Table 1:

<table>
<thead>
<tr>
<th></th>
<th>ANCA positive</th>
<th>ANCA negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>N of patients</td>
<td>3</td>
<td>24</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.3</td>
<td>27.5</td>
</tr>
<tr>
<td>Initial Scr (microles/L)</td>
<td>200</td>
<td>118.13</td>
</tr>
<tr>
<td>Proteinuria (g/l)</td>
<td>2.85</td>
<td>2.36</td>
</tr>
<tr>
<td>Hemoglobin (g/l)</td>
<td>9.8</td>
<td>11.9</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mmHg)</td>
<td>105</td>
<td>112</td>
</tr>
<tr>
<td>Systemic symptoms (%)</td>
<td>100</td>
<td>50</td>
</tr>
</tbody>
</table>

N : number, Scr : serum creatinine

REFERENCES

A CASE OF PODOCYTE DISEASE WITH AZOTEMIA FOLLOWING TREATMENT WITH INTRAVENOUS IBANDRONATE
Beom Kim1, Yerin Chung1, Woojin Jang1, Jin Seon Jeong1, Sanghee Lee1, Dong-Young Lee1, Kyounghyoub Moon1 and Huiseo Kim2

1Veterans Health Service Medical Center, Division of Nephrology, Department of Internal Medicine, Seoul, Rep. of South Korea and 2Gwangmyeong Sungae Hospital, Department of Nephrology, Gwangmyeong, Gyeonggi-do, Rep.of South Korea

Background and Aims: Bisphosphonate use may induce several types of nephrotoxicity. There are many reports on pamidronate-associated glomerular disease, such as focal segmental glomerulosclerosis and zoledronate-associated acute tubular necrosis. However, there are limited reports on ibandronate-associated nephrotoxicity. Herein, we describe a case of podocyte disease accompanied with azotemia following intravenous administration of ibandronate.

Method: Case report

Results: An 88-year-old female was referred to the emergency room due to grade 4 edema that developed 1 month before. The patient was diagnosed with osteoporosis 20 months earlier, for which she received quarterly intravenous administration of ibandronate (3 mg). The last dose was administered 2 weeks ago. The patient had no history of diabetes, hypertension, or chronic kidney disease. Laboratory tests revealed heavy proteinuria with a protein/creatinine ratio (PCR) of 32 and hypoalbuminemia (1.9 g/dL) with elevated serum creatinine (sCr) (1.8 mg/dL). Values of serum complement and electrophoresis were within normal ranges. The renal ultrasonogram was unremarkable. A renal biopsy was performed and light microscopy showed mild mesangial hypercellularity and segmental amorphous collagenous deposition in the glomerulus (Fig. 1-A). The tubules revealed focal marked atrophy and interstitial fibrosis (Fig. 1-B). Immunofluorescence studies were unremarkable. Electron microscopy showed diffuse effacement of foot processes and no electron-dense deposit (Fig. 1-C), consistent with podocyte disease favoring focal segmental glomerulosclerosis. The patient was treated with tacrolimus and fimasartan. Steroid use was spared owing to severe osteoporosis. Three months later, the edema subsided and laboratory findings improved (PCR 0.64, serum albumin 4 g/dL, sCr 1.23 mg/dL).

Conclusion: Compared to pamidronate and zoledronate, ibandronate is more highly protein-bound with a significantly shorter renal tissue half life, which might explain the rarity of ibandronate-related nephrotoxicity. Contrary to the trend of other bisphosphonates nephropathies, our case showed simultaneous podocyte disease and tubule damage. We recommend close monitoring of proteinuria and renal function for prompt nephrotoxicity detection in patients treated with ibandronate.
Figure 1: Renal Biopsy was consistent with podocyte disease favoring as focal segmental glomerulosclerosis. A. The light microscopy (Periodic acid-Schiff staining, X 400). showed normal size of glomerulus, mild mesangial hyper-cellularity and segmental amorphous collagenous deposition in glomerulus. B. Tubules revealed focal marked atrophy, interstitial fibrosis. C. Electron microscopy showed diffuse effacement of foot processes and no electron-dense deposit.

#4773
INFECTIVE ENDOCARDITIS COMPLICATED BY RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS: BEYOND ANTIBIOTICS - TO TREAT OR NOT TO TREAT?
Carla Nicolau, Miguel Bigotte Vieira, Maria Do Mar Menezes, Mário Góis, Helena Viana, João Sousa and Manuel Anibal A. Ferreira
Hospital Curry Cabral, Nephrology, Lisboa, Portugal

Background: A significant proportion of patients with infective endocarditis, present with acute renal failure related to infective endocarditis-associated glomerulonephritis (IEAGN). However, IEAGN differs from other infection-related glomerulonephritis because it may present with clinical and serological disturbances resembling autoimmune diseases such as antinutrophil cytoplasmic antibody (ANCA)-associated vasculitis. Its development introduces the dilemma of determining the best treatment approach. Immunosuppressive therapy added to antibiotic treatment may be beneficial for recovery of renal function in some cases of IEAGN with positive ANCA serology, although this approach is still controversial.

Case presentation: A 32-year-old man presented with fever, fatigue, purpura and rapidly progressive glomerulonephritis. He had a history of atrioventricular septal defect corrected at 9 years of age. Blood analysis showed anemia, acute kidney injury and positive ANCA proteinase 3 (PR3). Urine analysis revealed hematuria and proteinuria. Echocardiogram showed vegetation on the mitral valve with moderate to severe mitral regurgitation. Blood cultures showed Streptococcus mitis. After 14 days of intensive antibiotic regimen, kidney function rapidly deteriorated and ANCAtiters remained high. Arenal biopsy was performed and showed crescentic necrotizing glomerulonephritis with deposition of C3 and IgM – compatible with infection-related glomerulonephritis. Treatment was initiated with pulses of methylprednisolone, low dose of corticosteroids and intravenous immunoglobulin, combined with antibiotics. Renal function dramatically improved in less than a week. At three months of follow-up, kidney function remains stable and ANCA serology negative.

Conclusion: In infective endocarditis, ANCA antibodies might have an important pathogenic role rather than secondary phenomena. We suggest that patients with IEAGN, that despite adequate antibiotic regimen present, present with kidney deterioration and evidence of crescentic glomerulonephritis on kidney biopsy, might require addition of immunosuppressives.

#5009
GESTATIONAL COUNSELING DURING PREGNANCY IN PATIENTS WITH KIDNEY DISEASE: EXPERIENCE OF A MULTIDISCIPLINARY TEAM
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Background and Aims: Chronic kidney disease increases morbidity and mortality in pregnancy, being more prone to complications. Because it confers a risk to the fetus, this group of patients should be evaluated by a multidisciplinary unit, including nephrologists, rheumatologists, and obstetricians. Our study’s objective is to describe the clinical/analytical characteristics of patients with kidney disease (KD), assessed in a multidisciplinary consultation, to inform them of the risks and to be able to prepare them to reach pregnancy optimally. At the same time, detect patients with increased risk of complications and perform close follow-ups during pregnancy and postpartum.

Method: Demographic, clinical, analytical, and obstetric variables were collected in a retrospective study that included women with kidney disease (inflammatory/ autoimmune) between May 2020 to March 2022. In our hospital, the hereditary kidney disease unit offers reproductive advice to its patients, which was not considered in this study.

Results: A total of 24 patients with a median age of 35 years (18-39) were evaluated, classifying them into two independent groups: 1-pre-pregnancy (N=12) and 2-during pregnancy (N=12) and postpartum (N=10). All patients
from group 1 have kidney disease (100%). Lupus nephropathy (LN) was the most frequent (64%), followed by minimal change disease (17%) and IgA nephropathy (9%). Maternal-fetal risks were evaluated according to clinical and analytical parameters (age, blood pressure, renal function, proteinuria, and disease activity, among others). 17% of patients had a history of high blood pressure. Treatment modification was made in 25%. Renal biopsy was performed in 4/7 LN patients, and pregnancy was not recommended for one of them (class III LN). In group 2, 14% of the patients presented onset of disease one patient pre-rituximab therapy in LN and another one, an atypical hemolytic uremic syndrome in the immediate postpartum), the rest of them had previous KD: IgA Nephropathy (25%), and minimal change disease (17%), were the most frequent. 8% of the patients had a history of high blood pressure, 25% of them received ACE/ARBs that were discontinued. There were no cases of preeclampsia/eclampsia. The average gestation time was 38.3 weeks, 6.7% <37 weeks, and none <34 weeks. All newborns weigh greater than 2.5 Kg (mean birth weight 3.42 Kg). There were three inductions (two due to diabetes and one due to an altered topographic record). One peri-gestational complication (premature rupture of membranes) and one perinatal complication (respiratory distress) were observed. No other recorded/evidenced complications.

Conclusion: The gestational counseling and monitoring during pregnancy provide adequate support for patients with KD, being able to carry out a “guided” pregnancy with fewer complications. The strategies of our unit include modification of pre-conception treatment, activity control of underlying pathologies, and monitoring of kidney disease during pregnancy to reduce the risk of miscarriages, premature births, and low birth weight, among other complications.

#3767
THE IMPACT OF COVID-19 PANDEMICS ON THE OUTCOME OF 24 CHINESE PATIENTS DIAGNOSED OF MEMBRANOUS NEPHROPATHY RECEIVING RITUXIMAB THERAPY

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Background and Aims: Rituximab has been considered as the first-line immunosuppressive therapy in membranous nephropathy. Anti-CD20 depletion therapy is associated with prolonged B-cell depletion and has been reported to increase risk of severe COVID-19 infection in several rheumatic and neurologic diseases. However, few studies reported the impact of COVID-19 infection on membranous nephropathy in the status of B-cell depleletion. Our study aimed to describe the impact of prior rituximab therapy on clinical outcomes of a group of Chinese membranous nephropathy within 6-month follow-up during COVID-19 pandemics.

Method: We prospectively conducted a cohort study of adult patients diagnosed of membranous nephropathies receiving rituximab therapy from Aug 1st to Nov 30th in 2022, in one tertiary hospital, in Beijing. Patients’ baseline characteristics (including demographic data, serum albumin, serum creatinine, 24-hour proteinuria, serum IgG level, peripheral lymphocyte subsets, medications, past medical history, prior COVID-19 vaccination history), clinical outcomes were recorded. We followed up all the patient regularly until Jan 31st, 2023.

Results: We included 24 patients with median age of 55 (27, 83) years old. 13 (54.2%) patients were on chronic immunosuppression with corticosteroids, calcium urate inhibitors, and/or mycophenolate mofetil. We followed up the patients within median 4.6 months since last rituximab infusion at the dose of 1 gram. During follow-up, 18 (75%) patients got COVID-19 infection including 16 non-severe cases and two severe cases requiring hospitalization and treatment modification was made in 25%. Renal biopsy was performed in 4/7 LN patients, and pregnancy was not recommended for one of them (class III LN). In group 2, 14% of the patients presented de novo nephrotic syndrome and another one, an atypical hemolytic uremic syndrome in the immediate postpartum), the rest of them had previous KD: IgA Nephropathy (25%), and minimal change disease (17%), were the most frequent. 8% of the patients had a history of high blood pressure, 25% of them received ACE/ARBs that were discontinued. There were no cases of preeclampsia/eclampsia. The average gestation time was 38.3 weeks, 6.7% <37 weeks, and none <34 weeks. All newborns weigh greater than 2.5 Kg (mean birth weight 3.42 Kg). There were three inductions (two due to diabetes and one due to an altered topographic record). One peri-gestational complication (premature rupture of membranes) and one perinatal complication (respiratory distress) were observed. No other recorded/evidenced complications.

Conclusion: The gestational counseling and monitoring during pregnancy provide adequate support for patients with KD, being able to carry out a “guided” pregnancy with fewer complications. The strategies of our unit include modification of pre-conception treatment, activity control of underlying pathologies, and monitoring of kidney disease during pregnancy to reduce the risk of miscarriages, premature births, and low birth weight, among other complications.

#5547
SERUM PERIOSTIN IN KIDNEY TRANSPLANT RECIPIENTS AS A NOVEL BIOMARKER PREDICTING RENAL FUNCTION LOSS

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Background and Aims: Experimental studies have shown peristin is expressed throughout organogenesis, particularly within the kidney interstitium. Peristin is enhanced in different tissues of patients with nephropathy and has been considered as a candidate biomarker of kidney injury.

Method: Retrospective analysis of electronic medical record of one hundred and five kidney transplant recipients (KTRs) was performed. Only patients under sequential ambulatory care, with a history of at least 2 years post-transplant were included. Median (IQR) follow-up and time post-transplant was 4.42 (2.65, 4.58) and 4.29 (3.04, 8.07) years, respectively. Additionally, thirty-two health volunteers (HV) were enrolled. Biochemical testing was performed using commercially-available immunoassays.

Results: Median [IQR] serum peristin was significantly lower in KTRs as compared with HV (959 [732, 1204] vs. 1176 [997, 1408]; P<0.01). Higher serum peristin was observed in male patients (7.01 [6.84, 7.22] vs. 6.79 [6.64, 7.07], P<0.05) and a significant relationship was noted for interleukin 6 (IL6; r=0.24, P=0.01) and baseline estimated glomerular filtration (eGFR) (r=0.20, P=0.04). Patient age (P=0.60), body-mass index (P=0.08), cardiovascular disease (P=0.31), diabetes (P=0.45), current smoker status (P=0.27), nor anemia (P=0.25) were not associated with serum peristin. In a generalized additive model adjusted for baseline renal function and IL-6, serum peristin showed a significant nonlinear association (P=0.04) with eGFR change over follow-up.

Conclusion: Previous studies reported an association between peristin expression and the severity of histological injury within the kidney in both inflammatory and non-inflammatory conditions. Serum peristin may be a potential marker aiding in prediction of renal function in KTRs.
Background and Aims: The incidence of nephrolithiasis has risen in recent years, largely due to changes in diet and lifestyle. An association between nephrolithiasis and risk of cardiovascular disease has been described, including atherosclerosis. The underlying mechanisms linking the two conditions are not well understood, making it important to study the role of exercise and nutritional habits. This study aims to examine the incidence of cardiovascular comorbidities in patients with nephrolithiasis, considering demographic information and the timeline of disease diagnosis and follow-up. Conditions such as dyslipidemia, myocardial infarction, stroke, and metabolic syndrome are of particular interest in this population.

Method: We retrospectively analysed consecutive patients that were referred to our tertiary medical center nephrolithiasis clinic between 2021 and 2023. The demographic information collected included gender, age at first nephrolithiasis diagnosis, current age, and family history. The cardiovascular conditions analysed included metabolic syndrome, hypertension, diabetes, gout, smoking, stroke, and dyslipidemia. Additionally, renal function (GFR-EPI) was also taken into account. Appropriate tests for continuous and categorical variables were applied, recurring to SPSS v21.0.

Results: A total of 84 patients were included in the study. Of these, 51.2% (n=43) were women with a median age of 52 years (IQR: 13-83) and a median age of first nephrolithiasis diagnosis of 34 years (IQR: 9-75). The analysed comorbidities showed a high incidence of hypertension (n=35, 41.7%), obesity (n=33, 40.7%), dyslipidemia (n=50, 61%), and metabolic syndrome (n=20, 23.8%). Family history was identified in 37.3% (n=31) of patients, with a significant difference for men, where 64.5% (n=20) had a positive family history (p-value 0.033). The results showed a relationship between increased body mass index and younger age of first nephrolithiasis diagnosis (p-value 0.012) and lower renal function at diagnosis (p-value 0.005).

Conclusion: The diagnosis of nephrolithiasis requires a change in the patient’s diet and lifestyle, not only because of the risk of recurrence, but also because these patients are at a higher risk of developing serious cardiovascular events. This study highlights the high incidence of these comorbidities and underscores the importance of both the patient and the nephrologist being diligent in addressing these issues to achieve better kidney and overall health outcomes.

Figure 1: Crude Kaplan-Meier survival curve comparing dialysis-free survival among patients stratified into high and low serum periostin status groups. Cut-off is based on the middle tertile. Tick marks represent censored events. P-value is based on the log-rank test.
hematuria and 49.5% presented with gross hematuria, and 26.3% needed dialysis at presentation. The main associated causes of IgA nephropathy were liver disease in 46.3%, staphylococcal or streptococcal infections in 23.2%, autoimmune rheumatological disorders in 16.8%, respiratory tract disorders in 9.5% and inflammatory bowel disease in 4.2% of cases. 25 patients (26.3%) only received treatment of the cause, while 70 patients (73.3%) received an add-on therapy. 18 patients (18.9%) received as well cyclophosphamide and 20 patients (21.1%) mycophenolate. There were no differences in age, peak serum creatinine, proteinuria, hematuria, need of dialysis at presentation, histological parameters or associated comorbidities between patients treated with steroids ± immunosuppressants and patients who received supportive treatment. After a median follow-up period of 33 months, 28 patients (29.5%) progressed to ESKD and were on maintenance dialysis, and 32 patients (33.7%) died. There were no differences in progression to ESKD between immunosuppressed patients (28.6%) and those who only received treatment of the cause (32%, \( P = .747 \)). Survival analysis curves showed no significant differences between patients treated only with supportive measures and those who received an add-on steroid and/or immunosuppressive therapy in regards of renal survival (log-rank = 0.003, \( P = .956 \)) or overall survival (log-rank = 0.871, \( P = .351 \)). Cox regression analysis showed that the only factor associated with renal survival was serum creatinine at presentation (HR 3.09, 95%CI 1.39-6.86) independent from age, hematuria, hypertension, diabetes or the use of steroids and/or immunosuppression.

**Conclusion:** Secondary IgAN that presents with acute kidney injury or rapidly progressive glomerulonephritis has a poor prognosis, particularly when diagnosis is delayed at presentation. Adding steroid treatment with or without immunosuppression to supportive measures and treatment of the cause of secondary IgA nephropathy is not associated with an improved renal or patient survival.

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**#6213 RISK FACTORS FOR END-STAGE RENAL DISEASE IN IGA NEPHROPATHY**

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**Background and Aims:** Immunoglobulin A nephropathy (IgAN) is the most common primary glomerular nephropathy worldwide and one of the principal causes of chronic kidney disease. The presentation of this nephropathy is different between ethnic groups. The aim of our work is to describe the clinical, biological, and pathological symptoms of maghrebian patients diagnosed with IgAN.

**Method:** We conducted a retrospective descriptive study over 46 years from 1975 and 2021. This study included 213 patients with renal biopsy-proven IgAN whose clinical, biological, and pathological data were assessed and classified according to the Oxford classification.

**Results:** The mean age of the patients was 34.8 ± 15-80 with male predominance (sex ratio 1.77). Thirty-nine patients had a family history of kidney disease. 109 patients (51%) had hypertension. The median proteinuria was 2.6 g/24 h [0-46.17 g/24 h], Nephrotic proteinuria (>3 g/24h) was found in 98 patients (46%). The initial median glomerular filtration rate was 33.9 ml/min/1.73 m²/SC. At the end of the follow-up, it was 23.7 ml/min/1.73 m²/SC. Renal biopsy was performed in all the cases. The lesions observed in optical microscopy were mesangial proliferation M1 (63.8%), endocapillary proliferation E1 (8.5%), glomerulosclerosis S1 (71.4%), interstitial fibrosis or tubular atrophy T1-T2 (72.8%) and crescents C1 (16.9%). Fifty-two percent of the patients were managed conservatively whereas 9 (41%) were receiving immunosuppressive (steroid + mycophenolate mofetil) treatment.

**Conclusion:** Secondary IgAN that presents with acute kidney injury or rapidly progressive glomerulonephritis has a poor prognosis, particularly when diagnosis is delayed at presentation. Adding steroid treatment with or without immunosuppression to supportive measures and treatment of the cause of secondary IgA nephropathy is not associated with an improved renal or patient survival.

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**#2954 DAPAFLIJLOZIN IN IGA NEPHROPATHY: EARLY EXPERIENCE FROM A SINGLE CENTER IN CENTRAL INDIA**

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**Background and Aims:** IgA nephropathy (IgAN), a common glomerulopathy, may progress to end-stage kidney disease despite use of optimum treatment with immunosuppressants and renin-angiotensin aldosterone system antagonists. Recently, dapagliflozin (DAPA) has been shown to reduce the progression of kidney function decline in IgAN. The beneficial effects in kidney function could be because of reduction in the intraglomerular pressure. To assess the kidney function in terms of change in estimated glomerular filtration rate (eGFR) and urinary protein creatinine ratio (UPCR) with use of DAPA in patients with IgAN.

**Method:** We retrospectively collected the data of IgAN patients from our electronic database. Demographic, renal function parameters and biopsy findings were collected and compared in patients who received immunosuppression only (group I) and those who received DAPA in addition to immunosuppression (group II).

**Results:** We identified a total of 150 patients with IgAN from our database. Among these, 59 (39.3%) were managed conservatively whereas 91 (60.7%) were receiving immunosuppressive (steroid + mycophenolate mofetil) treatment.

**Conclusion:** Our initial experience in patients of IgA nephropathy suggests that the addition of DAPA to existing immunosuppressive treatment is useful in reducing the UPCR in short-term.

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**Table 1: MEST-C scoring in two groups.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N (group I/II)</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>M0</td>
<td>49/14</td>
<td>23 (46.9)</td>
<td>4 (28.6)</td>
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<tr>
<td>M1</td>
<td>49/14</td>
<td>26 (53.1)</td>
<td>10 (71.4)</td>
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<tr>
<td>E0</td>
<td>49/14</td>
<td>30 (61.2)</td>
<td>8 (57.5)</td>
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<tr>
<td>E1</td>
<td>49/14</td>
<td>19 (38.8)</td>
<td>6 (42.9)</td>
<td></td>
</tr>
<tr>
<td>S0</td>
<td>49/14</td>
<td>6 (12.2)</td>
<td>0</td>
<td>0.184</td>
</tr>
<tr>
<td>S1</td>
<td>49/14</td>
<td>43 (87.8)</td>
<td>16 (100.0)</td>
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</tr>
<tr>
<td>T0</td>
<td>49/14</td>
<td>13 (26.5)</td>
<td>6 (42.9)</td>
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<tr>
<td>T1</td>
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<td>28 (57.1)</td>
<td>8 (57.1)</td>
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<tr>
<td>T2</td>
<td>49/14</td>
<td>8 (16.3)</td>
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<tr>
<td>C0</td>
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<tr>
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<td>4 (33.3)</td>
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</tr>
<tr>
<td>C2</td>
<td>49/14</td>
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<td>1 (8.3)</td>
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**B4 - PREVENTION, TREATMENT & CLINICAL TRIALS**
**Table 2: eGFR and UPCR in two groups.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n=67)</th>
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<th>Group II (n=24)</th>
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<tr>
<td></td>
<td>n</td>
<td>Baseline</td>
<td>Follow-up (4.9 [1.6 to 13.4 months])</td>
<td>p</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>55/61</td>
<td>4.2 (2.0 to 7.1)</td>
<td>2.7 (1.5 to 6.4)</td>
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</tr>
<tr>
<td>eGFR (CKD-EPI)</td>
<td>55/61</td>
<td>14.5 (9.3 to 38.5)</td>
<td>27 (9 to 63)</td>
<td>0.065</td>
</tr>
<tr>
<td>UPCR</td>
<td>26/36</td>
<td>1.9 (1.0 to 3.2)</td>
<td>1.6 (0.3 to 2.6)</td>
<td>0.778</td>
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</table>

#3418
**DISAPPEARANCE OF GLOMERULAR C3 DEPOSITION MIGHT BE A PROGNOSTIC MARKER IN MEMBRANOUS NEPHROPATHY AFTER TREATMENT**

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**Background and Aims:** Membranous nephropathy (MN) is the most common cause of nephrotic syndrome (NS) in adults. In about 80% is primary and remaining 20% are secondary due to medications or other diseases. Treatment of primary MN remains controversial, and the prognosis is still difficult to predict despite the introduction of anti phospholipase A2 receptor (PLA2R) antibody. We evaluated pathological changes for predicting prognosis in patients of MN after methyprednisolone (MPD) pulse therapy.

**Method:** We performed 1,649 renal biopsies at the OPD during last 9 years, of which 31 subjects were MN. We performed follow up biopsy who showed normal urinary findings after treatment with MPD pulse therapy in 11 subjects of MN. Indications of the initial biopsy in MN were oral steroid resistant NS (9 subjects), massive proteinuria associated with hematuria (2 subjects). Among the 11 subjects of MN, 3 subjects were lupus nephritis (LN), 8 subjects were primary MN. One cycle of MPD consist of 10-20 mg/kg (max 1.0 g/day) for 3 consecutive days, performing every 10 to 14 days. Mean MPD pulse therapy were done 13 cycles

**Results:** Among the 11 cases of MN, male to female ratio was 6 to 5. Age distribution from 1 year old to 61years old (mean 40.8 y/o), Mean spot urine protein to creatinine before treatment was 4,182.5 mg/g and 189.4 mg/g after treatment, 9 subjects showed glomerular C3 deposition were noted at the initial biopsy and 2 subjects showed no C3 deposition. After treatment glomerular C3 deposition were disappeared in 8 subjects, and showed no relapse during 5.3 years follow up. However, 3 subjects who showed glomerular C3 deposition were lupus nephritis, relapsed during follow up period.

**Conclusion:** MPD pulse therapy might be still promising therapeutic modality in conventional oral steroid resistant MN. Although further larger number of studies are mandatory, disappearance of glomerular C3 deposition might be a prognostic marker for treatment response, instead of disappearance of proteinuria in MN.

#6929
**SGLT2 INHIBITORS IN IGA NEPHROPATHY: REAL LIFE EXPERIENCE AT OUR CENTRE**

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**Background and Aims:** SGLT2 inhibitors (SGLT2i) have a beneficial effect in diabetic and non-diabetic proteinuric chronic kidney disease (CKD), demonstrated in large randomized controlled trials. However, there is limited information about real life experience with SGLT2i in non-diabetic CKD like IgA nephropathy (IgAN).

**Method:** All patients with biopsy-proven IgA nephropathy since 2015 were evaluated for SGLT2 use. We collected data on age, gender, the use of renin-angiotensin-aldosterone system inhibitors (RAASi), eGFR, glycosuria and proteinuria at baseline, at 6 months and at one year of follow-up. Glomerular filtration rate (eGFR) was estimated using the CKD-EPI equation. Data was analyzed using Iamovi®.

**Results:** 51 patients had IgAN diagnosed by kidney biopsy from April 2015 until March 2021. Eleven of these started SGLT2i between December 2020 and February 2022 (at their physician’s description). Their median age was 52, nine were male and all were taking RAASi. The initial median proteinuria was 1 g/g (range 0.5-2.0 g/g), median eGFR was 57.5 mL/min (range 16.8-104 mL/min). At 6 months, the median proteinuria was 0.7 g/g (range 0.8-4.8 g/g), median eGFR was 42.6 mL/min (range 13.9-108 mL/min). One year after beginning SGLT2i, 8 patients have laboratory values and the median value of proteinuria was 0.85 g/g (range 0.2-3.0 g/g) and the median eGFR was 40.5 mL/min (range 14.5-85.4 mL/min). All patients had glycosuria at all urine evaluations confirming no discontinuations of the SGLT2i. No serious adverse events were reported and none of the patients needed dialysis or died. There were no significant differences between proteinuria and eGFR between evaluations at the start, 6 months and 1 year of follow-up.

**Conclusion:** SGLT2i have become important drugs in IgAN. Our first cases who started SGLT2i showed good compliance (using glycosuria as an indirect tool to monitor adherence) and no adverse events, irrespective of their initial eGFR. The small sample was probably a limitation to the lack of significant results.

#6930
**TOO ELDERLY FOR A KIDNEY BIOPSY?**

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**Background and Aims:** As we age, we lose kidney function and accumulate risk factors and comorbidities that predispose to kidney damage. However, kidney disease can develop at any time. Life expectancy continues to improve worldwide. For that reason, more elderly patients are undergoing diagnostic kidney biopsies (KB). There is a general reluctance in performing KB in those patients. It is important to know if a diagnosis KB in elderly patients can have a positive therapeutic impact.

**Method:** In this retrospective cohort study, we analyzed the medical charts of all patients aged ≥ 80 years who underwent a native kidney biopsy (KB) between January and December 2021, in a central hospital in Portugal.

**Results:** Between January and December 2021, 59 patients underwent a native KB, 6 of them over 80 years of age (10% of all patients). Between those elderly patients, the median age was 82 years. The indications for KB were chronic kidney disease with a nephrotic range proteinuria in 3 patients, nephrotic syndrome, acute glomerulonephritis and acute kidney injury in 1 patient each. Median serum creatinine was 2.27 mg/dL (minimum 0.8 and maximum 5.4 mg/dL) and median protein-to-creatinine ratio was 5.7 g/g (minimum 3.3 and maximum 13g/g). The pathological diagnoses found were focal and segmental glomerulosclerosis (FSGS) (n=2), pauci-immune crescentic glomerulonephritis (n=1), membranous nephropathy in a patient with a follicular lymphoma (n=1), acute interstitial nephritis (AIN) (n=1), and diabetic glomerulosclerosis in a patient with a monoclonal gammapathy of undetermined significance (n=1). 3 patients have received a kidney-specific treatment – the patient with AIN started corticosteroids, one patient with FSGS was submitted to corticosteroids plus tacrolimus, and the patient with pauci-immune crescentic glomerulonephritis plus rituximab. The patient with membranous nephropathy and follicular lymphoma received a specific chemotherapy regimen according with lymphoproliferative disease. An improvement in kidney function occurred only in one patient and the other three developed adverse effects (particularly corticosteroids induced diabetes and infections). One year later, one of patients who received treatment was dead, another one was on hemodialysis, and the other two patients had a glomerular filtration rate lower than 15mL/min/1.73 m².

**Conclusion:** Elderly patients have a higher risk of adverse effects from the kidney-specific treatment. It is important to assess the therapeutic risk/benefit when considering performing a renal biopsy in these patients.
CHRONIC KIDNEY DISEASE

C1 - BASIC SCIENCES & EXPERIMENTAL

COMPLEMENT C3 EXERTS DIRECT PRO-FIBROTIC EFFECTS ON KIDNEY TUBULES

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Background and Aims: Renal complement expression has been observed in both experimental and human kidney diseases. We have previously reported massive tubular C3 expression in fibrotic TGF-beta1 transgenic mice (Nephrol Dial Transplant 2015, 30; S3:FP301). Still, little is known whether this intra-renal complement is only an inflammatory marker of renal fibrosis or also exerts direct pro-fibrotic effects in the pathogenesis. In the present study we aimed to investigate the effect of C3a receptor activation in murine primary tubular epithelial cells.

Method: Primary tubular epithelial cells (TEC) were isolated from kidneys of four-weeks-old male C57Bl6 mouse. The cells were grown in DMEM/12 medium supplemented with 2% FBS and recombinant 5 ng/ml EGF, and characterized for epithelial and mesenchymal markers. Verified TEC cells were seeded on 6-well plates and treated for 24 hours with PBS (CTL, n = 3), 100 nM C3a receptor agonist peptide (C3aR, n = 3) or 10 ng/ml recombinant TGF-beta1 (TGFb, n = 3). Then, mRNA and protein expressions were assessed and evaluated using Kruskal-Wallis test (p < 0.05).

Results: TGF-beta induced a 2-fold Col1a1 and 1.6-fold Tgfb1 mRNA expression, accompanied by 4-fold Egr2 but not affect Ccl2 or C3 mRNA expression. In contrast, C3aR group depicted 1.6-fold C3 and 1.8-fold Ccl2 mRNA expression, an only 1.6-fold Egr2 but a 2-fold Col1a1 and 1.5-fold Tgfb1 mRNA expression. Despite the similar Tgfb1 mRNA overexpression in TGFb and C3aR groups, marked Tgfb1 protein overexpression (15-fold) was only observed in TGF-beta treated cells but not in the C3aR group.

Conclusion: Our study data indicate that renal complement C3 production can exert autocrine / paracrine direct pro-fibrotic effects on tubular epithelial cells unrelated to TGF-beta protein levels. Therefore, local C3 overexpression might play a significant pathogenetic role in kidney fibrosis.

MILD EXPERIMENTAL CKD IS ASSOCIATED WITH MYOCARDIAL FIBROSIS AND NOTCH/HEDGEHOG SIGNALING DYSREGULATION

Evdokia Bogdanova1, Airat Sadykov2, Olga Beresneva1, Vladimir Sharoyko3 and Vladimir Dobronravov4
1Pavlod University, Research Institute of Nephrology, Russia, 2Pavlod University, Raisa Gorbacheva Memorial Research Institute for Pediatric Oncology, Hematology and Transplantation, Russia and 3Pavlod University, Department for General and Bioorganic Chemistry, Russia

Background and Aims: Chronic kidney disease (CKD) is an independent cardiovascular risk factor. The initial mechanisms of myocardial remodeling (MR) in CKD are poorly understood. The major developmental signaling pathways Notch, Hedgehog, Wnt, and Bmp seem to be involved in many crucial steps of MR (cardiomyocytes survival and regeneration, fibrotic response, angiogenesis), while their role in MR due to CKD was not previously studied.

Phosphate (Pi) is essential for cellular signaling and its redistribution to the cardiovascular compartment in CKD could be one of the mechanisms of MR. Here we investigated the involvement of Pi/PPI transport, and reactivation of developmental signaling pathways in myocardial alterations associated with mild CKD.

Method: We induce mild CKD by 3/4 nephrectomy in adult male SHRs (SHR-Nx, n = 8) with normal phosphate intake (0.6%) and 2-month follow-up. Controls were sham-operated SHR (SHR-Sham, n = 8) and Wistar Kyoto rats (WKY-Sham, n = 8). We analyzed chronic kidney injury and Pi exchange parameters, serum intact parathyroid hormone (PTH), intact fibroblast growth factor 23 (FGF23), myocardial phosphorus content (ICP-AES), histomorphometry, PTV1 and PTV2 expression (IHC), and mRNA expression of Slco2a1, Slc20a2, Ankh, Mapk1, Mapk3, Bmp2, Bmp4, Cinnb1, Fzd2, Sfrp2, Dkk1, Wif1, Numb, Notch1, Jag1, Hes1, Lgr4, Tnfα, Tgfb1, and Ppil mRNA expression (Figure 2). We found no changes in Slco2a1 and Slc20a2 mRNA levels (Figure 2). An appearance of PTV2-positive fibroblasts-like cells in myocardial interstitium was apparent in SHR-Nx rats (data not shown).

Conclusion: Myocardial alterations in mild CKD are manifested in an increase in its phosphorus content, interstitial fibrosis, and dysregulation in genes likely related to the induction of the myofibroblasts and extracellular matrix remodeling.

<p>| Table 1: Parameters studied in Sham and Nx rats (median (IQR); *p &lt; 0.05, †p &lt; 0.005, ‡p &lt; 0.001). |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|</p>
<table>
<thead>
<tr>
<th><strong>Group</strong></th>
<th><strong>WKY-Sham (1)</strong></th>
<th><strong>SHR-Sham (2)</strong></th>
<th><strong>SHR-Nx (3)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, g</td>
<td>345 (336;361)</td>
<td>317 (311;337)</td>
<td>320 (300;370)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>135 (130-142)2,3*</td>
<td>170 (160-182) 3*</td>
<td>195 (180-205)</td>
</tr>
<tr>
<td>Myocardial mass index, mg/g</td>
<td>2.48 (2.13;2.79)2,3†</td>
<td>2.85 (2.79;3.09)</td>
<td>3.28 (2.82;3.46)</td>
</tr>
<tr>
<td>Cardiomyocyte diameter, um</td>
<td>15.4 (14.4;15.8)2,3*</td>
<td>16.9 (15.9;17.6)</td>
<td>17.7 (15.8;21.4)</td>
</tr>
<tr>
<td>Creatinine clearance, ml/min/100g</td>
<td>0.26 (0.20;0.36)2,3†</td>
<td>0.27 (0.20;0.35)2,3†</td>
<td>0.19 (0.16;0.23)</td>
</tr>
<tr>
<td>Albuminuria, mg/mg</td>
<td>0.026 (0.017;0.035)3†</td>
<td>0.043 (0.031;0.065)2,3†</td>
<td>0.327 (0.153-0.370)</td>
</tr>
<tr>
<td>Serum phosphate, mmol/L</td>
<td>1.47 (1.22-1.60)2,3*</td>
<td>1.89 (1.79;1.95)4,†</td>
<td>1.60 (1.56;1.84)</td>
</tr>
<tr>
<td>Urinary phosphate/creatinine, mg/mg</td>
<td>5.6 (4.5;6.5)</td>
<td>8.9 (6.9;10.1)</td>
<td>10.1 (7.6;12.7)</td>
</tr>
<tr>
<td>Parathyroid hormone, pg/ml</td>
<td>55.1 (12.7;112.9)</td>
<td>76.6 (18.4;111.0)</td>
<td>45.9 (21.2;76.6)</td>
</tr>
<tr>
<td>Fibroblast growth factor 23, pg/ml</td>
<td>351.9 (290.1;386.7)</td>
<td>361.7 (330.8;1530.3)</td>
<td>67.0 (330.9;793.7)</td>
</tr>
</tbody>
</table>

Abstract i1153
BACKGROUND AND AIMS: Autologous mesenchymal stem/stromal cells (MSCs) have emerged as a therapeutic option for many chronic diseases. Hypertensive kidney disease (HKD) might impair MSCs’ reparative ability by altering important biomolecular properties of the cell, but the characteristics of this impairment are unclear. In our previous pre-clinical studies, hypoxic preconditioning (HPC) enhanced MSC angiogenesis and reduced senescence through global gene and protein expression. Thus, we hypothesize that HPC would improve human MSCs by enhancing their functionality and angiogenesis, creating an anti-inflammatory and anti-senescence environment in MSCs from healthy control (HC), hypertensive patients (HTN), and hypertensive kidney disease patients (HKD).

METHOD: Human MSCs were collected from abdominal subcutaneous fat tissue biopsy of HC, HTN, and HKD patients (n=12 each). Samples were collected from healthy volunteers with no history of hypertension or kidney disease (HC), patients diagnosed with hypertension controlled with antihypertensive drugs (HTN), and hypertensive patients with eGFR<60 mL/min/1.73 m² (HKD). MSCs were harvested and cultured in Normoxic (20% O₂) or Hypoxic (1% O₂) conditions for 24-48 hours. MSC functionality was measured by migration and proliferation. Angiogenic and inflammatory secretome in conditioned media was assessed along with MSC senescence by senescence-
associated beta-galactosidase (SA-beta-gal) activity. In addition, transcriptome analysis using RNA-sequencing (n=3/group) and quantitative PCR (qPCR) were performed to evaluate gene expression.

**Results:** At baseline, Normoxic HTN-MSCs interestingly had higher proliferation compared to HC. HC-MSC subjected to HPC showed increased proliferation (Figure 1A). SA-β-gal activity tended to decrease after HPC, particularly in the HC group (P = .06). HPC did not affect the release of the pro-angiogenic protein VEGF from MSCs, but increased EGF in HC-MSC, and decreased HGF in HC and HKD-MSCs. HPC upregulated the pro-angiogenic genes, inflammatory gene, and a few senescence genes (Figure 1F).

**Conclusion:** HPC has a more favorable functional effect on HC- than on HKD-MSC, reflected in increased proliferation and EGF release, and tends to decrease senescence, whereas it has little effect on HTN or HKD-MSCs. These observations may assist in developing novel therapeutic strategies to improve the regenerative capacity of MSCs in patients with hypertensive kidney disease.

#4695

**LOSS OF NLRP6 INCREASES THE SEVERITY OF KIDNEY FIBROSIS**

Lara Valiño1, Chiara Favero 2, Aranzazu Pintor-Chocano2, Sol Carriazo2, Alberto Ortiz2 and Maria Dolores Sanchez-Nino2

1IIS Fundacion Jimenez Diaz, Nephrology, Madrid, Spain and 2IIS-Fundacion Jimenez Diaz, Nephrology, Madrid, Spain

**Background and Aims:** The burden of chronic kidney disease (CKD) is growing worldwide, illustrating the need for better prevention and therapeutic approaches. Kidney fibrosis is a hallmark of CKD that is not specifically addressed by current therapeutic options. The nucleotide-binding oligomerization domain-like receptor (NLR) family has 22 members. The NLRP3 inflammasome has been most extensively studied in the context of kidney disease where it plays a pathogenic role. However, the role of NLRP6 during CKD and kidney fibrosis remains unexplored. The aim of the study was to explore the role for endogenous Nlrp6 in protecting from kidney fibrosis.

**Method:** A hypothesis-driven analysis of non-biased human kidney disease transcriptomics databases was performed to identify NLRs other than NLRP3 of potential therapeutic interest, based on differential gene expression during CKD and the relationship of gene expression to severity of CKD. We explored Nlrp6 expression in preclinical accelerated CKD and kidney fibrosis (UUO) and characterized the function of endogenous Nlrp6 by inducing UUO in Nlrp6-deficient mice and validated the results in a second model of kidney fibrosis. Once tubular cells were identified as the key cells expressing NLRP6 and regulating Nlrp6 expression during UUO, we explored the drivers of Nlrp6 downregulation in tubular cells, as well as the consequences of Nlrp6 downregulation in these same cells.

**Results:** The role of Nlrp6 in experimental CKD was explored in wild-type and Nlrp6-deficient mice with unilateral ureteral obstruction (UUO). Whole kidney Nlrp6 mRNA and tubular cell Nlrp6 protein decreased following UUO. Low kidney Nlrp6 immunostaining was also observed in human CKD. Genetic Nlrp6 deficiency resulted in increased kidney p38 MAP kinase activation and more severe kidney inflammation and fibrosis, as assessed by kidney inflammatory gene expression, interstitial macrophage infiltration, expression of profibrotic cytokines and extracellular matrix encoding genes, Smad3 phosphorylation, Sirius red staining, collagen, and fibronectin deposition and myofibroblast numbers. Similar results were obtained in adenine-induced kidney fibrosis. Cytokines involved in the pathogenesis of kidney fibrosis, such as the profibrotic cytokine TGF-β1 and the proinflammatory cytokine TWEAK, decreased Nlrp6 expression in cultured tubular cells, while siRNA targeting Nlrp6 resulted in increased TGF-β1 and CTGF expression, which was limited by inhibiting p38 MAPK.

**Conclusion:** In conclusion, endogenous constitutive Nlrp6 dampens sterile kidney inflammation and fibrosis likely by dampening tubular cell responses. Loss of Nlrp6 expression may contribute to CKD progression.

#5129

**CLINICAL-FUNCTIONAL KIDNEY-LUNG LINK IN A POPULATION OF HEMODIALYZED PATIENTS**

Ersilia Satta1,2, Carmine Romano1, Ilaria Raiola1, Anna Scafarto2, Sandro Gentile1, Gioacchino Erbaggio1, Guido Gembillo3 and Mario Polverino4

1Nephrology and Dialysis Center, Nephrology and Diabetology Research, Naples, Italy, 2Nefrocenter Research S.crl, Nephrology and Diabetology Research, Naples, Italy, 3Institute of Nephrology The University of Messina, Institute of Nephrology, Messina, Italy and 4Nephrology and Dailyis Research, Nefrocenter, Naples, Italy

**Background and Aims:** We know that lung and kidney are intimately related from a functional standpoint, both in physiological conditions and in diseases. The close relationship between lung and kidney (kidney-lung link) is evidence of a homeostatic connection between all organs and systems in an attempt to maintain the body system balance. In a recent review [1] we emphasized the importance to search for the clinical signs of a disease not only in the primary affected organ but also in organ functionally related.

**Method:** For this purpose we examined 81 hemodialyzed patients, with a mean age of 66.6 ± 13 years (28 f and 53 M), undergoing hemodialysis treatment
**REFERENCES**


**#5730**

**PERLECAN AS A POTENTIAL BIOMARKER OF CARDIOVASCULAR RISK: ROLE OF ENDOTHELIAL GlicoCaLyX IN CHRONIC KIDNEY DISEASE**

**Gemma Valera Arévalo¹, Andrea Figuer Rubio², Paula Jara Caro Espada³, Claudia Yuste¹, Enrique Morales³, Noemi Ceprian Costoso¹, Guillermo Bodega¹, Rafael Ramirez², Matilde Alique² and Julia Carracedo¹**

¹Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Department of Genetics, physiology and microbiology, Biological science, Universidad Complutense de Madrid, Spain, ²Instituto Ramón y Cajal de Investigación Sanitaria (IRYCSIS), Department of Systems Biology, Universidad de Alcalá, Spain, ³Instituto de Investigación i+12, Department of Nephrology, Hospital Universitario 12 de Octubre, Spain, ⁴Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Department of Medicine/Department of Nephrology of Hospital de Octubre de Madrid, Spain and ⁵Department of Biomedicine and Biotechnology, University of Alcalá, Spain

**Background and Aims:** Chronic kidney disease (CKD) is associated with cardiovascular disease (CVD). CVD is in turn related to endothelial dysfunction, endothelial dysfunction, and degradation of the endothelial glyocalyx (EG), releasing its components into the bloodstream. The EG consists of glycosaminoglycans and proteoglycans, such as Perlecan. The aim of the study is to analyse the levels of perlecan in plasma in different stages of CKD and to relate them to age and inflammatory monocytes, as well as their adhesion capacity (CD54/ICAM-1).

**Method:** An observational cross-sectional study was carried out. 56 patients were included: advanced chronic kidney disease (ACKD) (n=13), haemodialysis (HD) (n=13), peritoneal dialysis (PD) (n=15) and transplant recipients (TX) (n=15). Thirty healthy subjects (CT) were analysed. Plasma perlecan levels were quantified using ELISA and phenotyping of monocyte subpopulations (classical (CD14+CD16+), intermediate (CD14+CD16+) and non-classical (CD14+CD16+)), as well as CD54 (ICAM-1) expression by flow cytometry. Statistical analysis: ANOVA and Spearman correlation.

**Results:** The mean values of PFT were globally no different between smokers with normal PFT and non smokers are summarized in Table 1: Although the never-smoking group was nearly twice as large as the smokers, and PFT were similar and normal, respiratory symptoms were predominant: daily cough (49 yes; 26 no); chronic phlegm (51 yes; 24 no).

**Conclusion:** In dialysis patients, cough and phlegm are common symptoms, regardless of smoking and spirometric values. Probably these results are the consequence of synergistic effects between lungs and kidneys, as recently demonstrated [2]. Hence the need to evaluate dialysis patients from the clinical-functional point of view of both, kidneys and lungs, in order to evaluate the appropriate, personalized, therapeutic strategy according to the last evidences of the literature [3].

**#5750**

**PERLECAN AS A POTENTIAL BIOMARKER OF CARDIOVASCULAR RISK: ROLE OF ENDOTHELIAL GUCASYLIX IN CHRONIC KIDNEY DISEASE**

**Gemma Valera Arévalo¹, Andrea Figuer Rubio², Paula Jara Caro Espada³, Claudia Yuste¹, Enrique Morales³, Noemi Ceprian Costoso¹, Guillermo Bodega¹, Rafael Ramirez², Matilde Alique² and Julia Carracedo¹**

¹Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Department of Genetics, physiology and microbiology, Biological science, Universidad Complutense de Madrid, Spain, ²Instituto Ramón y Cajal de Investigación Sanitaria (IRYCSIS), Department of Systems Biology, Universidad de Alcalá, Spain, ³Instituto de Investigación i+12, Department of Nephrology, Hospital Universitario 12 de Octubre, Spain, ⁴Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Department of Medicine/Department of Nephrology of Hospital de Octubre de Madrid, Spain and ⁵Department of Biomedicine and Biotechnology, University of Alcalá, Spain

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**Method:** An observational cross-sectional study was carried out. 56 patients were included: advanced chronic kidney disease (ACKD) (n=13), haemodialysis (HD) (n=13), peritoneal dialysis (PD) (n=15) and transplant recipients (TX) (n=15). Thirty healthy subjects (CT) were analysed. Plasma perlecan levels were quantified using ELISA and phenotyping of monocyte subpopulations (classical (CD14+CD16+), intermediate (CD14+CD16+) and non-classical (CD14+CD16+)), as well as CD54 (ICAM-1) expression by flow cytometry. Statistical analysis: ANOVA and Spearman correlation.

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**Conclusion:** In dialysis patients, cough and phlegm are common symptoms, regardless of smoking and spirometric values. Probably these results are the consequence of synergistic effects between lungs and kidneys, as recently demonstrated [2]. Hence the need to evaluate dialysis patients from the clinical-functional point of view of both, kidneys and lungs, in order to evaluate the appropriate, personalized, therapeutic strategy according to the last evidences of the literature [3].

**#6755**

**NOVEL ASPECT OF NATURAL FLAVONOL Fisetin VIA INHIBITING ACSL4-MEDIATED TUBULAR FERROPTOSIS AGAINST FIBROTIC KIDNEY DISEASE**

**Bo Wang, Letian Yang, Liang MA and Ping Fu**

West China Hospital, Sichuan University, Division of Nephrology, Kidney Research Institute, Chengdu, P.R. China

**Background and Aims:** Kidney fibrosis is the hallmark of chronic kidney disease (CKD) progression, whereas no effective anti-fibrotic therapies exist. We previously reported that natural flavonol fisetin alleviated septic acute kidney injury and protected against hyperuricemic nephropathy in mice. However, the versatile role and potential mechanism of fisetin against fibrotic kidney disease have not been well characterized. Recently, tubular ferroptosis contributes to the pathogenesis of CKD with a persistent inflammatory and profibrotic response.

**Method:** Here, we found that fisetin significantly improved tubular injury, as well as CD54 (ICAM-1) expression on monocytes, which is important for its contribution to the pathogenesis of CKD with a persistent inflammatory and profibrotic response.

**Results:** Patients with CKD had higher plasma levels of perlecan than healthy participants (p-value = 0.044 vs ACKD, 0.028 vs HD and 0.002 vs PD) (Fig. 1). These levels were associated with higher percentage of classical monocytes (p=0.011) intermediate monocytes (p=0.009) and non-classical monocytes (p=0.003) expressing ICAM-1 but not with a higher expression of ICAM-1 per monocyte. Perlecan levels correlate negatively with age (p=0.03) (Table 1).

**Conclusion:** Patients with ACKD, HD and PD have elevated plasma perlecan levels compared to CT and TX. Elevated perlecan concentrations are associated with increased ICAM-1 expression on monocytes, which is important for its possible role in the development of atherosclerosis. Perlecan may be postulated as a molecule of interest to assess endothelial and cardiovascular damage in CKD patients.

**Table 1: Correlation between perlecan levels in plasma, age and ICAM-1 expression in monocytes. MFI: mean fluorescence intensity. Pearson correlation test was performed. Statistical significance was denoted by *p<0.05.**

<table>
<thead>
<tr>
<th>Perlecan</th>
<th>Classical monocytes (%)</th>
<th>Intermediatemonocytes (%)</th>
<th>Non-classical monocytes (%)</th>
<th>Intermediate monocytes CD54+ (%)</th>
<th>Non-classical monocytes CD54+ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r = 0.159</td>
<td>r = -0.154</td>
<td>r = -0.086</td>
<td>r = 0.424*</td>
<td>r = 0.544*</td>
</tr>
</tbody>
</table>

**Figure 1:** (A) Perlecan plasma levels (ng/mL) in healthy subjects (HS), patients with advanced chronic kidney disease (ACKD); hemodialysis treatment (HD); peritoneal dialysis (PD) and patients with kidney transplantation (TX). *p < 0.05, **p < 0.01 vs CT; †p < 0.05 vs PD. Statistical analysis: Kruskal–Wallis test for perlecan (non-parametric).
Results: Mechanistically, fisetin inhibited ferroptosis in the kidneys of CKD mice as well as in injured tubular epithelial cells, as evidenced by a decrease of ACSL4, COX2, HMGB1, and an increase of GPX4. Meanwhile, fisetin effectively restored ultrastructural abnormalities of mitochondrial morphology and relieved the elevated iron, the downregulated GSH and GSH/GSSG, as well as the upregulated lipid peroxide MDA in the kidneys of CKD mice. Notably, abnormal expression of ferroptosis key marker ACSL4 was verified in renal tubules of CKD patients (IgAN, MN, FSGS, LN, and DN) and mice (adipine and UUO), which was also observed in injured tubular cells. Furthermore, ACSL4 knockdown inhibited tubular ferroptosis, while ACSL4 overexpression blocked anti-ferroptotic effect of fisetin and reversed the cytoprotective, anti-inflammation, and anti-fibrosis of fisetin in injured tubular cells.

Conclusion: In summary, we for the first time explored a novel aspect of fisetin via inhibiting ACSL4-mediated tubular ferroptosis against fibrotic kidney diseases.

#4623

A NOVEL ELECTRO-HYDRAULIC ACOUSTIC THERAPY REDUCES BLOOD PRESSURE IN HYPERTENSIVE PATIENTS WITH CHRONIC KIDNEY DISEASE: PRELIMINARY RESULTS

Talya Wolak1,2, Amir Lerman3, Michael Glikson1,2, Ivetta Sukholutsky2, Shuli Silberman2 and Lilach Lerman3
1Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel, 2Shaare Zedek Medical Center, Jerusalem, Israel and 3Mayo Clinic, Rochester, United States of America

Background and Aims: Arterial hypertension (HTN) in association with chronic kidney disease (CKD) is a global healthcare burden, yet clinically proven treatments are limited. electro-Hydraulic Acoustic Therapy (eHAT), using ~10% of the energy used in shockwave lithotripsy, is a promising technique which was also observed in injured tubular cells. Moreover, eHAT has been demonstrated to enhance healing in tissues such as bone, muscle, and myocardium, via several mechanisms, particularly by promoting neovascularization. Furthermore, previous animal studies demonstrated that eHAT reduces blood pressure (BP) and preserves renal function after ischemic kidney injury. The present pilot study explored the clinical safety and efficacy of eHAT and tested the hypothesis that eHAT would reduce BP and preserve renal function in patients with medically-treated hypertension and CKD.

Method: So far, a total of 15 patients with HTN and Stage III a/b CKD were enrolled in this prospective, single-arm study. The patients were treated with six sessions of eHAT during a 3-week period. At each session, 2400 shockwaves were applied to each kidney with 0.9 mJ/mm2 at 2.66Hz (NephrospecTM by Curespec LTD, Yehud, Israel). Follow-up (FU) visits were performed at 1, 3, and 6 months.

Results: The treatment was well tolerated with no major adverse events or need for analgesic treatment. Average Automated Office BP (AOBP) showed a strong tendency for a decrease in diastolic BP from baseline to the Primary Efficacy Objective at FU II (3 months post last treatment), which progressively decreased further at FU III (6 months) (Table 1). Similarly, average Office BP (OBP) detected a strong trend for a progressive decrease in systolic BP from baseline to the Primary Efficacy Objective (Table 1). Levels of eGFR appeared to slightly rise throughout the study, but this change has not reached statistical significance levels (Table 1).

Conclusion: The current study demonstrates that the eHAT procedure is tolerable and safe in this cohort. Moreover, a 3-week regimen tended to reduce BP and preserve eGFR in patients with controlled HTN and CKD. Therefore, electro-Hydraulic Acoustic Therapy may emerge as a novel, safe, and non-invasive alternative therapeutic approach in the management of HTN in the context of CKD.

Table 1:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baselinea</th>
<th>EoTb</th>
<th>FU Ic</th>
<th>FU IIId</th>
<th>FU IIIe</th>
<th>PValuef</th>
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<tbody>
<tr>
<td>Office BP</td>
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<tr>
<td>Systolic</td>
<td>135.69±17.98</td>
<td>139.50±18.25</td>
<td>133.40±25.98</td>
<td>124.38±13.04</td>
<td>120.50±22.84</td>
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<tr>
<td>Diastolic</td>
<td>77.23±5.64</td>
<td>80.42±9.09</td>
<td>79.3±11.44</td>
<td>75.25±8.12</td>
<td>72.00±8.83</td>
<td>0.1185</td>
</tr>
<tr>
<td>AOBP</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>125.17±13.82</td>
<td>134.46±19.29</td>
<td>125.33±23.56</td>
<td>119.65±16.37</td>
<td>113.19±14.39</td>
<td>0.1146</td>
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<tr>
<td>Diastolic</td>
<td>76.27±6.92</td>
<td>79.44±7.51</td>
<td>77.57±7.16</td>
<td>75.41±9.53</td>
<td>71.83±5.76</td>
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<td>eGFR</td>
<td>42.15±17.38</td>
<td>40.50±17.18</td>
<td>42.00±18.87</td>
<td>50.13±16.49</td>
<td>49.25±18.01</td>
<td>0.2483636</td>
</tr>
</tbody>
</table>

Note: N=13, N=12, N=10, N=8, N=4
EoT= End of Treatment
f Two sample t-test for means

#4561

VOLUNTARY EXERCISE EXACERBATES CHRONIC KIDNEY DISEASE INDUCED BY FOLIC ACID IN MALE C57BL/6 MICE

Raisa Brito Santos1, Gabriel Estrela2, Alexandre Budu1, Adriano Arruda1 and Ronaldo Araujo1
1Federal University of São Paulo Unifesp, Nephrology, São Paulo, Brazil, 2Biophysics, São Paulo, Brazil

Background and Aims: Voluntary exercise is of utmost importance to avert a plethora of diseases and to ameliorate other conditions, such as neuromuscular diseases, however in some occasions, the inflammation can be exacerbated by intense physical activity. The folic acid kidney disease model is of key interest since it is non-invasive and leads to conspicuous fibrosis. Our main objective was to determine the influence of voluntary exercise on chronic kidney disease in folic acid-treated mice.

Method: Male C57Bl6 mice were divided into 3 groups, vehicle (V), folic acid (FA), and folic acid + voluntary exercise (FA + E). The animals were kept in cages with or without voluntary wheels (sedentary or exercised groups) for 30 days, and then received a single injection of folic (240 mg/kg i.p.) in 0.3 mol/L sodium bicarbonate. The animals were euthanized after 28 days.

Results: Chronic kidney disease in the folic acid model is exacerbated by voluntary exercise. Voluntary exercise decreases the survival level in animals treated with folic acid (V- 100%, FA- 85,71%, FA + E- 60%). On day 28 after folic acid administration the urea levels (FA vs. FA + E P= 0.003) and creatinine (V vs. FA + E P= 0.0004; FA vs. Fa + E p= 0.0001). Renal injury marker such as KIM-1 (V vs. FA + E p= 0.00131, FA vs. Fa + E p= 0.0213) was higher in animals that went to the wheel, but NGAL showed no significant differences. Inflammation markers as IL-6 (V vs. FA + E p= 0.0037 FA vs. Fa + E p= 0.0254) and TLR4 (V vs. FA + E p= <0.0001 FA vs. Fa + E p= <0.0001) were exacerbated as well as apoptosis relation BAX/BCL2 (V vs. FA + E p= 0.0001 FA vs. Fa + E p= <0.0001). Picrosirius red staining was used to assess tubulointerstitial fibrosis and the kidney architecture; animals from the FA + E group showed the highest destruction of kidney architecture.

Conclusion: We established that previous voluntary exercise has deleterious effects on nephrotoxic folic acid–Induced CKD.
COMPENSATORY HYPTERTROPHY OF THE KIDNEY CONTRIBUTES TO LOSS OF KLOTHO KIDNEY THROUGH PAKT SIGNALING

Aurora Pérez-Gomez, Juan Miguel Díaz-Tocados, Juan Diego Domínguez Coral, Maite Caus Enríquez, Alicia García-Carrasco, Ana Martínez Bardají and José Manuel Valdivielso Revilla

IRB Lleida, Experimental Nephrology, Lleida, Spain

Background and Aims: Chronic kidney disease (CKD) represents a significant public health burden worldwide, mainly driven by the increase of the incidence of associated risk factors like diabetes. Decreased renal Klotho expression is an early feature of CKD, driving an increase on circulating FGF23 and phosphate. These alterations in mineral metabolism have a direct negative impact on the progression of renal dysfunction and can cause bone alterations, vascular calcification and heart failure. In parallel, during the early stages of CKD, kidneys activate molecular mechanisms of hypertrophy in an attempt to counteract the loss of renal function. The PI3K/Akt/mTOR pathway, activated by growing factors like insulin-like growing factor-1 (IGF-1) participates in compensatory renal growth. The aim of the present study is to investigate the possible role of PI3K/Akt activation on renal Klotho levels during renal compensatory hypertrophy.

Method: We generated a mice model of kidney compensatory hypertrophy (UNX mice) in which kidney klotho levels and circulating mineral metabolism parameters were analyzed. Furthermore, some of the mice were treated with inhibitors of the PI3K/Akt/mTOR pathway. In vitro, proximal tubular epithelial human cells (PTEC) were stimulated with IGF-1 in order to activate the PI3K/Akt pathway, and the effects on Klotho expression were determined.

Results: UNX mice present with an activation of the PI3K/Akt/mTOR pathway in kidney, which correlates with the loss on renal Klotho expression. Moreover, UNX mice showed an increase on both, plasma phosphate and FGF23, and a decrease in the fractional excretion of phosphate (% FEPi). Renal function, estimated by BUN plasma levels, was unaltered. Pharmacological inhibition of the pathway restored Klotho and decreased FGF23 levels, normalizing renal phosphate excretion and blood levels. In vitro, IGF-1 stimulated PI3K/Akt activation in PTEC and induced a decline on Klotho expression, which was restored with PI3K/Akt inhibitors.

Conclusion: The overactivation of PI3K/Akt/mTOR pathway in renal hypertrophy modulates Klotho expression and has direct effects on FGF23 and phosphate. Our findings constitute an important breakthrough in the research of new therapeutic targets in order to maintain renal Klotho levels, and it may be useful in the treatment of kidney disease patients.

C2 - PATHOPHYSIOLOGY, RISK FACTORS & PROGRESSION

#5799

RENAAL TUBULAR TOXICITY OF ORGANOPHOSPHATE FLAME RETARDANTS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Department of Internal Medicine, Kaohsiung, Taiwan, Rep. of China and
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Background and Aims: Organophosphate flame retardants (OPFRs) are widely utilized flame retardants and considered less harmful than legacy brominated flame retardants. However, owing to their widespread utilization, OPFRs have led to extensive and persistent human exposure, with potentially hazardous effects on human health such as nephrotoxicity. Experimental and clinical studies have revealed that OPFR exposure is associated with renal tubular toxicity and renal impairment. However, the nephrotoxic mechanisms of OPFRs have not yet been clarified, and their impact on renal tubular injury has less been evaluated in patients with chronic kidney disease (CKD).

In this cross-sectional observational study, we assessed the urinary OPFR concentrations in CKD patients to evaluate the associations between OPFR exposure and renal tubular injury in this population.

Method: Adult CKD patients in Taiwan (≥ 20 years of age and with nondialysis-dependent CKD stage 3–5) were recruited from the Kaohsiung Chang Gung Memorial Hospital between January 2020 and May 2021. The first-void urine samples in the morning were collected to measure the concentrations of 10 common OPFR compounds using an ultra-performance liquid chromatography-tandem mass spectrometry (Waters, Milford, MA, USA). The urinary novel renal biomarkers were also measured using enzyme-linked immunosorbent assays (kidney injury molecule-1 [KIM1] and 8-hydroxy-2-deoxyguanosine [8-OHdG]; Abcam, Trumpington, Cambridge, UK). OPFRs with concentrations below a limit of quantitation (LOQ) were considered undetectable, and LOQ/√2 was assigned to the non-detected samples for analysis. The associations between urinary renal biomarkers and urinary OPFR concentrations (i.e., the sum of 10 OPFR compounds) were assessed via Spearman’s correlation analysis. Simple linear regression analyses were conducted to evaluate the correlations between urinary renal biomarkers, urinary OPFR concentrations, and baseline patient characteristics. The effects of OPFR exposure on the urinary concentrations of KIM1 and 8-OHdG in the enrolled CKD patients were examined in multiple linear regression analyses, adjusting for age, sex, body mass index, diabetes, hypertension, renal function, proteinuria, and covariates with a p-value < 0.1 in univariate analyses via the enter method.

Results: In this study, 163 CKD patients were enrolled for analysis (stage 3: n = 79 [49.47%]; stage 4: n = 48 [29.45%]; stage 5: n = 36 [22.08%]). The overall detection frequency of urinary OPFRs was 98.77% in the study cohort, with a median SOFR of 2.04 μg/g Cr (interquartile range [IQR], 0.84–4.27). The median urinary KIM1- and 8-OHdG concentrations were 185.89 ng/g Cr (IQR, 83.05–441.60) and 71.23 μg/g Cr (IQR, 37.87–149.73), respectively. In our analysis, urinary OPFR concentrations were positively correlated with urinary KIM1 and 8-OHdG concentrations (r = 0.267 for KIM1, p = 0.001; r = 0.281 for 8-OHdG, p < 0.001) (Figure 1). In the multiple linear regression analyses, urinary OPFR concentration was identified as an independent predictor positively associated with urinary renal biomarkers in the enrolled patients, with a 0.260 log ng/g Cr (95% confidence interval [CI], 0.140–0.380, p < 0.001) increase in urinary KIM1 and a 0.227 log μg/g Cr elevation (95% CI, 0.124–0.330, p < 0.001) in urinary 8-OHdG by per log μg/g Cr urinary OPFR (Figure 2).

Conclusion: OPFR exposure is common and associated with renal tubular injury as well as increased oxidative stress in CKD patients, which highlights its nephrotoxic potential in this vulnerable population.
Background and Aims: Through metabolomics research, it was found that in mice with chronic kidney disease, the distribution of lipids in the kidneys was different from that of healthy individuals, and medium-chain fatty acids were reduced. In order to explore the role of medium-chain fatty acids in kidney metabolism and disease, we conducted this systematic review.

Method: Systematic review. The pubmed database was used to search for keywords such as medium chain fat acids, medium chain triglyceride, MCFRA, MCT, chronic kidney disease, CKD, and renal fibrosis.

Results: In chronic kidney disease, long-chain fatty acids decrease and medium-chain fatty acids increase. The increase of medium-chain fatty acids may be a compensatory mechanism. Compared with long-chain fatty acids, medium-chain fatty acids are more easily metabolized through the tricarboxylic acid cycle, thus providing more energy. MCFAs are readily absorbed and transported across the intestinal barrier, with less interference from dietary factors. MCFAs can be rapidly metabolized to provide energy and can also be converted into ketone bodies, which can be used as an alternative energy source in cases of glucose deprivation.

Abstract

THE ROLE OF MEDIUM-CHAIN FATTY ACIDS IN RENAL METABOLISM AND DISEASES

Wu Yiting

Chengdu, P.R. China

Background and Aims: Through metabolomics research, it was found that in mice with chronic kidney disease, the distribution of lipids in the kidneys was different from that of healthy individuals, and medium-chain fatty acids were reduced. In order to explore the role of medium-chain fatty acids in kidney metabolism and disease, we conducted this systematic review.

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oxidized by cells, including cardiomyocytes, and provide a very efficient source of energy production. MCFAs display metabolic, biological, and physical properties that are distinct from LCFA, which may contribute to their reported benefits on the kidney's energy status and function. Only few deleterious effects have been reported with the use of MCFAs, many of which have been reported mainly when MCTs were administered as the main dietary energy source representing 50% of the total energy intake. These include decreased absorption of LCFA, which may result in deficiency in essential polyunsaturated LCFA, steatorrhea, gastrointestinal discomfort, increased risk of ketogenesis and acidosis, and in some studies, though not all, changes in blood lipid profile such as a raise in triglycerides or non-high-density lipoprotein cholesterol.

Conclusion: Studies in animal models indicate that MCFAs may favourably modulate kidney disease progression. Medium-chain fatty acids have protective effects on the kidney and provide new ideas for the relief and treatment of chronic kidney disease.

#4051

FGF-23 IN CHRONIC KIDNEY DISEASE: CORRELATION WITH BONE AND CARDIOVASCULAR PARAMETERS – A PRELIMINARY STUDY

Lina Maria Leon Machado 1,2, Gloria del Peso Gilsanz 1,2, María González Casaus 3, Marta Osorio 1,2, Yaniele Hernandez Perdomo 1, Carolina Tornero Marín 1, Pilar Aguado Acín 1, Mónica Coronado Poggio 1, Luisa Fernanda Giraldo 1, Teresa López Fernández 1, María Auxiliadora Bajo Rubio 1,2


Background and Aims: The FGF-23/Klotho ratio increases from early stages of chronic kidney disease (CKD) in parallel with kidney function decline. In some cases, serum FGF-23 levels increase is unbalanced, causing organ damage and increasing cardiovascular risk. The aim of our study was to evaluate the intact FGF-23 (iFGF-23) levels in a cohort of CKD patients and to establish its correlation with cardiovascular and bone mineral metabolism parameters.

Method: A prospective observational study in 59 adult normophosphatemic patients with CKD stage 2-4, was performed. Clinical and analytical variables (serum calcium, phosphorus, intact parathyroid hormone (iPTH), iFGF-23, calcidiol and calcitriol) were evaluated. Basal transthoracic echocardiogram, bone densitometry (Lunar prodigy, GE iDXA), software trabecular bone score (TBS), iNightingal clinical data analyzer and carotid Doppler ultrasound were performed. We excluded patients with background of primary hyperparathyroidism, hepatorenal polycystic disease, kidney transplant, tumoral nephrectomy, active neoplasm, tubulopathies or treatment with active vitamin D or calcimimetics. For statistical analysis, we use SPSS software (T Student, Pearson correlation with cardiovascular and bone mineral metabolism parameters.

Conclusion: Studies in animal models indicate that MCFAs may favourably modulate kidney disease progression. Medium-chain fatty acids have protective effects on the kidney and provide new ideas for the relief and treatment of chronic kidney disease.
Table 1: Baseline Characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n=359)</th>
<th>Progressors (n=220)</th>
<th>Non-progressors (n=139)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.8±8.9</td>
<td>59.2±8.7</td>
<td>50.2±9.3</td>
<td>0.04</td>
</tr>
<tr>
<td>BMI</td>
<td>26.0(23.4-29.6)</td>
<td>26.9(23.9-29.6)</td>
<td>25(24.3-29.0)</td>
<td>0.5</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>91.7</td>
<td>95.2</td>
<td>63.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>23.2</td>
<td>24.2</td>
<td>21</td>
<td>0.325</td>
</tr>
<tr>
<td>Proteinuria (%)</td>
<td>86.7</td>
<td>77.7</td>
<td>25.3</td>
<td>0.00</td>
</tr>
<tr>
<td>24 hr protein(g/day)</td>
<td>1.8(0.6-4.0)</td>
<td>2.0(0.8-4.4)</td>
<td>0.85(0.36-1.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>GFR-Decline</td>
<td>20ml/1.73 m²/year (8-40)</td>
<td>12 ml/1.73 m²/year (8.5-19.3)</td>
<td>1.6 ml/1.73 m²/year (0-3.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>CKD stages(%)</td>
<td>G1 19.7</td>
<td>17</td>
<td>26.7</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>G2 22.5</td>
<td>23</td>
<td>20.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G3a 21.7</td>
<td>24.3</td>
<td>14.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G3b 15.3</td>
<td>17.4</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G4 20.3</td>
<td>18.1</td>
<td>25.7</td>
<td></td>
</tr>
<tr>
<td>Diabetic retinopathy(%)</td>
<td>86.7</td>
<td>77.7</td>
<td>25.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diabetic neuropathy(%)</td>
<td>25.8</td>
<td>31.2</td>
<td>12</td>
<td>0.007</td>
</tr>
<tr>
<td>CVD(%)</td>
<td>40.8</td>
<td>45.8</td>
<td>28.3</td>
<td>0.04</td>
</tr>
<tr>
<td>CVA(%)</td>
<td>10.6</td>
<td>12.1</td>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>PVD(%)</td>
<td>6.9</td>
<td>8.1</td>
<td>4.1</td>
<td>0.17</td>
</tr>
<tr>
<td>AKI-Episodes(%)</td>
<td>50.8</td>
<td>57.3</td>
<td>34.3</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 2: Prediction of Risk factors.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>4.7</td>
<td>2.2-9.88</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>0.24</td>
<td>0.1-0.5</td>
<td>0.01</td>
</tr>
<tr>
<td>AKI episodes</td>
<td>2.18</td>
<td>1.2-3.7</td>
<td>0.003</td>
</tr>
</tbody>
</table>

DIFFERENCES IN PROTOCOLS FOR MEASURING GLOMERULAR FILTRATION RATE USING IOHEXOL

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Background and Aims: When assessing kidney function, measurement of glomerular filtration rate (mGFR) using an exogenous marker such as iohexol is the gold standard. In this study, we aim to identify similarities and differences between iohexol-based mGFR protocols.

Method: Detailed data on iohexol measurement protocols were obtained using a standardized survey sent to centres in Europe and the US. It was completed by 15 participants. Data are reported as number and percentage (n, %).

Results: In the participating centres, measurements are performed after referral by a nephrologist (n=6, 40%), other specialties (n=5, 33%) or for research purposes (n=4, 27%). Most common indications for mGFR are evaluation of kidney donors (n=5, 33%), drug dosing (n=4, 27%), abnormal body composition (n=3, 20%) and transplant evaluation (n=4, 27%). Most participants perform measurements in the morning (n=10, 67%), with patients withholding caffeine (n=5, 33%), fasting (n=4, 27%) or avoiding heavy meals (n=3, 20%). Most centres use an IV iohexol dose of 5 mL 300 mg I/mL (n=10, 67 %) or a dose based on weight (n=2, 13%). The timing of sample collection is shown in Figure 1, most often a single sample per time point (n=12, 80%). Iohexol is measured by LC-MS (n=8, 53%) or LC-UV (n=7, 47%). Within-assay variability ranges between <2% (n=3, 20%) and 6-8% (n=1, 7%) and the between-assay variability ranges between <2% (n=2, 13%) and 6-8% (n=2, 13%). When asked about assumptions and corrections, most centres make a one-compartment assumption in their PK model (n=8, 53%), others making two-compartment (n=2, 13%) or measurement-dependent (n=1, 7%) assumptions. mGFR is standardized for body surface area according to the DuBois-formula (n=6 (40%), Haycock and Schwarz formula (n=2, 13%) or not-specified (n=7, 47%). Some participants correct their measurements for eGFR (n=9, 60 %). Most centres participate in external quality control (Equalis, n=12, 80%).

Figure 1: Timing of samples after iohexol administration. Samples are drawn within the first hour (n=3, 20%), between 1-2 hours (n=13, 87%), 2-3 hours (n=8, 53%), 3-4 hours (n=11, 73%), 4-5 hours (n=9, 60%) or 5-7 hours (n=3, 20%) after iohexol administration.
Conclusion: There is a large variation in protocols for iohexol-based mGFR, which highlights the need for a standardized mGFR protocol before widespread use in clinical routine.

#3788
PROGNOSTIC ROLE OF THE NEUTROPHIL-TO-LYMPHOCYTE RATIO IN PATIENTS WITH CHRONIC KIDNEY DISEASE
Eun Hui Bae1, Jin Kim1, Su In Kim1, Da Hae Cho1, Sang Yoeb Lim2, Seong Kwon MA1, Soo Wan Kim1 and Hong Sang Choi1
1Gwangju, Rep. of South Korea and 2Ansan, Rep. of South Korea

Background and Aims: The neutrophil-to-lymphocyte ratio (NLR) has been demonstrated to have prognostic value in cardiovascular disease, infection, inflammatory disease, and several types of cancer. Therefore, it is expected that NLR has predictive value in patients with chronic kidney disease (CKD) but it has not been validated. Here, I aimed to investigate the possibility of NLR as a predictor of progression of CKD.

Method: This retrospective observational study included 141 patients with non-dialysis CKD. Subjects were divided into terciles (T1, T2, and T3) according to NLR. The primary outcome of interest was defined as a composite renal event, which included a decline in the estimated glomerular filtration rate (eGFR) of at least 50% or onset of end-stage renal disease (ESRD) during the follow-up period.

Results: The median follow-up duration was 5.45 ± 2.11 years. The median NLR for each group was 1.35 ± 0.05 in T1 (n=47), 2.16 ± 0.04 in T2 (n=47) and 4.29 ± 0.73 in T3 (n=47). The group with the highest NLR (T3) had higher baseline CKD and serum creatinine and lower eGFR levels than the group with the lowest NLR (T1). The cumulative incidence of composite renal events was significantly increased in T3, compared to T1 (p < 0.001, log-rank test). Cox regression analysis revealed that high NLR was independently associated with the risk of composite renal events (adjusted hazard ratio 2.85, 95% confidence interval 1.18-6.93).

Conclusion: A higher NLR reflects the more advanced stage of CKD and suggests that a role for NLR as a biomarker for predicting CKD progression.

Figure 1: Flow diagram of the study participants.

Figure 2A: Kaplan-Meier survival curve for cumulative incidence of renal events by Neutrophil-to-Lymphocyte ratio.
Figure 2B: Kaplan-Meier survival curve for cumulative incidence of decline of kidney function by Neutrophil-to-Lymphocyte ratio.

Figure 2C: Kaplan-Meier survival curve for cumulative incidence of initiation of RRT by Neutrophil-to-Lymphocyte ratio.

Figure 3: Kaplan-Meier survival curve for cumulative incidence of all-cause death by Neutrophil-to-Lymphocyte ratio.
Background and Aims: Increased urinary sodium-to-potassium (Na/K) ratio has been associated with chronic kidney disease. However, we demonstrated that urinary Na/K ratio does not accurately reflect dietary Na/K ratio. Rhythmic patterns of sodium storage and release from the skin interstitium are associated with aldosterone and cortisol levels and previous studies linked tissue sodium accumulation to water conservation. Therefore, we investigated whether the discrepancy between urinary and dietary Na/K ratio could be explained by these factors.

Method: For this post-hoc analysis, we used data from the long-term sodium balance studies Mars105 and Mars520. These studies collected 24-hour urine samples and controlled dietary salt intake for 105 (4 men) and 205 days (6 men) at levels of 6, 9 and 12 grams per day. We calculated the difference between urinary and dietary Na/K ratio. We tested whether this difference varied across salt intake levels in a linear mixed-effects model. Furthermore, we fitted two linear mixed-effect models to explain discrepancies between urinary and dietary Na/K ratio. In the first model, sodium intake, potassium intake, urinary aldosterone and urinary cortisol were fixed effects and each factor random slopes per participant were allowed. In the second model, sodium intake, potassium intake, urinary aldosterone and urinary cortisol were fixed effects and for each factor and dietary Na/K ratio. Furthermore, we investigated whether the discrepancy between urinary and dietary Na/K ratio could be explained by sodium intake, aldosterone, cortisol and urine volume. This suggests that tissue sodium accumulation contributes to the inaccuracy of a single 24-hour urine collection for estimation of dietary sodium and potassium intake.

Results: The median difference between 24-hour urinary and dietary Na/K ratio was −0.08 (IQR: −0.47 to 0.09). At higher salt intake levels the underestimation was significantly larger (mean difference −0.11, −0.22 and −0.36 for 6, 9 and 12 grams salt intake, respectively; P < 0.001). At each salt intake level, higher urinary aldosterone was associated with underestimation of the dietary Na/K ratio (Figure 1A). In contrast, higher urinary cortisol and higher urine volume were associated with relative overestimation of the dietary Na/K ratio (Figure 1B and C, respectively).

Conclusion: The discrepancy between dietary and urinary Na/K ratio can be explained by sodium intake, aldosterone, cortisol and urine volume. This suggests that tissue sodium accumulation contributes to the inaccuracy of a single 24-hour urine collection for estimation of dietary sodium and potassium intake.
Table 1: shows the results of all the patients and stratified according to the GFR (CDK-EPI greater or less than the median 21.7 ml/min).

<table>
<thead>
<tr>
<th>Age</th>
<th>eGFR &lt;21.7 ml/min (n=16)</th>
<th>eGFR ≥21.7 ml/min (n=16)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, woman (%)</td>
<td>66±±18.2</td>
<td>66.7</td>
<td>0.093</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>28.1</td>
<td>63</td>
<td>0.008</td>
</tr>
<tr>
<td>CKD-EPI (ml/min)</td>
<td>23.2±7.8</td>
<td>67±±2.4</td>
<td>0.000</td>
</tr>
<tr>
<td>IACR (mg/g)</td>
<td>26.8±±6.68</td>
<td>353±±6.08</td>
<td>ns</td>
</tr>
<tr>
<td>Copetin (pmol/l)</td>
<td>26.9±±22</td>
<td>30.6±±27.3</td>
<td>ns</td>
</tr>
<tr>
<td>GDF-15 (pg/ml)</td>
<td>4703±±2683</td>
<td>6274±±2854</td>
<td>0.002</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>5.7±±8.2</td>
<td>4.6±±1.9</td>
<td>ns</td>
</tr>
</tbody>
</table>

#4023
FEELINGS OF SAFETY AND SOCIAL BEHAVIOURS AFTER COVID-19 VACCINATION IN PEOPLE LIVING WITH KIDNEY DISEASE AND THEIR SIGNIFICANT OTHERS

Gurneet K Sohanahoa1,2, Naeema A Patel1,2, Ella Ford1,2, Thomas Wilkinson1,3, Courtney J Lightfoot1,2, Alice Smith1,2
1Leicester Kidney Lifestyle Team, Department of Population Health Sciences, University of Leicester, Leicester, United Kingdom, 2Leicester NIHR Biomedical Research Centre, Leicester, United Kingdom and 3NIHR Applied Research Collaboration East Midlands, Leicester Diabetes Centre, Leicester, United Kingdom

Background and Aims: Throughout the majority of 2020, the COVID-19 pandemic forced the UK population, and especially clinically vulnerable people such as those with chronic kidney disease (CKD), to isolate and cease their usual activities outside the home. The COVID-19 vaccine became available in early 2021, with the aim of protecting against COVID-19 infection, reducing the risk of serious illness or death, and consequently allowing a return to more normal social behaviours. In May 2021 we conducted a survey to explore perceptions of increased COVID-19 safety and resultant changes in social mixing behaviour in people with non-CKD CKD (ND-CKD), kidney transplant recipients (KTRs), and their significant others (SOs) after receiving the COVID-19 vaccination.

Method: ND-CKD, KTR and SO participants from 11 hospital sites across England were invited to complete an online survey in May 2021. The survey included items asking about changes to their feelings of COVID-19 risk and safety, and their social behaviours after receiving the COVID-19 vaccine. Participants ranked questions on 7-point Likert scales (perceived COVID-19 safety, 1: feel not safe at all to 7: feel completely safe; changes in social behaviour, 1: no change to 7: complete change), and provided free-text explanations for their ranked responses. Question ratings were analysed by ANOVA, and free-text responses by content analysis to identify common themes.

Results: A total of 59 elder men and 34 females (>65 years) of age with estimated glomerular filtration rate (eGFR) ≥45mL/min/1.73 m² followed up in renal clinics. They were looked for progression to ESRD and morbidity and mortality over time. The age, basic disease, systolic blood pressure, underlying heart disease and stroke was admitted to Nephrology for severe renal failure (P = 0.001), the degree of proteinuria among men was found to be statistically significant as compared to women in this cohort. During a median follow-up of 2.9 years, (22.3% men) developed ESRD while 7.2 % died. The adjusted risks for ESKD and mortality were higher in men as compared to the women in this cohort.

Conclusion: Elderly men have a steeper decline in eGFR along with higher proteinuria as compared to women indicating that the decline in the mean GFR in women was slower than in men, independent of health status.

#4758
IMPACT OF GENDER ON CHRONIC KIDNEY DISEASE IN ELDERLY

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Background and Aims: Men with chronic kidney disease (CKD) progress to end-stage CKD at a faster rate than women Data for the association of sex with chronic kidney disease (CKD) progression are conflicting, a relationship between the two especially among elderly population needs understanding.

Method: We conducted a prospective study among all elderly population with CKD attending Nephrology OPD between between Jan 2019-Jan 2022 in Tertiary care hospital, Lucknow and assessed for the stage of CKD and their fall in eGFR over the period of fall in eGFR within a year’s time.

Results: A total of 59 elder men and 34 females (>65 years) of age with estimated glomerular filtration rate (eGFR) <60mL/min/1.73 m² followed up in renal clinics. They were looked for progression to ESRD and morbidity and mortality over time.

Conclusion: Elderly men have a steeper decline in eGFR along with higher proteinuria as compared to women indicating that the decline in the mean GFR in women was slower than in men, independent of health status.

#6475
AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE WITH COMPLETE SITUS INVERSUS: A CASE REPORT

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Background and Aims: Association between complete Situs inversus and autosomal polycystic kidney disease is rare. The Medline search revealed only three such cases. We report the fourth one. Recent studies have revealed ciliary dysfunction as a cause of both conditions.

Method: We report a case of association of familial hereditary polycystic kidney disease with a situs inversus.

Results: A 52-year-old patient with a familial history of polycystic kidney disease and stroke was admitted to Nephrology for severe renal failure with hypertension. On examination, the patient had a blood pressure of 160/100mmHg. The abdomen was soft, with bilateral palpable renal masses persist in today's environment and highlight the need for communication of high-quality research evidence to encourage uptake of booster COVID-19 and flu vaccines, and effective public education campaigns, to allow clinically vulnerable people to confidently return to pre-pandemic social activity.
with irregular surfaces. Neurological examination was without abnormalities. The most affected creatininemia at 82μmol/L, urea at 44mmol/L, correct ionogram, CO2 at 19 mmol/L, calcium at 1.98mmol/L and uric acid at 860 μmol/L. The 24-hour proteinuria was 1.5g. The cytobacteriological examination of the urine was negative. The chest X-ray showed a situs inversus of the heart. On abdominal ultrasound, the kidneys were polycystic, the liver was seen on left and the spleen on the right. The patient was put on antihypertensive treatment with a calcium channel blocker and Purinol. Given the new and biological improvement, the patient was discharged without monitoring at the outpatient clinic with possible preparation for hemodialysis. In addition, a cerebral MRI angiography was requested to detect cerebral damage because of the family history of stroke.

Conclusion: Polycystic kidney disease is caused by mutations in the polycystic kidney and hepatic disease (PKHD1) gene. Several proteins that are encoded by genes associated with polycystic kidney disease have been identified in primary cilia in renal tubular epithelia. These findings have suggested that abnormalities in cilia formation and function may play a role in the pathogenesis of PKD. Treatment options for PKD are still being explored but further research can develop solutions to increase the life expectancy of patients diagnosed with PKD. Cases like this are rare but could provide more information on the causes of PKD and Situs Inversus leading to these new developments.

#6672
THE DEVELOPMENT OF A COMMUNITY-Nephrology, MULTI-DISCIPLINARY SERVICE
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Background and Aims: The Walsall Together clinical and operational leads constructed a collaborative initiative between nephrology and community services. Driven to provide multi-agency, patient-focused care. The aim of the community nephrology MDT service is to identify and optimally manage individuals with acute nephrological presentations and optimally manage individuals with secondary complications of chronic kidney disease (CKD) at home, while maximally utilising outpatient community services to prevent hospital admissions.

Method: Nephrology and community teams, including rapid-response, complex-case management, enhanced-care and frailty teams devised a MDT service for individuals with either community-acquired acute kidney injury (AKI) or complications of CKD. The MDT service can consist of, a nephrologist, community-CKD nurse, a member from each of the above teams, a community pharmacist and an MDT coordinator. Patients are identified from the MDT attendee’s caseload, from the community heart failure and the community geriatrician patient cohort. A weekly MDT meeting is held on Microsoft Teams, this allows for efficient working across a large geographical area. The MDT coordinator is essential for the efficient performance of the community nephrology MDT. They are responsible for: organising meetings, producing minutes, requesting laboratory investigations (including urine album in creatinine ratio), chasing results from clinical investigations and finally ensuring that the actions generated from the MDT are completed. The community pharmacist is an independent prescriber and immediately actions any medication changes. The community teams consist of advanced clinical practitioners or band 7 above nurse prescribers. All clinical staff perform home visits and fully utilise outpatient services including ambulatory-care unit services for medical assessment, urgent imaging and intravenous electrolyte replacement. The medical-day-case unit services for the administration of blood transfusions. The community outpatient access team services for intravenous iron therapy and antibiotic therapy.

Results: Currently, the community nephrology MDT is actively managing over 60 patients. This excludes patients who have been successfully managed and discharged from the community MDT service. The multimorbid, patient cohort with recurrent hospital admissions appear to have benefited the most. A reduction and/or cessation is noted, in hospital admissions after the introduction of interventions from the community nephrology MDT. The service works with secondary care teams to establish the community MDT service in the community and manage individuals with CKD. This reduces the number of admissions related to secondary complications of CKD. Furthermore, by managing acute illness in the community, the service reduces the number of individuals admitted to hospital with community acquired AKI. Finally, in the unfortunate event of terminal, irreversible pathology, the MDT service allows for advanced care planning and referral to community palliative care services.

Conclusion: The Walsall Together collaboration has demonstrated that utilising a multi-agency approach to managing acute and chronic renal disease, can result in a reduction in hospital admissions. Furthermore, the cooperative multi-speciality approach, has led to improved monitoring and management of housebound individuals with CKD.

#2708
THE EFFECT OF PERCEIVED TEMPERATURE ON THE MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS
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Background and Aims: With the global warming, the interest in health risks from the high temperature exposure is growing. The perceived temperature is an equivalent temperature based on a complete heat budget model of the human body. We aimed to analyse the effect of perceived temperature on the overall mortality among patients with chronic kidney disease.

Method: A total of 32,870 patients with chronic kidney disease living in Seoul metropolitan region were recruited in a retrospective cohort (2001-2018). The perceived temperature during summer season (from July to September, at each year) was calculated using various climate factors including air temperature nearby automated weather station, dew point temperature, wind velocity, height of anemometer above ground, and total cloud amount. We assessed the association of perceived temperature using inverse distance weighting on mortality in patients with chronic kidney disease in the Cox proportional hazard model that was adjusted for sex, age, body mass index, estimated glomerular filtration rate, hypertension, and diabetes mellitus status.

Results: During the 6.14±3.96 years, 3,863 deaths (13%) were observed. We confirmed the significant effects of perceived temperature (average perceived temperature: hazard ratio [HR] 1.21, 95% confidence interval [CI] 1.18-1.23; minimum perceived temperature: HR 1.02, 95% CI 1.00-1.05; maximum perceived temperature: 1.20, 95% CI 1.18-1.22) on mortality among patients with chronic kidney disease in univariable analysis. In multivariable analysis, average perceived temperature (HR 1.22, 95% CI 1.19-1.25) and maximum perceived temperature (HR 1.20, 95% CI 1.17-1.23) showed increased risk for overall mortality among patients with chronic kidney disease.

Conclusion: Long-term exposure to high perceived temperature during summer season increased the risk of mortality among patients with chronic kidney disease.

#3880
REDUCED EGFR IS ASSOCIATED WITH IMPROVED SURVIVAL IN PATIENTS WITH RENAL CANCER WHO RECEIVED TARGETED SYSTEMIC ANTI-CANCER THERAPY
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Background and Aims: Treatment with vascular endothelial growth factor signalling pathway inhibitors (VSP1) and immune checkpoint inhibitors (ICI) has transformed outcomes in advanced renal cancer. A significant proportion of people with renal cancer have co-existing chronic kidney disease (CKD) and concerns persist about the usage of these agents in patients with CKD. We sought to analyse the effect of reduced kidney function on the survival of patients with renal cancer treated with VSI or ICI.

Methods: The Chemocare and NHS West of Scotland SafeHaven databases were linked (data collection spanning 2008–2020), to identify adults from the Greater Glasgow and Clyde Health board who had received either a VSI or ICI as an anti-cancer therapy. We included participants with two available serum creatinine values (at least 3 months apart) before the date of initiation of treatment. The estimated glomerular filtration rate (eGFR) was calculated using CKD-EPI (2009), the average of the two eGFR results (at least 3 months apart) was included in the analyses. Proteinuria was defined as any positive urine albumin: creatinine (>3 mg/mmol) or protein:creatinine (>15 mg/mmol) ratio before treatment. Factors associated with all-cause mortality were analysed using Cox proportional hazards models with R Software.

Results: We identified 349 patients with renal cancer who received at least one cycle of ICI and/or VSI. Sufficient serum creatinine results were available for analysis in 337 of these patients. The average age at first treatment was 63.0 (IQR 55-71) years, 62.5% were male and the median BMI was 28.2kg/m² (IQR 23.9-31.6). Proteinuria results were recorded in 125 patients and 149 patients had nephrectomy prior to treatment. The majority of patients received VSI (88.7%). Over a median follow-up of 335 days (IQR 131 days – 840 days),
281 patients died (Table 1). On univariable analysis, lower baseline eGFR (per 10mL/min/1.73 m² decline in eGFR: HR 0.89, CI 0.84-0.95, p = <0.001) and prior nephrectomy (HR 0.65, CI 0.52-0.83, p = <0.001) were associated with a higher hazards of death. Age (HR 0.99, CI 0.98-1.00, p = 0.245), sex (HR 0.93, CI 0.74-1.18, p = 0.570), BMI (HR 0.99, CI 0.96-1.03, P = .775) and treatment class (HR 0.76, CI 0.51-1.14, p = 0.253) were not associated with higher hazards of death. After adjustment for age, sex and prior nephrectomy, lower eGFR was associated with lower hazards of death (per 10mL/min/1.73 m² decline in eGFR: HR 0.91, CI 0.84-0.97, p = 0.007). In a sensitivity analysis in people who had complete eGFR and proteinuria data available, the presence of proteinuria was associated with greater hazards of death (HR 1.63, CI 1.05-2.12, p = 0.029) after adjustment for age, sex, eGFR and nephrectomy (Figure 1).

Conclusion: Lower baseline eGFR before treatment was associated with reduced hazards of death. This finding was not fully explained by the association of prior nephrectomy with better cancer outcomes. This suggests that other factors may contribute to these discrepancies, such as underlying selection bias of patients for treatment, or bias from the marker used to estimate GFR in this group of patients. The presence of proteinuria was associated with an increased hazards of death and maybe a better marker of renal-associated risk in this group than eGFR and warrants further investigation.

#3859
THE TREND OF RENAL REPLACEMENT THERAPY IN N. MACEDONIA FROM 2015 TO 2020: DATA FROM THE ERA-EDTA ANNUAL REGISTRY

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Background and Aims: Kidney Failure (KF) is treated with three modalities of renal replacement therapy (RRT): kidney transplantation (Tx), hemodialysis (HD), and peritoneal dialysis (PD). Our study aimed to present the trend of RRT in N. Macedonia from 2015 to 2020.

Method: The epidemiological retrospective study analyzed the patients with kidney failure by gender, age, etiology of kidney disease, and modality of RRT. The data were processed from the annual reports of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA). The study patients were divided into group 1 (prevalent) with patients on the RRT at the current year, group 2 (incidence at Day 1) with patients on the RRT with a duration of at least 1 day, and group 3 (incidence at Day 91) with patients on the RRT with a duration beyond 91 days.

Results: A total of 10395 patients were analyzed with a mean age of 59.2 ± 9.5 years (median 60.4 years), of which 60.2% were male. From 2015 to 2019, there was an increasing trend in all groups, and most patients were reported in 2019. In group 1, 1598 patients were registered in 2015, and 1762 patients were registered in 2020, which is an increasing trend of 10.3%. The number of patients in group 2 was increasing every following year, with the highest growth
in 2019 up to 12.1%, compared to 2018. The number of patients in group 3 also showed significant growth from 253 patients in 2015 to 324 patients in 2019, but there was a decrease of 16.4% in 2020 (271 patients). Deviations are observed in 2020, with a decrease in the number of patients in group 1 and group 3, as well as a slowdown in the growth dynamics of patients in group 2, which might be associated with the start of the SARS-CoV-2 pandemic. According to the modality, most of the patients (84.7%) were on HD in 2015 and 85.9% in 2020. The most frequent age group of patients was from 45 to 64 years, from 36.3% to 49.4%. There was an increasing trend of patients from older age groups (over 64 years) and male patients. The increasing number of patients from the age group 75+ years was also noted in all groups. Etiology of kidney disease: hypertension (25.8%) and diabetes mellitus (17.4%) were the leading causes of KF in patients requiring RRT.

Conclusion: The study showed a constantly increasing trend of patients with KF requiring RRT. The largest number of patients were men, aged from 45 to 64 years. Hypertension and diabetes mellitus were the leading causes of KF, and most of the patients were treated with HD.

C4 - CO-MORBIDITIES (ANAEMIA, CARDIOVASCULAR, CKD-MBD, ETC.)

#3750
SERUM AMYLOID A AS PROGNOSTIC MARKER FOR CKD AND NON-CKD COVID-19 PATIENTS ADMITTED TO THE EMERGENCY ROOM
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Background and Aims: Patients with chronic kidney disease (CKD) and a SARS-CoV-2 infection are at higher risk of developing acute kidney injury (AKI) and of mortality after hospital admission. Herein, we assessed whether serum amyloid A (SAA) was associated with outcomes (AKI and/or death). Method: The study group included 160 patients: 70 Covid-19-positive CKD patients (eGFR <60 mL/min), 50 Covid-19-positive patients with no history of kidney disease, 20 Covid-19-negative CKD patients, and 20 healthy controls. We collected data on patients' gender, age, co-morbidities, and laboratory results from blood and urine samples taken at admission into the ER, and from healthy volunteers. All participants gave their informed consent for trial with protocol № 12/31.05.2022 approved by the ethical committee KENIMUS of the Medical University of Sofia, Bulgaria. Laboratory values included calculated eGFR (by the CKD-EPI 2021 formula), highly sensitive inflammatory markers, D-dimer, blood-cell counts, and changes in urine parameters. Co-morbidities included hypertension, obesity, diabetes mellitus, vascular disease, and CKD. All patients had been treated by the official protocol of the Republic of Bulgaria for SARS-CoV-2. We determined the levels of SAA across the four groups to assess if this biomarker could predict AKI, risk of mortality, and if there was a significant difference between the CKD and non-CKD patients.

Results: Overall, median age of Covid-19 patients was 56.4 years; gender ratio was 50% M/F in all groups. Median duration of symptoms before hospitalization was 6 days. Of the 160 patients, 30% were febrile with temperatures >38°C. Overall, creatinine level on admission was elevated in 40% of cases; eGFR was <60 mL/min/1.73 m² in 37.5% of patients. Mean value of eGFR on admission was 82.3 mL/min/1.73 m² for the non-CKD Covid-19-positive group, 49.5 mL/min/1.73 m² for the CKD Covid-19-positive group, 62.3 mL/min/1.73 m² for the CKD patients without COVID-19, and 111.1 mL/min/1.73 m² for the healthy control group. In total, three Covid-19 patients needed renal-replacement therapy: two patients from the CKD group and one...
from the non–CKD group. AKI occurred in 38 Covid-19 patients (23.7%). Of those, 76.3% of the Covid-19 patients with AKI had a serum creatinine level within our cohort of 160 patients, in-hospital mortality was 14.3% (23 patients): of these, 82.6% had AKI (19 patients). Overall, 100% of patients that did not survive Covid-19 also had CKD. We analyzed the levels of SAA across the groups. The reference limits considered for negative results were < 7 pg/mL; the ELISA could measure values up to 300 pg/mL. Of the 23 patients that died, 19 had levels > 300 pg/ml (82.6%), whilst the remainder had results >250 pg/mL. The other patients who survived the infection in our cohort had levels well below 200 pg/ml. When the patients with AKI and without AKI were compared on the basis of SAA, patients with AKI had significantly higher biomarker values (p = 0.02). When compared across the four groups, no significant differences were found except when comparing the healthy control group with the other three groups, where there was significance of p<0.0001 in each comparison.

Conclusion: We confirm that SAA was a reliable biomarker for predicting AKI in Covid-19 patients. It also acted as a predictor for a fatal outcome in patients with severely Covid-19 infection. In conclusion, SAA is a reliable marker, highly informative in the emergency department setting, enabling us to have an early prognosis for the outcome of the Covid-19 infection for the patients in our cohort.

#4399
ALGORITHM-MANAGED DOSING AND PHARMACIST-MANAGED DOSING OF ERYTHROPOIETIN STIMULATING AGENTS IN RENAL ANEMIA: A SYSTEMATIC REVIEW
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Background and Aims: In clinical practice, the treatment of renal anemia is challenging. The attainment of target levels for hemoglobin is often low, due to the high incidence of infections, hyporesponsiveness to erythropoietin stimulating agents (ESA), and suboptimal prescribing of ESA and iron. Several interventions to improve the treatment of renal anemia have been developed, two of them being algorithm-managed dosing and pharmacist-managed dosing of ESA. We performed a systematic review to identify and summarize these two types of interventions and to determine their effectiveness in improving the treatment of renal anemia.

Method: We followed the PRISMA guidelines for systematic reviews. Studies that explored the effect of algorithm-managed and pharmacist-managed dosing of ESA in adult patients with renal anemia were evaluated for inclusion. No restrictions were set on outcome parameters. All observational and interventional studies that included a control group and had a follow-up of at least six months, were eligible for inclusion. Only full-length articles were considered for inclusion. PubMed, Embase, Web of Science, and the Cochrane Library were searched from their inception through July 2022. All included studies were evaluated by two independent reviewers. The quality of studies was assessed by the Newcastle Ottawa Scale and the risk of bias was assessed by the ROBINS-I and RoB1 tools. Data were summarized and tabulated. Studies were grouped according to intervention type, study design, and risk of bias. The protocol of this study was registered in PROSPERO (International Prospective Register of Systematic Reviews) with ID CRD42021243678. This study was funded by the Francisca Gasthuis and Vlietland hospital.

Results: A total of 120 articles were assessed for inclusion, and after screening, 16 articles were included with a total number of 3777 patients. Available evidence was scarce and generally of low to moderate quality; only two RCTs could be identified. All but one of the other studies were observational in nature. The risk of bias was serious in all but one study. Study follow-up was relatively short, varying between six and thirteen months. In six studies, ESA dosing was pharmacist-managed and in one study ESA dosing was algorithm-managed, in nine studies a combination was used. The quality of the intervention description was low to moderate and interventions generally were not reproducible. Although heterogeneity was substantial for outcome parameters, four types of outcome parameters could be determined: hemoglobin/hematocrit, ESA dose and expenditure, iron status, and iron dose. Quantitative synthesis of data was not possible due to the substantial heterogeneity in outcome parameters and the high risk of bias. Therefore, the effectiveness of algorithm-managed and pharmacist-managed dosing of ESA in renal anemia could only be qualitatively assessed for the four types of outcome parameters. In six of the fifteen studies that reported on hemoglobin or hematocrit, the percentage of patients within target levels was significantly higher for the intervention group, whereas in four studies no significant difference was found. Six of the ten studies that reported on ESA dose or ESA expenditure found a significant decrease in ESA dose or expenditure in the intervention group, whereas two studies reported no significant difference. In five of the seven studies that reported on iron status, a significantly higher iron status was found in the intervention group, whereas one non-inferiority study reported no significant difference. In three of the four studies that reported on the iron dose, no significant difference was found between the intervention and the control group, whereas in one study the iron dose was significantly higher in the intervention group.

Conclusion: Available evidence was scarce with a high risk of bias, and quantitative data synthesis was not possible. Therefore, no definite conclusions could be drawn on the effectiveness of algorithm-managed and pharmacist-managed dosing of ESA in renal anemia. Consequently, no recommendations on the implementation of either of the two interventions could be made.

#4405
CHANGES OF VITAMIN D BIOMARKERS ACCORDING TO CAUSE-GLOMERULAR FILTRATION RATE-ALBUMINURIA (CGA) CLASSIFICATION OF CKD PATIENTS
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Background and Aims: The monitoring of vitamin D status is important to manage metabolic bone disease in patients with chronic kidney disease (CKD). 25(OH)D is used as the vitamin D marker in CKD patients, but vitamin D metabolite ratio (VMR) is also becoming useful as the marker, too. The classification of CKD is based on the cause-glomerular filtration rate (GFR)-albuminuria (CGA) in the KDIGO guidelines. This classification is importantly used in the management decision of CKD and predicts well the prognosis related to CKD. However, there are no study on the changes in various vitamin D markers according to CGA classification. We aimed to investigate the changes of vitamin D biomarkers according to classification by cause of CKD, estimated GFR (eGFR), and proteinuria of CKD patients.

Method: We prospectively analyzed blood and urine samples from a total of 206 patients who received informed consent with CKD class G2-G5. After classifying each group according to the presence or absence of diabetes, eGFR degree, and proteinuria amount, the differences in various vitamin D biomarkers in each group were compared. VMR was the ratio of 24,25(OH)2D to 25(OH)D.

Results: The mean age of the 206 patients was 64.1±12.72 years old. The patients with DM were 46.6% and the most common cause of CKD was glomerular disease (51.4%) including diabetic nephropathy (DN). There was no significant difference in all vitamin D markers we measured in the comparison between the DKD group and the non-DKD group. Among DKD patients, the DN group had significantly lower levels of 25(OH)2D (p=0.012) and bioavailable 25(OH)D (p=0.044) than the no DN group. When divided into three groups according to the degree of eGFR, the mean value of 24,25(OH)2D (p=0.003) and VMR (p<0.001) were significantly lower as the eGFR decreased but all 25(OH)D markers showed no significant decrease with the change in eGFR. In the diabetic patients, when divided into four groups according to the amount of proteinuria, the group with high proteinuria had significantly lower levels of total 25(OH)D (p=0.011), bioavailable 25(OH)2D (p<0.001), free 25(OH)D (p=0.001), and 24,25(OH)2D (p=0.029) compared to the group with low proteinuria but there was no significant difference in VMR. In the non-diabetic patients, when divided into three groups according to the amount of proteinuria, the group with high proteinuria had significantly lower levels of total 25(OH)D (p=0.032), bioavailable 25(OH)D (p=0.010), and free 25(OH)D (p=0.035) compared to the group with low proteinuria but there was no significant difference in 24,25(OH)2D and VMR levels. In these CKD patients, there was no significant difference in the level of VDBP despite the presence or absence of diabetes, the degree of eGFR, and the amount of proteinuria.

Conclusion: As eGFR decreased, the levels of 24,25(OH)2D and VMR significantly decreased. All vitamin D markers we measured showed no significant difference depending on the presence or absence of diabetes except for the low 24,25(OH)2D and bioavailable 25(OH)D levels in DN patients. Regardless of the presence or absence of diabetes, all 25(OH)D
markers decreased significantly as proteinuria increased. Although we showed that significant changes in vitamin D markers differed according to CGA classification, large-scale study and long-term follow-up are necessary for meaningful use in diagnosis and treatment.

#4568
C-REACTIVE PROTEIN / SERUM ALBUMIN RATIO IN PATIENTS WITH COVID-19 AND ADVANCED CHRONIC KIDNEY DISEASE DUE TO TYPE 2 DIABETES MELLITUS

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Background and Aims: The patients with laboratory confirmed COVID-19 and advanced chronic kidney disease (CKD) due to type 2 diabetes mellitus (T2DM) are at a high risk of adverse outcomes of COVID-19. The mortality in both subgroups was rather high (38.2% vs 38.5% resp.). The median of CPR in (1) was 96 (IQR 27; 144) mg/l (survivors) vs 158 (IQR 43; 193) mg/l (nonsurvivors), \( P = .025 \). The median of SA in (1) was 37.0 (IQR 32.0; 38.5) g/l (survivors) vs 30.0 (IQR 29.6; 33.0) g/l (nonsurvivors), \( P < .001 \). The median of CPR (2) was 69 (IQR 39; 133) mg/l (survivors) vs 90 (IQR 33; 156) mg/l (nonsurvivors), \( P = .246 \). The median of SA in (1) was 34.8 (IQR 32.0; 37.0) g/l (survivors) vs 33.0 (IQR 28.0; 35.0) g/l (nonsurvivors), \( P = .84 \). CPR/SA in (1) subgroup was 2.7 (IQR 0.8; 4.0) (survivors) and 4.9 (IQR 2.6; 5.9) (nonsurvivors), \( P = .012 \). CPR/SA in (2) subgroup was 2.4 (IQR 1.3; 4.3) (survivors) and 2.6 (IQR 1.0; 5.9) (nonsurvivors), \( P = .457 \). Determination of the cut-off point for CPR/SA ratio was based on the receiver operating characteristic (ROC) analysis. Cut off point CPR/SA ratio for (1) subgroup is 3.6 and cut off point for CPR/SA ratio for subgroup (2) is 2.4. 55-days cumulative proportion surviving (Kaplan-Meier method) are presented on the Fig. 1 and Fig. 2. In subgroup (1), a threshold value of the CPR/SA ratio was revealed, which significantly affects the survival of patients. In subgroup (2), it was not possible to identify the threshold value of the CPR/SA ratio, which significantly affects the cumulative survival rate of patients.

Conclusion: CPR/SA ratio >3.6 in patients with advanced DKD not requiring MHD is a laboratory indicator of adverse outcome of COVID-19. The studied parameter did not differ in patients on MHD regardless of the COVID-19 outcomes.

#5868
PREVALENCE AND MANAGEMENT OF CHRONIC COMPLICATIONS IN PATIENTS WITH DIABETES AND ADVANCED CHRONIC KIDNEY DISEASE: A RETROSPECTIVE AUDIT

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Background and Aims: Current guidelines recommend that all patients with Chronic Kidney Disease (CKD) stage 3b or higher should be monitored and treated for anaemia, mineral bone disorder (BMD) and metabolic acidosis. We audited the prevalence and management of these complications in a cohort of patients with diabetes and advanced CKD.

Method: A retrospective audit was undertaken using KDIGO guidelines as standard and necessary approvals were secured from the governance team at University Hospitals Birmingham. We included patients with (a) diabetes (b) eGFR 30 and 15 ml/min/1.73 m² and (c) attending diabetes clinics as of 30/09/2022. Using electronic patient records, we collected: demographics, co-morbidities, complications, treatments, body weight, BMI, blood pressure and serial biochemistry (creatinine, Hb,ic, cholesterol, UAab/Creat ratio, bicarbonate, haemoglobin, vitamin D, parathyroid hormone (PTH). Following definitions were applied: anaemia as Hb <13 g/dl for men and <12 g/dl for women, BMD as vitamin D <40 nmol/l plus raised PTH, acidosis as bicarbonate <22 meq/l. Data was analysed using SPSS 26. Descriptive statistics (frequencies and cross tabulations) were used to estimate prevalence. Independent means test was used for continuous variables. Comparison between groups was undertaken using the Chi Square test and one way ANOVA test.

Results: Data for 192 subjects (110 European (EUR), 40 South Asian (SA), 42 African-Caribbean (AFC) /other) was analysed. Mean age (SD) was 73 (±11) years. There were no significant differences in general characteristics between the ethnic groups except for albuminuria which was greater in SA and AFC compared to EUR (193 v 133 v 95.5mg/mmol; \( P = .038 \)). 47% of the cohort had at least one diabetes related complication. 63/192 (32.8%) had cardiovascular disease, 49/192 (25.3%) had retinopathy and 19/192 (9.9%) had neuropathy. Insulin was the most common prescribed glucose lowering agent 105/192 (55%) with proportionately more SA treated with insulin (65%). Anaemia was present in 171/183 (93.4%) of the patients. 82/101 (81.2%) had BMD, and 135/168 (82.8%) of patients had metabolic acidosis. 65/192 (33.9%) of patients had all 3 complications. Only 38/133 (22%) of those with anaemia were receiving treatment out of which only 56.8% were treated adequately with a Hb of >10g/l. Corresponding figures for BMD and metabolic acidosis were: BMD: 39/82 (47.6%) treated and 42% optimally corrected, metabolic acidosis: 54/135 (40%) treated and 53% optimally corrected. There were no significant differences between ethnic groups in prevalence or treatment of these complications.
Table 1: Prevalence and management of CKD-related complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Prevalence n (%)</th>
<th>Treated n (%)</th>
<th>Treated and adequately corrected %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>171 (93.4)</td>
<td>38 (22.0)</td>
<td>36.8</td>
</tr>
<tr>
<td>BMD</td>
<td>81 (81.2)</td>
<td>39 (47.6)</td>
<td>42.0</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>135 (82.8)</td>
<td>54 (40.0)</td>
<td>53.0</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of CKD related complications is high. The management of these complications however, is suboptimal. Increased emphasis on the management of these complications is required to improve outcomes in patients with advanced CKD.

#4424
FREQUENCY OF RED BLOOD CELL TRANSFUSION USE IN PATIENTS WITH ANEMIA OF CHRONIC KIDNEY DISEASE (CKD) IN EUROPE: A SYSTEMATIC LITERATURE REVIEW

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Background and Aims: Anemia of CKD is common and managed with oral or intravenous iron, erythropoiesis-stimulating agents (ESAs) and, when necessary, red blood cell transfusions (RBCT). Reducing RBCT use is a goal in the management of anemia of CKD due to known short term (e.g., hyperkalaemia, heart failure) and longer term risks (e.g., allosensitization), but there is limited collated data on their use in Europe. A systematic
literature review was conducted to evaluate the frequency of RBCT use among dialysis and non-dialysis (ND) patients, and associated data reported for predictors of RBCT receipt, complications, healthcare resource use (HCRU), and costs.

Method: A comprehensive search strategy was used to retrieve real-world (RW) studies and randomized controlled trials (RCTs) conducted in DD and ND CKD patients with anemia using Embase and Medline (1980 to June 2022). Searches of conference abstracts, bibliographies and grey literature were also conducted. Studies which included European patients' data are described here.

Results: Of the 3495 citations retrieved, 182 relevant studies were identified including 54 studies with European patients. Thirteen were RW studies including 12 quantifying the frequency of RBCT use (Table). In RW studies, the overall frequency of RBCT use ranged from 4.3–35.0% across studies and for key subgroups (n=10 studies: DD only studies, 8.4–33.9%; ND only studies, 4.3–35.0%). The number of RBCT units per patient-year (PY) ranged from 1.4–2.7 among DD patients (n=2 studies; no ND studies found). RBCT use appeared to vary by patient factors (iron/ESA use, CKD stage), by study design (e.g., length of follow-up) and across countries (but with no clear patterns in geographic variation). For the 41 RCTs including European patients (single country, n=3 studies, multi-country, n=38 studies), the overall frequency of RBCT use ranged from 0–21.6% (DD only studies, 0–21.6%; ND only studies, 0–14.8%), which was lower than those recorded in the RW studies. The rate of RBCT use in trials ranged from 3.5–66.0 events per 100 PY overall (DD only studies, 3.5–66.0; ND only study, 8.0); the number of RBCT units per PY ranged from 0.20–1.65 among DD patients (n=2 studies; no ND studies found). No studies used statistical modelling to quantify predictors of RBCT use while adjusting for potential differences between groups. One RW study from 1986 reported detection of human T-lymphotropic virus type III (HTLV-III; subsequently known as HIV) antibodies in 4 patients who had received RBCT (in a sample of 276 screened chronic HD patients). Of three RW studies reporting data on costs, two were >30 years old and one provided costs relating to receipt of inpatient RBCT in ND patients stratified by oral iron, low dose, or high dose intravenous iron use from 2013–2015 (n=111).

Conclusion: RBCT use forms part of the management of anemia of CKD in Europe and its use is variable but not infrequent. RBCT risk in RW studies appeared elevated compared to RCTs. There were no consistent patterns in geographic variation, but risk varied by patient factors and study design. There is currently limited European data reporting on frequency of associated complications, predictors of RBCT use, associated HCRU and costs. Funding: GSK (Study 211829).

#5963
THE ASSOCIATION OF FRAILTY, DENTAL STATUS, INFLAMMATION AND MALNUTRITION IN HEMODIALYSIS PATIENTS

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Background and Aims: Persistent low-grade inflammation and malnutrition in chronic kidney disease (CKD) are associated with so many CKD complications. Frailty, the state of increased vulnerability often associated with aging, had a higher incidence in CKD patients regardless of age. In this study, we aimed to investigate the frequency of frailty among hemodialysis patients and volunteers with normal kidney function to define its relationship with inflammatory markers, biochemical parameters and dental status.

Method: A cohort of 86 CKD patients with hemodialysis (HD) and 74 volunteers with normal kidney function (similar in terms of age and gender distribution) were included in this study. Both groups were evaluated by the Clinical Frailty Scale in three groups as non-frile, pre-frail and frail. Demographic characteristics, biochemical parameters and dental status were recorded.

Results: 21 of 86 patients (24.4%) were frail in CKD patients with HD, and 4 of 76 patients (5.4%) in the control group were frail (p<0.001). The frail individuals in the HD group were older (p<0.001), had more systemic diseases (p<0.001), had higher serum C-Reactive Protein (CRP) levels (p<0.001), lower serum albumin levels (P = .001), lower serum creatinine levels (p<0.003). When the number of teeth was evaluated: the number of patients with more than 20 teeth was significantly lower in the frail group than in the non-frail group (p<0.001).

Conclusion: In our study, the frequency of frailty in hemodialysis patients was found to be significantly higher than in the control group. The lower albumin and serum creatinine levels, the higher CRP levels and the lower number of teeth suggest the relationship between frailty with dental status, malnutrition and inflammation in hemodialysis patients. It can be concluded that improvements in oral health and/or inflammation status can contribute to the improvement of frailty in this patient group.

#6754
THE EFFECT OF REDUCED RFN FUNCTION ON SEXUAL FUNCTION IN PATIENTS WITH HEART FAILURE

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Background and Aims: Sexual Dysfunction is a common and often undiagnosed complication in patients with Heart Failure (HF) or Chronic Kidney Disease (CKD). Sexual dysfunction presents a strong association with cardiovascular disease and death. This study aims to evaluate the possible effect of reduced renal function on the sexual dysfunction in patients with heart failure.

Method: This is a prospective case-control study in patients with Heart Failure (clinical diagnosis based on relevant symptoms and/or signs) with preserved or reduced renal function, defined as estimated glomerular filtration rate (eGFR) >60 and <60 ml/min/1.73 m², matched for age (± 5 years). The eGFR was calculated with the CKD-EPI equation. Sexual dysfunction was evaluated with the validated Female Sexual Function Index Scoring (FSFI) and the International Index of Erectile Function (IIEF) questionnaires in the native language.

Results: A total of 214 (107 per group) patients were included in this study. Patients’ age 74.10±8.97 vs 75.81±8.66; P = .157), gender (males: 65.4% vs 57.9%; P = .261) and BMI (28.10±4.90 vs 28.99±4.43; P = .164) were not different between the two study groups. In total population, sexual dysfunction was more prevalent in patients with eGFR>60 compared to <60 ml/min/1.73 m² (75.7% vs 88.8%; P = .012). In females, no significant differences were evidenced in sexual dysfunction based on FSFI score <26.0 (91.9% vs 95.6%; P = .490). In contrast, males with preserved renal function had lower prevalence of sexual dysfunction (IIEF<22) compared to those with reduced renal function (67.1% vs 83.9%; P = .027). In regression analysis eGFR was an independent factor associated with sexual dysfunction.

Conclusion: Renal dysfunction may be an important factor predisposing heart failure patients to more frequent sexual dysfunction.

#6794
CALCIUM/MAGNESIUM RATIO IN PATIENTS WITH DIABETES AND CHRONIC KIDNEY DISEASE: A RISK FACTOR FOR CARDIOVASCULAR DISEASE

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Background and Aims: Chronic Kidney Disease (CKD) and Diabetes Mellitus (DM) are significant risk factors for Cardiovascular (CV) Disease. Patients with CKD and/or DM exhibit higher incidence and prevalence of CV events compared to the general population. Hypomagnesemia and elevated calcium-magnesium (Ca:Mg) ratios have been identified as independent risk factors for CV-related deaths. The aim of this study is to determine the relationship between Ca:Mg and the prognosis of CV disease in patients with CKD and DM.

Method: This cross-sectional study enrolled patients with DM and CKD followed at Diabetic Nephrology appointments in a hospital. The study population was divided into two groups: Group 1 (G1) - patients who had a previous hospitalization due to a CV event, and Group 2 (G2) - patients without CV-related hospitalizations. A logistic regression model was employed to evaluate the predictive factors for CV hospitalization for the variables studied.

Results: A total of 223 patients were included in the study: 92 females and 131 males, with an estimated glomerular filtration rate of 38±42 mL/min/1.73 m² and 41% had been hospitalized due to a CV event. G1 had higher age (P = .02), higher serum phosphate (p = .001), parathormone (p = .01), interleukin-6 (p = .01), FGF-23 (p = .01), oxidized-LDL (p = .01), Ca:Mg (p = .01), and pulse pressure (p = .01), as well as lower eGFR (p = .01) and magnesium
Conclusion: In this population, Ca:Mg and FGF-23 were predictors of CV patients. These parameters may be valuable in clinical practice to identify high-risk morbidity. Further studies are necessary to fully understand the relationship of -0.54 kg was found between FFMBIS and FFMCT (LoA: -14.88 to 13.7 kg, p=0.544). Between LTM_BIS and FFM_CT a mean difference of -12.2 kg was apparent (LoA: -28.7 to 4.2 kg, p<0.001). Compared with FFM_CT, the highest occurrence of accurate predicted protein requirements was found for FFM_BIS. Mean difference between protein requirements according to FFM_BIS and FFM_CT was -0.7 ± 9.9 grams in males and -0.9 ± 10.9 grams in females.

Conclusion: FFM_BIS seems a valid surrogate measure for the estimation of FF as compared to FFM_CT. As expected, large clinically relevant differences were observed in calculated protein requirements when comparing multiple methods, with FFM_BIS having the best accuracy compared to FFM_CT.

#4852
LATE REFERRAL OF PATIENTS WITH AN UNKNOWN CAUSE OF CHRONIC KIDNEY DISEASE AND MALIGNANT HYPERTENSION
Tamar Tevdoradze1, Irma Tchokhonelidze1, Miranda Tsilosani2, Nora Sarishvili1, Tamar Kasradze1, Dalakishvili Ketevan1, Nona Babutsidze1, Gvantsa Metshkharishvili1, Nino Buadze1, Tamar Bagashvili1, Rusudan Rusia1, Giorgi Gazdeliani1, Mariam Beridze1, Ana Tchikaberidze1, Teona Khelasvili1, Ketevan Kapanadze1 and Nani Khidasheli1
1Tbilisi State Medical University/HMT University Clinic, Nephrology, Tbilisi, Georgia and 2V.Iverieli Endocrinology Metabology Dietology Center "ENMEDIC", Pathology, Tbilisi, Georgia

Introduction: Systemic sclerosis (SS) is a rare connective tissue disorder characterized by widespread vascular dysfunction and progressive skin and internal organ fibrosis. Scleroderma renal crisis (SRC) is a life-threatening complication of SS. The estimated incidence of SS is approximately 20 cases per million per year, and SRC affects about 5-15% of these patients.

Case Description: A 32-year-old female was admitted to the hospital with dyspnea, edema, HTN, COPD. 4 months before the hospitalization, she had an abrupt onset of HTN (230/120 mmHg) and seizures (no abnormal waveforms on EEG). Vital signs: HR 90’, RR 22’, BP 197/121 mmHg, SpO2 90% on room air. PEx: severe jugular venous dilation, crackles in both lungs, 3+ pitting edema bilaterally. The skin appeared abnormal with a modified Rodnan score “9” out of “51” with puffy hands, sclerodactyl, telangiectasia, and Raynaud’s phenomena. Lab: creatinine 406 mcmol/L, urea 20.8 mmol/L, T.Ca 2.04 mmol/L, P 1.71 mmol/L, PTH 255.5 pg./mL, Alb 33 g/L, LDH 596 U/L. Urinalysis: UPCR of 4.169 mg/mg creat. microhematuria ANA

Figure 1: Patient’s hands with Raynaud’s phenomena.

Figure 1: Bland-Altman plots of muscle compartment measurements. (A) FFM_BIS versus FFM_CT; (B) FFM_BIS versus FFM_CT in males. (C) FFM_BIS versus FFM_CT in females. Abbreviations: FFM_CT = computed tomography derived fat free mass, FFM_BIS = bio impedance spectroscopy derived weight fat free mass. Differences were calculated by subtracting FFM_CT from FFM_BIS.
Figure 2: Telangiectasias.

Figure 3: Microthrombi in small interlobar arteries.

Figure 4: Intimomedial mucoid degeneration of the vascular wall.
Figure 5: Late changes in small arteries manifested by intimal thickening and proliferation (vascular “onion-skin” appearance).

Figure 6: Ischemic changes in glomeruli.

Figure 7: Acute tubular injury.
were positive for centromere pattern with a titer of >400 AU/mL (N = 40). CENP-B + anti-CCP, ANA, Anti-Jo1 and anti-Sm antibodies. A kidney biopsy showed acute tubular injury in the early stage, and later stages of interstitial fibrosis and tubular atrophy; chronic active thrombotic microangiopathy (TMA), vascular abnormalities including intimal accumulation of myxoid material, thrombosias, fibrinoid necrosis consistent with Scleroderma Renal Crisis (Fig 3; 4; 5; 6; 7) The patient started treatment with losartan 100mg. 3 months she started hemodialysis due to diuretic refractory overhydration with severe pulmonary edema resulting in acute kidney injury hospital readmission.

Discussion: SRC was at one time almost uniformly fatal, with the kidney histopathology workup, neither clinical presentation nor lab tests inevitably leading to irreversible changes resulting in CKD. Notably, until damage to the kidney, presenting with combined nd-SRC and SSc-TMA, eventually leads to microvascular thrombosis. Our case demonstrates severe significant hypertension. The pathology of SSc-TMA shows abnormalities in the capillary wall which eventually leads to microvascular thrombosis. Our case demonstrates severe damage to the kidney, presenting with combined nd-SRC and SSc-TMA, inevitably leading to irreversable changes resulting in CKD. Notably, until the kidney histopathology workup, neither clinical presentation nor lab tests revealed typical TMA. SRC was at one time almost uniformly fatal, with death often occurring within a few weeks. With the development of ACE-I, sur Ethiopians, hyperphosphatemia and hyperkalemia in elderly Koreans. In 12% of cases, both 2% with the Limited cutaneous systemic sclerosis (lcSS) and 12% in the Diffuse cutaneous systemic sclerosis (dcSS). Histopathologically SRC can be divided into narrowly defined nd-SRC and SSc-associated TMA: nd-SRC is a typical type of SRC, which shows acute renal failure and abrupt onset of moderate-to-significant hypertension. The pathology of nd-SRC shows injured endothelial cells and subsequent intimal thickening in the arcuate and interlobar arteries. The pathology of SSc-TMA shows abnormalities in the capillary wall which eventually leads to microvascular thrombosis. Our case demonstrates severe damage to the kidney, presenting with combined nd-SRC and SSc-TMA, inevitably leading to irreversible changes resulting in CKD. Notably, until the kidney histopathology workup, neither clinical presentation nor lab tests revealed typical TMA. SRC was at one time almost uniformly fatal, with death often occurring within a few weeks. With the development of ACE-I, sur

Conclusion: SSc should be considered in any patient presenting with malignancy or AKI. SRC can occur in patients without evidence of skin thickening or other manifestations of SSc. Early diagnosis improves outcome. A kidney biopsy should be gold standard in all patients with “unknown” causes of the CKD. ACEi remains the cornerstone of the treatment. Renal Transplantation: to discuss after two years after start of dialysis.

#4964

ASSOCIATION OF DIETARY INTAKE WITH SERUM LEVELS OF PHOSPHORUS AND POTASSIUM IN THE ELDERLY HEMODIALYSIS PATIENTS IN KOREA

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Background and Aims: Dietary management of elderly (>60 years old) hemodialysis (HD) patients is very important for solving health problems and improving quality of life. Hyperphosphatemia and hyperkalemia in elderly HD patients are closely related to intake of dietary phosphorus and potassium from Koreans’ unique eating patterns. It is very difficult to manage the diet of hemodialysis patients due to the unique eating patterns of elderly Koreans. In the daily meal pattern, sodium and potassium contents are high in grain-based foods, soups, stews, and seasoned vegetables. And, there are various recipes for meals using a range of condiments, which increase serum phosphorus level. For this reason, it is necessary to educate dietary management using real-time Apps for the elderly in Korea. This study was designed to provide the base data for the development of a self-dietary management App for Korean elderly HD patients.

Method: This study was conducted on 237 elderly HD patients (149 males and 88 females) at nationwide 18 university hospitals. We collected anthropometric data, biochemical parameters, and dietary data of the subjects. Dietary data for usual intake were obtained by use of a food-frequency questionnaire (FFQ) consisting of 23 food meal items based on the Korean usual diets. For this dietary status evaluation, a newly constructed potassium and phosphorus content DB was used.

Results: The average age of the patients was 69.7±11.6 years for men and 69.2±6.9 years for women and the duration of HD was 5.4 ± 4.9 years for men and 5.5±4.2 for women. The mean body mass index (BMI) was 23.24 ± 2.99 kg/m², mean serum phosphorus level was 5.03 ± 9.59 mg/dL, and mean serum potassium level was 5.41 ± 8.58 mEq/L. Hyperphosphatemia (> 4.5 mg/dL) was found in 45.8% of the subjects, and hyperkalemia (> 5.0 mEq/L) in 35.4%. Energy and protein intake were significantly lower than recommended intakes of HD patients (P = .027, P = .015). Lower intake of energy and protein was more significant in women. The intake of sodium and potassium was

significantly higher than recommendation (P = .014, P = .021), which was more excessive in men. Serum phosphorus levels showed positive correlation with intake frequency of mixed grains rice (P = .011), noodle without broth (P = .000), vegetable soup (P = .039), and roasted beef (P = .047) in male patients. In case of female patients, intake of sweet potatoes was correlated with hyperphosphatemia (P = .047). Serum potassium levels showed a positive correlation with intake of Kimchi (P = .000), noodle without broth (P = .000), and ham (P = .018) in men. In women, sweet potatoes (P = .027) and medium- sized potato (P = .047) were correlated with serum potassium level. On the other hand, intake of white rice showed negative correlation with serum potassium levels (P = .037) in both sex.

Conclusion: Dietary management along with medical treatment is essential for maintaining serum phosphorus and potassium levels within acceptable ranges because the composition of the daily routine diet is very unique and varies in Korea. The results of this study showed that the intake of white rice rather than mixed grains is an important factor in sustaining normal serum phosphorus and potassium levels in the elderly Korean HD patients. In addition, limiting intake of sweet potatoes, medium and high potassium vegetables & fruits to under three servings per week is recommended. Therefore, customized dietary management needs to be regulated according to each individual’s dietary pattern for the Korean elderly HD patients. Major variables found in this study can be used in the development of new App for customized self-dietary management.

#2538

HEALTHY PLANT-BASED DIET IN CHRONIC KIDNEY DISEASE THROUGH USE OF SODIUM ZIRCONIUM CYCLOSILICATE (HELPFUL TRIAL): LABORATORIAL FINDINGS

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Background and Aims: Patients with chronic kidney disease (CKD) and hyperkalemia (HK) are counselled to follow a diet restricted in potassium (K) which limits the intake of fruits and vegetables. This is a cause of complaints for many patients. The use of the K lowering medication sodium zirconium cyclosilicate (SZC) has the potential to treat HK and allow a healthy plant-based diet (PBD). We designed a clinical trial to explore the safety and feasibility of prescribing a healthy PBD to CKD patients with HK with the concomitant use of SZC.

Method: The HELPFUL trial is an ongoing single-arm study with patients with CKD stage 4-5 on dialysis and with plasma K between 5.1 to 6.5 mmol/L at inclusion. Patients are followed for 6 weeks. In the first 3 weeks, SZC is prescribed to normalize plasma K (pK) while ingesting a low protein diet with low K+ content. In the subsequent 3 weeks, a healthy PBD with a target pK of 3700 mg/day is prescribed maintaining the use of SZC. A food basket with the PBD is delivered to the participants weekly. A weekly monitoring of pK and titration of SZC to keep normokalemia is performed. Other laboratory measurements and food intake are assessed at baseline, week 3 and week 6. Food intake is evaluated using the 24-hour food record (24HFR). Data was analyzed by repeated measures-ANOVA or by Friedman test for related samples, as appropriate. The protocol is registered at www.clinicaltrials.gov (identifier NCT04207203).

Results: 22 patients were included (59±13 years; 13 men, 59%). Table 1 describes the main findings. During the study, eGFR did not change, serum urea decreased, and P-carbon dioxide increased significantly. Inflammatory markers, 24hour urinary sodium and K excretion did not change. Potassium intake from 24h-FR increased, as well as the intake of fruits, vegetables and nuts after the PBD. The mean pK normalized in week 3 and 6. After the start of PBD, 3 patients (13.6%) had pK between 5.1 and 5.3 mmol/L. Most patients needed SZC dose of 10g/day. No changes were observed in dose of RAAS.

Conclusion: The strategy of PBD food basket with concomitant use of SZC allowed an increase in dietary K intake with higher intake of fruits, vegetables and nuts. P-carbon dioxide, a surrogate of bicarbonate improved as well. The pK was kept within normal values for most of the patients.
**Table 1:**

<table>
<thead>
<tr>
<th></th>
<th>Week 0</th>
<th>Week 3</th>
<th>Week 6</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea, mmol/L</td>
<td>19.1 ± 5.6</td>
<td>16.8 ± 5.3</td>
<td>17.8 ± 5.9</td>
<td>0.01</td>
</tr>
<tr>
<td>P-carbon dioxide, mmol/L</td>
<td>21 ± 2</td>
<td>22 ± 2</td>
<td>23 ± 2</td>
<td>0.02</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73m²</td>
<td>17.5 ± 4</td>
<td>18.6 ± 5.6</td>
<td>18 ± 5.5</td>
<td>0.23</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>1.5 (1.3)</td>
<td>1 (1.3)</td>
<td>2 (1.3)</td>
<td>0.80</td>
</tr>
<tr>
<td>Interleucine-6, pg/mL</td>
<td>2.8 (2.6)</td>
<td>3.3 (2.5)</td>
<td>2.7 (2.5)</td>
<td>0.59</td>
</tr>
<tr>
<td>Plasma K+, mmol/L</td>
<td>5.5 ± 0.3</td>
<td>4.7 ± 0.4</td>
<td>4.8 ± 0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Urinary K+, mmol/day</td>
<td>51.9 ±19</td>
<td>43 ±11</td>
<td>53 ± 24</td>
<td>0.13</td>
</tr>
<tr>
<td>Urinary Na, mmol/day</td>
<td>177 (125; 199)</td>
<td>186 (144; 250)</td>
<td>215 (142; 242)</td>
<td>0.11</td>
</tr>
<tr>
<td>Potassium intake, mg/day</td>
<td>2655 ± 777</td>
<td>2333 ± 768</td>
<td>2840 ± 927</td>
<td>0.03</td>
</tr>
<tr>
<td>Fruits*/day</td>
<td>1.5 (1;2.3)</td>
<td>1.3 (1;2)</td>
<td>3.2 (3;4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vegetables*/day</td>
<td>1 (0;6.2)</td>
<td>1.1 (1.2)</td>
<td>2 (1;3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Nuts*/week</td>
<td>0.3 (0.7)</td>
<td>0 (0.7)</td>
<td>13 (7;22)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Urinary Na, mmol/day</td>
<td>177 (125; 199)</td>
<td>186 (144; 250)</td>
<td>215 (142; 242)</td>
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<td>1.5 (1;2.3)</td>
<td>1.3 (1;2)</td>
<td>3.2 (3;4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vegetables*/day</td>
<td>1 (0;6.2)</td>
<td>1.1 (1.2)</td>
<td>2 (1;3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Nuts*/week</td>
<td>0.3 (0.7)</td>
<td>0 (0.7)</td>
<td>13 (7;22)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SZC dose</td>
<td>20; 91</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>30g; n, %</td>
<td>2; 8</td>
<td>18; 82</td>
<td>20; 91</td>
<td>–</td>
</tr>
<tr>
<td>10g; n, %</td>
<td>4; 18</td>
<td>2; 8</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5g; n, %</td>
<td>–</td>
<td>–</td>
<td>3; 14</td>
<td>–</td>
</tr>
<tr>
<td>HK+ (&gt;5&lt;6.5 mmol/L); n, %</td>
<td>22; 100</td>
<td>4; 18</td>
<td>3; 14</td>
<td>–</td>
</tr>
</tbody>
</table>

Data described as mean ± standard deviation or median and interquartile range. *Servings; HK+: hyperkalemia

#3642

**SERUM APELIN AND RENAL PROGNOSIS IN PATIENTS WITH NON-DIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE**

Nao Kani1, Michinori Hirata2, Shuzo Makino1, Tomoya Naka1, Kazuhiro Okamoto1, Hiromitsu Miyakawa1, Ryuta Uwatoko1, Sakii Bessho1, Nobuhiro Hashimoto1, Rei Iio1, Yoshiyasu Ueda1 and Terumasa Hayashi1

1Osaka General Medical Center, Kidney Disease and Hypertension, Osaka, Japan and 2Chugai Pharmaceutical Company, Co., Ltd., Tokyo, Japan

**Background and Aims:** The apelin/APJ system is a novel pleiotropic system with an essential role in renal and cardiovascular physiology and disease. A role for the apelin/APJ system in diverse pathological states, including disorders of sodium and water balance, hypertension, heart failure, pre-eclampsia, acute kidney injury, sepsis and diabetic nephropathy, has recently been reported. Especially, the impact of apelin/APJ system on cardiovascular system has been attracting attention, but scarce data is available in chronic kidney disease (CKD).

**Method:** We measured serum apelin-36 by ELISA in 411 outpatients with non-dialysis dependent (NDD) CKD and analyzed factors associated with serum apelin. Furthermore, we examined the association of serum apelin with renal outcome (renal replacement therapy, RRT) using multivariate Cox proportional hazards model.

**Results:** Median age and eGFR were 71 years and 21.7 ml/min/1.73 m², respectively and the prevalence of male gender and diabetes was 26.8% and 50.8%, respectively. Median serum apelin was 0.81 pg/ml. There was no significant difference in serum apelin level between male and female patients, or those with and without diabetes. Moreover, serum apelin level had no significant association with age and eGFR; however, there was a significant relationship between serum apelin and brain natriutetic peptide. During the follow-up period of 38 months, 126 patients started RRT. eGFR and age were associated with the time to RRT induction. Serum apelin was not associated with renal outcome (HR, 1.05; 95%CI, 0.64-1.71; P=0.86); however, this association was interacted by diabetes and gender (P for interaction, 0.073 and 0.070, respectively).

**Conclusion:** Serum apelin could be a predictive marker of renal prognosis in male and non-diabetic CKD patients.

#3647

**RELATIONSHIP BETWEEN MONOCYTE-LYMPHOCYTE RATIO AND RENAL OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES**

Yue Gu, Yingying Ren and Jing Zhou

Henan Provincial People’s Hospital; Zhengzhou University People’s Hospital; Henan University People’s Hospital, Department of Nephrology, Henan Provincial Clinical Research Center for Kidney Disease, Henan Provincial Key Laboratory of Kidney Disease and Immunology, Zhengzhou, P.R. China

**Background and Aims:** Acute kidney injury (AKI) is a common complication of hospitalized adults with increased risk of chronic kidney disease and end-stage kidney disease. Sepsis is the most common reason of AKI in patients admitted in intensive care unit (ICU) with the incidence over 50%. Soluble urokinase-type plasminogen activator receptor (suPAR) is an important immune mediator involved in kidney injury. Numerous studies have shown that the suPAR is associated with a variety of kidney diseases. However, it remains unknown on the diagnosis and prognosis value of suPAR in sepsis-associated acute kidney injury (S-AKI). Hence, this study aimed to explore the diagnostic value for the prediction of S-AKI courses and 28-day death.

**Method:** In this prospective study, adult patients with sepsis admitted to the ICU of Henan people’s Hospital from December 2020 to February 2022 were enrolled. Plasma suPAR levels at 0, 12, 24 and 48 hours after admission to ICU were measured by enzyme-linked immunosorbent assay. We assessed the development of S-AKI as the primary outcome and the occurrence of death within 28 days in patients who had S-AKI as a secondary outcome. The prediction of the suPAR level on S-AKI and death was tested using receiver operating characteristic curve (ROC) analysis, by calculating the area under the curve (AUC), and 95% confidence interval (CI).

**Results:** Of the 182 sepsis patients, 66 (36.3%) developed AKI during hospitalization, of whom 31 (46.9%) died. At 12, 24 and 48 hours after admission to ICU, the plasma suPAR level was significantly higher in patients with S-AKI than in patients without AKI (P<0.05). (Fig. 1) In sepsis patients dead with 28 days after admission in ICU, the plasma suPAR level was significantly higher at 0 and 48 hours after admission in ICU compared to the survival patients (P<0.05). (Fig. 1) Diagnostic performance of plasma suPAR level improved over time with the highest area under the receiver operating characteristic curve of 0.701 (95% CI, 0.623–0.779) 24 hours after study inclusion. Additionally, plasma suPAR levels at 0h have the highest area under the receiver operating characteristic curve of 0.647 (95% CI, 0.512–0.782) in predicting 28-day death. The best discrimination ability for the S-AKI was achieved for suPAR 24 hours after inclusion by applying a cutoff value of greater than or equal to 6.31 ng/ml (sensitivity 62.1, specificity 71.6). The suPAR at 0h after inclusion performed best in discriminating 28-day death by using a cutoff value of greater than or equal to 4.57 ng/ml (sensitivity 87.1, specificity 51.4). (Table 1)

**Conclusion:** Plasma suPAR level can be a potential biomarker for early diagnosis of S-AKI and has a certain clinical value in predicting the short-term death of S-AKI. However, further clinical studies with larger sample size is needed.
Figure 1: Comparison of suPAR levels between the S-AKI vs non-AKI groups and the survival vs death groups at 0, 12, 24 and 48 hours after admission to ICU.

Table 1: The receiver operating characteristic analysis for predicting S-AKI and death based on the suPAR level.

<table>
<thead>
<tr>
<th>Time after admission to the ICU</th>
<th>S-AKI</th>
<th>Death</th>
<th>AUC</th>
<th>P</th>
<th>95% CI</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Predict S-AKI</th>
<th>AUC</th>
<th>P</th>
<th>95% CI</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 h</td>
<td>66</td>
<td>31</td>
<td>0.557</td>
<td>0.198</td>
<td>0.468 - 0.647</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.647</td>
<td>0.04</td>
<td>0.512 - 0.782</td>
<td>4.57 ng/ml</td>
<td>87.10%</td>
<td>51.40%</td>
<td></td>
</tr>
<tr>
<td>12 h</td>
<td>66</td>
<td>31</td>
<td>0.686</td>
<td>&lt; 0.001</td>
<td>0.608 - 0.764</td>
<td>5.24 ng/ml</td>
<td>74.20%</td>
<td>56.90%</td>
<td>0.586</td>
<td>0.232</td>
<td>0.447 - 0.725</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>24 h</td>
<td>66</td>
<td>31</td>
<td>0.701</td>
<td>&lt; 0.001</td>
<td>0.623 - 0.779</td>
<td>6.31 ng/ml</td>
<td>62.10%</td>
<td>71.60%</td>
<td>0.613</td>
<td>0.116</td>
<td>0.473 - 0.753</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>48 h</td>
<td>66</td>
<td>31</td>
<td>0.672</td>
<td>&lt; 0.001</td>
<td>0.593 - 0.751</td>
<td>4.72 ng/ml</td>
<td>77.30%</td>
<td>51.70%</td>
<td>0.644</td>
<td>0.044</td>
<td>0.507 - 0.782</td>
<td>8.27 ng/ml</td>
<td>45.20%</td>
<td>88.60%</td>
<td></td>
</tr>
</tbody>
</table>

#3074
CHANGES IN THE CLINICAL CHARACTERISTICS AND MANAGEMENT OF PATIENTS WITH AHUS OVER 10 YEARS: TRENDS FROM THE GLOBAL AHUS REGISTRY

Andrew Siedlecki, Imad Al-Dakkak, Katerina Anokhina, Gema Ariceta, Gianluigi Ardissino, Laurence A. Greenbaum, Christoph Licht and Johan Van de Walle

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Background and Aims: Atypical haemolytic uraemic syndrome (aHUS) is a rare disease predominantly caused by alternative complement pathway dysregulation. Prior to 2011, before the targeted complement inhibitor eculizumab became available, aHUS frequently led to end-stage kidney disease (ESKD) and early death. Treatment with eculizumab led to notable improvements in outcomes; whether patient characteristics and management has continued to change over time is unknown. Using data from the Global aHUS Registry, we assessed clinical characteristics and management of patients with aHUS over 10 years to identify any potential trends.

Method: All patients enrolled in the Global aHUS Registry from 2012–2022 were included. Patients were categorised according to age at aHUS onset (adult [≥ 18 years] vs paediatric [< 18 years]); onset of aHUS was defined as the earliest of initial symptom presentation, aHUS diagnosis, or first recorded thrombotic microangiopathy (TMA). Patient characteristics were summarised using descriptive analysis.

Results: Of the 1994 patients enrolled in the registry between 2012 and 2022, 33 (1.7%) were missing data on age at aHUS onset. Of the remaining 1961 patients, 813 (41.5%) were paediatric and 1148 (58.5%) were adult. Changes in patient characteristics and management are presented in Fig. 1. Plasma exchange/plasma infusion (PE/PI) prior to and including the year of enrolment was less common in paediatric than adult patients (58.5% vs. 71.3%) between 2012–2013 and declined substantially in paediatric (19.6%) relative to adult (55.1%) patients by 2020–2022. Similar proportions of paediatric patients required dialysis at the time of enrolment between 2012–2013 (5.1%) and 2020–2022 (6.5%), while numerically lower proportions of adults required dialysis over time (2012–2013, 15.2%; 2020–2022, 6.5%). The rate of paediatric patients requiring a kidney transplant prior and up to enrolment dropped from 2012–2013 (28.4%) to 2020–2022 (5.9%); however, the rate among adult patients remained comparable (2012–2013, 29.2%; 2020–2022, 27.1%). A decrease in the proportion of patients with a reported identified pathogenic variant and/or anti-CFH antibodies was observed in paediatric and adult patients between 2012–2013 (paediatric, 59.1%; adult, 45.5%) and 2020–2022 (paediatric, 49.0%; adult, 38.8%). The proportion of patients with a reported triggering event increased from 2012–2013 (paediatric, 6.3%; adult, 12.4%)
to 2020–2022 (paediatric, 9.8%; adult, 28.0%). In this cohort, a total of 1208 patients were treated with eculizumab/ravulizumab between 2012 and 2022 (paediatrics, 476; adults, 732). Between 2012–2013, the median time from aHUS onset to treatment initiation was 94.9 days for paediatric patients (blue) and 51.1 days for adult patients (orange); this fell to 13.1 days in paediatrics and 24.1 days in adults between 2020–2022 (Fig. 2).

**Conclusion:** Utilisation of PE/PI to treat aHUS has decreased more in paediatric than adult patients over time. A decreased requirement for transplant in paediatric patients was evident, suggesting more paediatrics are now being diagnosed and treated earlier, leading to better outcomes with fewer patients progressing to renal failure and requiring kidney transplant. The proportion of both paediatric and adult patients with reported pathogenic variants and/or anti-CFH antibodies decreased over time and may reflect

*Figure 1:* Changes in characteristics of patients in the Global aHUS Registry.

*Figure 2:* Gap between aHUS onset and treatment start for patients in the Global aHUS registry.
the rate at which a clinical constellation consistent with aHUS is identified. Moreover, aHUS may not be recognised as frequently in the presence of a triggering condition, or a lower barrier for clinicians to suspect aHUS in recent years. Patients were more rapidly treated with a complement inhibitor, likely due to better awareness in the clinical community around complement inhibitors and the importance of early treatment initiation. Although patients with aHUS are being treated more promptly in recent years than 10 years ago, more work is needed, especially in adults, to move towards optimal clinical practice.

#3169 EXPERIENCE IN INTRAOPERATIVE AUTOLOGOUS BLOOD SALVAGE IN PEDIATRIC CARDIAC SURGERY
Bratislav Stankovic¹, Gordana Vidakovic² and Željko Vidakovic³
¹The high school of professional health studies, Zemun, Belgrade, Serbia, ²Special Hospital for Cerebral Palsy and Developmental Neurology, Belgrade, Serbia and ³Livanova, Italy

Background and Aims: Due to the drastic reduction in the number of voluntary blood donors has led to the need for the development of alternative strategies for allogeneic blood transfusion, which include the use of different strategies for autologous transfusion. Display: a) the use of "Cell-Saver" pediatric cardiac surgery at the Department of Cardiothoracic Surgery, Institute for Health Protection of Mother and Child of Serbia; Dr Vukan Cupić; b) to analyze the reduced use of allogeneic blood and/or chemo products using "Cell-Saver" pediatric cardiac surgery; c) to evaluate the "cost benefit" of this strategy (e.g. the ratio of prices set, "Cell-Saver") and pretransfusion rates processing one unit of allogeneic blood; d) to identify increased intraoperative security in complex, reconstructive and redo cardiac surgery using the "Cell-Saver" combined with ultrafiltration (conventional or modified), particularly in cyanogenic congenital heart defects; e) to establish and improve the hemodynamic status of hemoreologic operated child.

Method: A retrospective study was conducted. Experimental group included 63 patients (aged 12 years - 16 years and 4 months, body weight of patients that ranged between 2.9 kg and 80 kg - the mean body weight was 28.3 kg). In the experimental group patients were performed following cardiac surgery: 46 patients underwent reconstructive surgery (most often reparations for cyanogenic congenital heart defects); 3 patients who underwent cardiovascular, and 3 patients who underwent cardio-surgical procedures had hematological disorders. The control group included 60 patients of similar age and body mass who underwent the cardio-surgical procedure without the use of "Cell-Saver" with application of allogeneic blood and/or chemo products during transfusion care. The following laboratory parameters were accompanied: hematocrit, platelet count, fibrinogen, prothrombin time (PT) and activated partial thromboplastin time (aPTT), after 3, 6, and 12 hours postoperatively compared to the control group. We compared the volume of postoperative bleeding by patients of the experimental group with the control group (1h, 4h, 7h, 11h, 15h, 21h and 24h) and analyzed the amount of used allogeneic and autologous blood and/or hemoglobin products used in the transfusion care during hospitalization the experimental group compared with the control group.

Results: Postoperative administration of allogeneic blood and/or hemoproducts was statistically significantly lower in the experimental group using "Cell-Saver" than in the control group. The amount of salvaged blood after surgery ranged from 210 ml - 620 ml. Intraoperative hematocrit "rescued" autologous blood ranged between 0.32 / 1/l and 0.38 / 1/l. e range of values preoperative and postoperative hematocrit were lower in the experimental group than in the control group that used "Cell-Saver". The total volume of postoperative drainage content was significantly lower in the experimental group, which used "Cell-Saver" compared to the control group. The postoperative hematocrit was higher in the experimental group patients who used "Cell-Saver", compared with the same operating using allogeneic blood and/or hemoproducts patients in the control group. The mean platelet count, fibrinogen, PT and aPTT results showed no statistically significant difference between the experimental group of patients in whom we used "Cell-Saver" in comparison to the control group.

Conclusion: The results obtained by the retrospective analysis of above mentioned data indicate a positive therapeutic effect of the application of the "Cell-Saver" that is most clearly expressed in patients with the presence in the "bell" of small volume, the use of the Cell Saver has become an integral part of the pediatric cardiac surgery - perfusion, regardless of body weight, age and body surface area of the child. The performance of intraoperative "rescue" of autologous blood using the "Cell Saver", while the follow-up of pediatric patients in the perioperative and postoperative period has immeasurable significance of teamwork perfuser, expert specialist nursing, pediatrician, cardiac surgeon and transfusion.

#3713 NEPHROLOGISTS’ AND PRIMARY CARE PHYSICIANS’ KNOWLEDGE ABOUT NOVEL TREATMENT OPTIONS FOR TYPE 2 DIABETES AND CKD AUGMENTED BY ONLINE MEDICAL EDUCATION
Joachim Trier¹, Jolanta Malyszko² and Rita Moreira Da Silva³
¹WebMD Global LLC, Medscape Education, New York, United States of America and ²Medical University of Warsaw, Department of Nephrology, Warsaw, Poland

Background and Aims: Diabetes is the number one cause of kidney failure and chronic kidney disease (CKD) associated with type 2 diabetes (T2D) increases the risk for cardiovascular events 2 to 3-fold thus highlighting the crucial need for early detection of CKD and comprehensive vascular risk control. Recently, novel treatment options with clear benefits for the prognosis of patients with T2D and CKD have emerged. The goal of this activity for primary care physicians (PCP) and nephrologists (NEPH) was to improve their understanding of the clinical benefits as well as safety considerations of selective non-steroidal mineralocorticoid antagonists (sMRA) in the management of their patients with T2D and CKD.

Method: Two nephrology experts joined a 20-minute online video discussion in the synchronization slides. Educational effect was assessed using a repeated-pair design with pre-/post-assessment. 3 multiple choice questions assessed knowledge, 1 question rated on a Likert-type scale assessed confidence. A paired samples t-test was conducted on overall average number of correct responses and for confidence rating, a McNemar's test was conducted at the question level (5% significance level). Cohen’s d with correction for paired samples estimated the effect size of the education on number of correct responses. Data collection from 8/2/22 to 10/17/22.

Results:

• 42% of PCP (n=212, p<.001, d=0.36) and 35% of NEPH (n=146, p<.001, d=0.31) improved their knowledge regarding the clinical benefits and safety aspects of novel selective sMRA for patients with T2D and CKD
• 47% of PCP and 37% of NEPH had greater confidence (score increased by 73% and 50%, respectively) in their ability to treat patients with CKD and T2D with a selective sMRA
• 92%/93% of participating PCP and 96%/97% of NEPH expect that the education will improve their performance and patient outcomes.

Conclusion: Participation of PCP and NEPH in an online video expert discussion improved their understanding of the clinical benefits and safety aspects of selective sMRA as well as their confidence in using such novel therapies for their patients with T2D and CKD in clinical practice.

#3739 SHUNT PORTOSYSTEMIC COMPLICATED BY HYPERAMMONEMIA AND HEPATIC ENCEPHALOPATHY SUPPORTED BY DAILY DIALYSIS IN A CHRONIC HEMODIALYSIS PATIENT
Nabil Hamouche, Sara Bouhjar, Mariam Chettati, Wafaa Fadili and Inass Laoud
Mohammed VI University center of Marrakesh, Nephrology, Marrakech, Morocco

Background and Aims: Hepatic encephalopathy is a neuropsychiatric syndrome that may develop as a consequence of liver insufficiency. In acute liver failure, hepatic encephalopathy suggests the severity of the disease. In end-stage chronic liver diseases, episodes of hepatic encephalopathy are frequently fully and spontaneously reversible. Clinical manifestations vary from mild neuropsychiatric disorders to coma. The pathogenesis of hepatic encephalopathy is complex and not clearly understood. Ammonia plays a key role. In the healthy individual, ammonia is, during its first hepatic passage, directly degraded into urea, itself excreted by the kidney and the stools, and to a lesser degree in glutamine. Ammonia is also metabolized by the muscle stripped. In case of liver failure and/or shunts portosystemic, there is a defect in hepatic clearance ammonia which is then found in excess in systemic circulation. Decreased muscle mass, linked to malnutrition, frequent
in the patient cirrhotic and chronic hemodialysis, also helps to decrease brain barrier, the brain is exposed to excessive concentrations ammonia causing functional brain abnormalities and structural, which can partly explain the signs neurology of hepatic encephalopathy. In end stage chronic renal failure, clearance of ammonia via extracorporeal treatment has not been systematically evaluated. Several studies with small samples have demonstrated the effectiveness of hemodialysis, compared to peritoneal dialysis, in terms of ammonia elimination in chronic renal failure, on dialysis or not on dialysis.

The aim of this study was to evaluate the effectiveness of daily dialysis for the purification of ammonium a chronic hemodialysis patient with hepatic encephalopathy.

Case Report: A 40-year-old man undergoing chronic hemodialysis was referred to gastroenterology department of Mohammed VI University Center of Marrakech for inoperable shunt portosystemic complication by hyperammonemia causing hepatic encephalopathy consisting of headaches and seizures. His medical history was significant for liver cirrhosis caused by infection with hepatitis B, end stage kidney disease due to membranoproliferative glomerulonephritis, for which the patient is on hemodialysis at the rate of 3 sessions per week.

The patient went on to develop portal hypertension and ascites requiring frequent hospital admissions and treatment with diuretics. He was on a low-protein and low-sodium diet. While on oral furosemide 250 mg daily and spironolactone 100 mg daily, his diuresis was adequate. Before referral, this patient had already suffered 4 episodes of tonic clonic seizures. His 1st hemodialysis session in our training was on January 10, 2023, he was given daily hemodialysis sessions with daily blood tests, including immediate pre and post dialysis ammonia. Pre-dialytic ammonia levels varied between 24 and 37 μmol/l, as well as post-dialytic ammonia levels varied between 103 and 161 μmol/l, knowing that the normal value of laboratory ammonia varied between 10 and 31 μmol/l.

The evolution was marked by a clear clinical improvement, with a disappearance of the seizures without a significant drop in ammonia after 14 daily hemodialysis sessions. Serum creatinine and urea declined, and sodium increased. Accumulation of ascites slowed and the patient could eat and sleep normally and was again independent with self care. The patient returned home on January 24.

Conclusion: This study shows the interest of daily hemodialysis sessions as a potential treatment for hyperammonemia in a patient on chronic intermittent hemodialysis, with a portosystemic shunt. The interest lies in the fact that the improvement is mainly clinical than biological (persistent hyperammonemia).

ASSESSMENT OF THE PROGRESSION OF CKD TAKING INTO ACCOUNT METABOLIC CHANGES

Guzal Karimdzhanova, Dano Egamberdieva and Iroda Ruzmetova
Tashkent Pediatric Medical Institute, Internal Disease, Nephrology and Hemodialysis, Tashkent, Uzbekistan

Background and Aims: To study was to study the relationship between the metabolic syndrome and the risk of CKD progression in a representative sample of patients who were hospitalized at the Department of Cardiology and Interventional Cardiology of the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation.

Method: In the prospective part of the study, information on demographic characteristics, including age, gender, education, and occupation, was collected from doctor’s visits using a standard questionnaire. Metabolic syndrome was defined according to international guidelines in the presence of three or more of the following risk factors: waist circumference > 102 cm in men or > 88 cm in women; serum triglyceride level ≥ 1.70 mmol/l; HDL cholesterol level < 1.04 mmol/l in men or < 1.30 mmol/l in women; BP ≥ 130/85 mm Hg, including achieved serum glucose level ≥ 6.11 mmol/l. The criteria for determining the metabolic syndrome were used.

Results: Demographic characteristics of patients are presented in the table. Mean serum creatinine was similar, but GFR was estimated to be lower among those with metabolic syndrome compared to those without. The percentage of individuals with CKD and elevated serum creatinine was statistically significantly higher among those with metabolic syndrome. It turned out low HDL cholesterol, elevated plasma glucose and abdominal obesity were statistically significantly associated with the risk of developing C5 CKD and elevated serum creatinine. In addition, there was a significant relationship between the number of metabolic syndrome components and the percentage of C5 CKD or elevated serum creatinine (P < 0.015 and P = 0.02, respectively). In the multivariate model, patients with 1, 2, 3, and 4 or 5 components of the metabolic syndrome had 1.51; 1.50; 2.13 and 2.72 times higher chances of C5 CKD, respectively, compared to individuals without metabolic syndrome components. Overall, patients with metabolic syndrome had a 64% increase in risk of C5 CKD compared to the comparison group without metabolic syndrome.

Conclusion: In the present study, a positive and significant relationship was found between the metabolic syndrome and the risk of C5 CKD in the examined patients. The risk of C5 CKD increased progressively with an increase in the number of components of the metabolic syndrome.
Table 1: Baseline characteristics of participants.

<table>
<thead>
<tr>
<th></th>
<th>Total (n=198)</th>
<th>HD (n=116)</th>
<th>PD (n=11)</th>
<th>KT (n=22)</th>
<th>CKD (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male), n (%)</td>
<td>109 (55)</td>
<td>65 (56)</td>
<td>6 (54)</td>
<td>12 (55)</td>
<td>26 (54)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54 (11)</td>
<td>56 (11)</td>
<td>53 (12)</td>
<td>51 (10)</td>
<td>54 (13)</td>
</tr>
<tr>
<td>Vaccine, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pfizer-BioNTech, n (%)</td>
<td>25 (13)</td>
<td>9 (8)</td>
<td>3 (27)</td>
<td>5 (23)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Moderna, n (%)</td>
<td>42 (21)</td>
<td>25 (22)</td>
<td>4 (36)</td>
<td>6 (27)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>AstraZeneca, n (%)</td>
<td>28 (14)</td>
<td>15 (13)</td>
<td>2 (18)</td>
<td>4 (18)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Sputnik V, n (%)</td>
<td>36 (18)</td>
<td>20 (17)</td>
<td>1 (9)</td>
<td>5 (23)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>ZF-UZ-VAC2001, n (%)</td>
<td>67 (34)</td>
<td>47 (40)</td>
<td>1 (9)</td>
<td>2 (9)</td>
<td>17 (35)</td>
</tr>
</tbody>
</table>

#3008
SERENDIPITY OF SGLT2 INHIBITION – DIABETIC AND NON DIABETIC CKD
Vjollca Godanci-Kelmendi1,2, Mimoza Ramadani Piraj3, Fatime Ymeri1 and Shega Konjufca4
1 UCCK, Nephrology Clinic, Prishtina, Kosovo*, 2 UCCK, Nephrology Clinic, Prishtina, Kosovo*, 3 UCCK, Endocrinology Clinic, Prishtina, Kosovo* and 4 Asklep Med, Ministry of Health Private Practice, Prishtina, Kosovo*

Background and Aims: Ever since their therapeutic introduction, SGLT2 inhibition class of medicaments did impress physicians of related fields, nephrologists, internal medicine doctors, endocrinologists etc. Their natriuretic and glucoretic effects besides lowering the plasma glucose does produce a important effect on lowering intraglomerular pressure, this became an added value and a strong point to recommend these drugs on all CKD population irregardless the main cause of the disease.

Method: Observational retrospective study on 125 patients, three groups: G1 50 pt with diabetic nephropathy treated with empagliflozine vs control group G2 50 pt with diabetic nephropathy treated with other glucose lowering agents, and G3 25 nondiabetic pt with CKD and proteinuria treated with SGLT2i. Inclusion criteria was proteinuria and T2D for G1 and G2, and patients with proteinuria and CKD for G3. Patients with T1D and eGFR > 20 where excluded. Intervention - the SGLT2i drugs where started, median follow up 18 months. We followed on four periods creatinine levels, 24 hour proteinuria in g/24 h, HbA1c, cholesterol level, BMI.

Results: In our study the G1 showed a decrease in proteinuria average – 811 mg/24 h, serum creatinine showed increase on the first three months and it did get back to baseline afterwards, the eGFR increased + 15.44 ml/min; Hba1c decreased with -1.41%, levels, the reduction BMI – 0.9 kg/m² and LDL cholesterol -1.11 mmol/L. G2 results decrease on 24 hour proteinuria with – 121 mg/24 hours, a drop on eGFR with - 3.3 ml/min, a drop on HbA1C – 1.45 %, - 0.3 mmol/l decrease on cholesterol level and average increase on BMI with + 0.8 kg/m²; G3 results on patients without T2D but with CKD different causes and proteinuria where: - 690 decrease proteinuria, + 14.4 increase on eGFR, Hba1C NA, we did have 2 cases that experienced hypoglycemic symptoms, both of them where improved with dose reduction, a – 0.9 decrease on cholesterol level and 0.3 kg/m² was registered on our G3.

Conclusion: In our observation the 18 month follow up showed remarkable improve in kidney function tests, other benefits were noted such as optimal glycemic control, total body cholesterol lowering and a significant reduce of body weight expressed on BMI. Treatment with SGLT2i drugs does present a safe and efficient treatment modality for diabetic nephropathy and for all other CKD with proteinuria.
Table 1:

<table>
<thead>
<tr>
<th>Group</th>
<th>T2D SGLT2i</th>
<th>Ur Prot 24</th>
<th>eGFR MDRD</th>
<th>HbA1c</th>
<th>Chol</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 50 pt</td>
<td>T2D SGLT2i</td>
<td>-811 mg/24 h ▼</td>
<td>+15.44 ml/min ▲</td>
<td>-1.41 % ▼</td>
<td>-1.11 mmol/l ▼</td>
<td>-0.9 kg/m² ▼</td>
</tr>
</tbody>
</table>


Table 2:

<table>
<thead>
<tr>
<th>Group</th>
<th>T2D CONTROL GROUP</th>
<th>Ur Prot 24</th>
<th>eGFR MDRD</th>
<th>HbA1c</th>
<th>Chol</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2 50 pt</td>
<td>T2D CONTROL GROUP</td>
<td>-121 mg/24 h ▼</td>
<td>-3.3 ml/min ▼</td>
<td>-1.45 % ▼</td>
<td>-0.3 mmol/l ▼</td>
<td>+0.8 kg/m² ▲</td>
</tr>
</tbody>
</table>


Table 3:

<table>
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<tr>
<th>Group</th>
<th>CKD non diabetes</th>
<th>Ur Prot 24</th>
<th>eGFR MDRD</th>
<th>HbA1c</th>
<th>Chol</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>G3 20 PT sGTL2i</td>
<td>CKD non diabetes</td>
<td>-690 mg/gl ▼</td>
<td>+14.4 ml/min ▼</td>
<td>NA</td>
<td>-0.9 mmol/l ▼</td>
<td>-0.3 kg/m² ▲</td>
</tr>
</tbody>
</table>


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#4927

**DARBEPOETIN ALFA ONCE IN 4 WEEKS CORRECTS ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE NOT ON DIALYSIS**

Mooyong Park¹, Soo Jeong Choi² and Jin Kuk Kim³

¹Soonchunhyang University Bucheon Hospital, Bucheon, Rep. of South Korea

**Background and Aims:** In anemia management in patients with CKD not on dialysis (CKD ND), darbepoetin alfa (DA), which has shorter half-life but lower cost than continuous erythropoietin receptor activator (C.E.R.A.), is preferred in actual clinical practice in Korea. The current study evaluated the efficacy and safety of DA every 4 weeks (Q4W) compared to C.E.R.A. Q4W administration for in erythropoiesis-stimulating agent (ESA)-naive patients with CKD ND.

**Method:** In this randomized, prospective, non-inferiority study, 40 ESA-naive patients with CKD ND were randomized 1:1 to receive either DA or C.E.R.A. Q4W during a 12-week correction period and 24-week efficacy evaluation period (EEP). Two primary efficacy end points were analysed: 1) the mean difference in the changes in haemoglobin (Hb) levels between baseline and EEP and 2) the Hb response rates defined as the proportion of patients who reached the target Hb level range (10-11 g/dL) during correction period. The non-inferiority margin is pre-defined as: 1) The lower limit of the 95% confidence interval (CI) is > -0.75 g/dL for the mean difference in the changes in Hb levels and 2) >60% for Hb response rates. Safety profiles including changes in blood pressure (BP), laboratory safety parameters, and frequency of all adverse events (AEs) were monitored and analysed during study period.

**Results:** The mean difference in the changes in Hb levels between the two groups was [0.375 g/dL; 95% confidence interval (CI), -0.446 to 1.196] and [-0.070 g/dL; 95% CI, -0.730 to -0.590] in the intent-to-treat (ITT) and per-protocol (PP) population, respectively (Fig. 1). The Hb response rates in correction period were comparable between DA and C.E.R.A. group; [100%; 95% CI, 81.4 to 100] versus [94.1%; 95% CI, 71.3 to 99.8] and [100%; 95% CI, 79.4 to 100] versus [100%; 95% CI: 88.2 to 100] in ITT and PP population, respectively (Fig. 2). The mean estimated glomerular filtration rate, systolic and diastolic BP, sodium, and potassium level over time were not different during total study period between two groups (P = 0.264, 0.999, 0.823, 0.941, and 0.978). All of the AEs in each group were reported to be mild to moderate in intensity. Peripheral edema, neck pain, herpes zoster, and dyspnea occurred in DA group (20%) and urinary tract infection, dyspnea, and femur neck fracture occurred in C.E.R.A. group (15%). There were no serious AEs which led to discontinuation of the treatment. All AEs were mild to moderate in severity, and they are probably not associated with the study drugs and were successfully cured. The reasons for discontinuation of the drugs were starting HD or follow-up loss, but not due to the administered study drugs. No subjects received RBC transfusion or iron replacement therapy in both groups. There was no death during the study period.

**Conclusion:** These study results suggest that DA Q4W has non-inferiority in anemia correction efficacy and similar safety profiles compared to C.E.R.A. Q4W in ESA-naive patients with CKD ND.

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Figure 1: The mean difference in the changes in Hb levels with Darbepoetin alfa (DA) and continuous erythropoietin receptor activator (C.E.R.A.) between baseline and evaluation period (ITT and PP populations). ITT, intent-to-treat; PP, per-protocol.
Supplemented low-protein diet (sLPD) versus a conventional diet on the is a comparative study that aimed to assess the effects of a ketoanalogue-supplemented low-protein diet (sLPD) versus a conventional diet on the progression of CKD and proteinuria in patients with advanced DKD.

**Background and Aims:** Low-protein diets seem to have an important role in the management of advanced chronic kidney disease (CKD). In addition, this type of nutritional regimen may defer kidney replacement therapy by improving metabolic abnormalities. However, low-protein diets (LPDs) may be more difficult to integrate in patients with diabetic kidney disease (DKD), because of the already complex dietary intervention in these patients. This is a comparative study that aimed to assess the effects of a ketoanalogue-supplemented low-protein diet (sLPD) versus a conventional diet on the progression of CKD and proteinuria in patients with advanced DKD.

**Method:** Ninety-seven adult patients with DKD and heavy proteinuria (>3 g/g creatininuria) who proved to be compliant to protein restriction in a 3-month run-in phase were enrolled to receive a LPD (0.6g mixed protein/kg-day) supplemented with ketoanalogues of essential amino acids (Ketosteril®, Bad Homburg, Germany, 1 tbl/10 kg dry ideal body weight per day) for 12 months. Ninety-two patients completed the study (5 patients received preemptive kidney transplant). The control group was made up of seventy-four adult patients with DKD and heavy proteinuria who received a conventional diet for 12 months. Efficacy outcomes were variation of the estimated glomerular filtration rate (eGF) and variation of proteinuria.

**Results:** At baseline, patients from the sLPD group had a median age of 61 years (95% CI 58 to 67), were mostly male (66%) and predominantly on insulin (68%). In the control group, the median age of 60 years (95% CI 56 to 61), 62% were male and, similarly, the majority were on insulin (62%). All patients had poorly controlled diabetes, with a glycated hemoglobin of 8.1% (95% CI 8.0 to 8.3) in the sLPD group and 8.2% (95% CI 7.9 to 8.6) in the conventional-diet group respectively (P = .84). Although the median eGF was different between groups: 24.78 mL/min (95% CI 20.00 to 30.00) in sLPD patients versus 12.61 mL/min (95% CI 11.70 to 13.11) in conventional diet patients (p < 0.0001), proteinuria was similar at baseline: 5.26 g/g creatininuria (95% CI 4.98 to 5.22) in sLPD patients and 4.05 g/g creatininuria (95% CI 3.70 to 5.80) in control group patients (P = .44). After 12 months, the decline of eGF (mL/min/month) was four-times slower in the sLPD group versus the control group [0.11 (95% CI 0.1 to 0.14) versus 0.43 (95% CI 0.30 to 0.57), p < 0.0001]. A twofold reduction in proteinuria (g/month) was observed in sLPD patients compared to conventional diet patients [0.29 (95% CI 0.28 to 0.32) versus 0.12 (95% CI 0.09 to 0.15), p < 0.0001].

**Conclusion:** Low-protein diets supplemented with ketoanalogues of essential amino acids seem to be more efficient in reducing kidney function decline and proteinuria than conventional diets.

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**DIALYSIS**

**D1 - EXTRACORPOREAL TECHNIQUES & ADEQUACY**

**#2726**

**DUAL DIALYSER HAEMODIALFILTRATION: A NEW EXTRACORPOREAL DIALYSIS TREATMENT MODALITY FOR PATIENTS WITH END STAGE KIDNEY DISEASE**

Gerald Glancey

1 Ipswich Hospital, Renal unit, Ipswich, United Kingdom

**Background and Aims:** The introduction of High Flux (HF) haemodialysers and their application in single dialysers haemodialfiltration (sdHDF) for patients on extracorporeal dialysis (ECD) therapy has improved the extraction of ureaemic toxins including the low molecular weight protein (LMWP) beta 2 microglobulin (#2M, 11.6kDa). Similar increases in the extraction of protein-bound ureaemic toxins (PBUT) and larger LMWP (15-50kDa) remain elusive. High concomitant losses of albumin prohibit the use of Medium Cut-Off (MCO) or protein-losing haemodialysers in sdHDF to increase the convective transfer of these molecules.

**Method:** A new extracorporeal dialysis treatment modality, dual dialyser haemodialfiltration (ddHDF), has been designed together with an accompanying mathematical model to compare its predicted performance to that of sdHDF in the extraction of solute. The extra process that distinguishes ddHDF from sdHDF is the secondary ultrafiltration and partial re-infusion of the effluent haemodiafiltrate from the initial or primary haemodialyser. This allows MCO and protein-losing haemodialysers to be used to increase the extraction of both LMWP and PBUT without excessive concomitant loss of albumin.

Glancey GR. Modeling the transfer of low molecular weight proteins during haemodialfiltration and online haemodialfiltration. *Artificial Organs* 2021;45(4):419-426.

**Results:** Data from the mathematical model show that ddHDF could increase the extraction of smaller and larger LMWP by an extra 102% and 220% respectively compared to standard HF sdHDF whilst restricting the loss of albumin to 0.83 grams per hour of treatment. In using albumin as a recyclable carrier molecule for the extraction of PBUT from plasma ddHDF has the potential to increase PBUT reduction ratios (RRs) to 49% by convection alone. Even higher RRs are possible if the dialysate volume flow rate can be increased beyond 600 ml/min.
Conclusion: ddiHDF provides an opportunity for a step change increase in the level of extraction of both larger LMWP and PRMT in patients with end stage kidney disease.

#5633
USE OF HEPARIN GRAFTED DIALYZER (EVODIAL) FOR HEMODIALYSIS IN PATIENTS WITH HIGH RISK OF BLEEDING: A SINGLE CENTER EXPERIENCE

Vladimir Pusheski, Zhaklina Shterjova- Markovska, Julijana Usprcov, Nikola Gjorgjievski, Lada Trajcheska, Mimoza Milenkova and Irena Rambabova-Bushnjletik
University clinic for nephrology- Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Republic Of North Macedonia

Background and Aims: During hemodialysis exposure of the blood to the dialysis membrane and the tubing system can activate blood cells and promote clotting activation. So usually, some form of anticoagulation, most frequently heparin, is used to prevent blood coagulation. However, there are patients with increased risk for bleeding (patients with active bleeding, major surgery in past 72 hours, severe trombocytopenia) where use of heparin free regime is mandatory. Evodial dialyzer (Gambro-Hospital, France) [1] contains a heparin-grafted membrane aiming to provide a system with a low thrombogenicity that can be used without or with low dose heparin in order to reduce the patients’ bleeding risk. As high-quality evidence of the optimal choice of anticoagulation in these patients is limited we wanted to show our experience with the use of Evodial dialyzer.

Method: During 12 months 106 dialysis sessions in 59 patients were performed. Reasons for using Evodial : active bleeding, hematological conditions, complications of vascular access. Changes in the dialyzer or the blood lines, or any additional interventions were examined.

Results: Low dose unfractionated heparin (1250 IE total) was used in 10 (9.4%) sessions, and it was added in 15 (14%) more sessions because of problems with the coagulation. In 4 (2.8%) sessions we had to terminate dialysis because of clotting.

Conclusion: Heparin grafted dialyzers can be safely used in patients with high risk for bleeding. Although results are worse than the ones reported in literature [2] where regional citrate anticoagulation (RCA) is used, it can be reasonable alternative when RCA is unavailable.

REFERENCES

#5203
THE INCESSANT QUEST FOR DRY WEIGHT: SHOULD WE ADOPT NEW STRATEGIES?

Amel Ayed, Hadj Brahim Mayssa, Lazhar Jaballah, Amel Echouk, Habiba Ben Alaya and Zohra Elati
Taher Safar Hospital, Nephrology, Mahdia, Tunisia

Background and Aims: The estimate of the hydration state in the chronic hemodialysis patient is a key point of his care. Currently, there is no Gold Standard feasible in routine despite the increasingly numerous tools such as impedancepenetry and pulmonary cardiac ultrasound.

The objective of our study is to compare the results of the clinical estimation of dry weight with the results of impedancepenetry and cardiac ultrasound results.

Method: This is a transverse study in the dialysis unit of Taher Safar Mahdia hospital. The estimation of the hydration state was assessed before and after the hemodialysis session by the three above methods. The volume evaluation was carried out by a clinical score (NYHA= III dyspnea, orthopneic; jugular turgor (TJ), hepatojugular reflux (HRJ), crackling in auscultation, peripheral edema and pre-dialysis hypertension); as well as by cardiac ultrasound (diameter of the lower vein, E/E ratio and systolic pulmonary arterial pressures).

Results: The values measured by the different techniques decreased significantly after the hemodialysis session (p <0.001). At the two -stroke studied, we have objectified a significant correlation between the results of the impedancepenetry, the index of the lower vein and its compliance. A significant difference between the results provided by the techniques studied and the results of the clinical evaluation was found in 64 % of patients. Only the orthopnea (p = 0.03) and the hepatojugular reflux (p = 0.04) were significantly associated with the ultrasound overdiagnosis.

Conclusion: The existence of a difference between the subjective and objective target weight suggests the incessant need for a mixture between the different techniques evaluated. Our strategy requires to be adapted to the particularities of each patient.

#4431
PREPARATION OF IMIDAZOLE QUATERNARY AMMONIUM SALT MICROSPHERES WITH HIGH BILIRUBIN ADSORPTION PERFORMANCE AND SELF-ANTICOAGULATION ABILITY

Ningyue Deng, Lunqiang Jin2 and Baihai Su2
P.R. China and , P.R. China

Background and Aims: Bilirubin is a crucial toxin in liver metabolism. Increase of bilirubin is one of common manifestations in patients with abnormal liver function, and large accumulation of bilirubin in the blood can lead to more severe hepatic dysfunction and even death. Due to the poor therapy effect and the shortage of available donor organs, the artificial liver support system has been introduced to maintain the liver function and bridge patients to transplantation. Previous studies have found that imidazole quaternary ammonium salts have great potential to adsorb bilirubin. This work is to develop a novel bilirubin adsorption column by simple and general method, and evaluate the removal efficiency, anticoagulant property and biocompatibility of the bilirubin adsorption column.

Method: Multifunctional microspheres were fabricated by in situ polymerization of 1-vinylimidazole and divinylbenzene. Nuclear magnetic resonance (NMR), thermo-gravimetric analysis and X-ray photoelectron spectroscopy (XPS) etc. were performed to characterize the chemical compositions of the microspheres. Meanwhile, hemolysis test, blood routine test and clotting time test etc. were leveraged to evaluate the biocompatibility of the microspheres. Both static adsorption test and dynamic adsorption test were performed in vitro to evaluate adsorption performance.

Results: A variety of methods had proved successful synthesis of the adsorption performance. The hemolysis ratios of microspheres were less than 5%. Compared with BS330 microspheres and PES microspheres, the activated partial thromboplastin time (APTT) and thrombin time (TT) were longer in this work. Moreover, the microspheres showed a high adsorption clearance. In PBS solution of bilirubin, the adsorbent could decrease bilirubin from 200 mg/L to 45-55 mg/L.

Conclusion: The results suggested that the multifunctional microspheres can significantly reduce bilirubin concentration without obvious adverse interactions and could exhibit anticoagulation activity.

#4059
MICROBIOLOGICAL ANALYSIS OF HEMODIALYSIS WATER AT THE DOUALA GENERAL HOSPITAL, CAMEROON

Cedric Gueguim, Alain Ragon1, Halle Marie Patrice3, Francois Jerome Kaze Folefack1 and Hortense Gonsu Kamga1
Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Central region, Cameroon, Microbiology, Cameroon, 1Division of Uro-Nephrology Laboratory, Hospital of Conception, Marseille, France, pharmacology, France, 3Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Littoral Region, Cameroon, Nephrology, Cameroon and 4Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Central region, Cameroon, Cameroon

Background and Aims: Rigorous control of the microbiological quality of water in hemodialysis services is important because the immune system of patients with chronic renal failure is weakened. The aims of this study was to determine the microbiological quality of water for hemodialysis in Nephrology Unit of the Douala Général Hospital in order to improve the disinfection strategy.

Method: Twelve water samples were collected each month at different sites of the hemodialysis circuits A (inlet of filters), B (Outlet of filters / inlet of Reverse Osmosis (RO) device) and C (outlet of the RO device / close to the generator) between November 2015 and February 2016 to be analyzed. The bacteria were isolated after filtration of 100 ml of water at each site through nitrocellulose membrane with 0.45 μm microporosity deposited on the surface of the Tryptone Glucose Extract Agar (TGEA) and then incubated at room temperature (20 to 22°C) for 7 days. After transplanting to different environments, pure bacterial isolates were identified by their cultural characters and marketed biochemical galleries.

Results: The colony count was well above the required international standards (>100 CFU / ml), for the hemodialysis water with a percentage of 50% of non-
compliance. Among the bacteria identified, seven (07) were Gram-negative bacilli including Pseudomonas fluorescens, and Klebsiella pneumoniae subsp. ozaenae, three (03) Gram-positive bacilli all Bacillus sp and three (03) Gram-positive cocci all of coagulase-negative staphylococci. The most frequently isolated bacterial genera were Pseudomonas sp (38,5%), Staphylococcus sp (23%), Bacillus sp (23%) and Klebsiella sp (15,5%).

Conclusion: The high bacteriological contamination of the hemodialysis water with the detection of a variety of bacteria shows that the disinfection procedure of the distribution loop is not efficient and cannot prevent the development of a biofilm. A higher frequency of disinfection (almost every week), an increase of the concentration and time of contact of the chlorine disinfection product or the use of peracetic acid and a regular monitoring can contribute to improve the quality of the hemodialysis water at the Douala General Hospital to ensure a better quality of life for patients undergoing this treatment.

#4837
CLINICAL OUTCOMES OF HEMOPERFUSION WITH MG350 AMONG RT-PCR-CONFIRMED SEVERE AND CRITICAL COVID-19 PATIENTS IN A TERTIARY HOSPITAL IN LA UNION
Mayene Alyssa Echave and Chrysanta Octaviano
Ilocos Training and Regional Medical Center, Internal Medicine, San Fernando City, The Philippines

Background and Aims: Hemoperfusion (HP) refers to the circulation of anticoagulated blood through an extracorporeal circuit with a disposable, adsorbent-containing cartridge. Earlier studies showed that HP stabilizes the plasma levels of cytokines in sepsis and septic shock. Case reports demonstrated the benefit of HP among COVID-19 patients with severe and critical illness but local data on the outcome of HP in COVID is still lacking. This study aimed to determine the clinical outcomes of HP with MG 350 cartridge among RT-PCR confirmed severe and critical COVID-19 patients admitted in a tertiary hospital in La Union in terms of the trend of clinical parameters before and after HP, mean duration of ventilatory support, mean duration of hospital stay and patient’s clinical parameters before and after HP. Patients with higher oxygen saturation, PaO2 and lower fraction of inspired oxygen (FiO2) had shorter duration of ventilatory support. Increased FiO2, CRP, D-dimer, ferritin, white blood cell (WBC) count and Neutrophil Lymphocyte Ratio (NLR) are highly correlated with increased mortality. Early hemoperfusion correlated with shorter duration of ventilatory support, shorter hospital stay and decreased mortality. Interestingly, those with higher oxygen saturation, PaO2, ferritin and procalcitonin correlated with longer duration of hospital stay after HP. Patients with critical illness and late HP had longer duration of ventilatory support. Patients with bilateral infiltrates on chest X-ray and those on mechanical ventilator had longer duration of hospital stay. Increased COVID severity and decreased mean arterial pressure (MAP) had higher likelihood of death even after HP.

Conclusion: Hemoperfusion significantly decreased the level of inflammatory markers thereby lowering the risk for cytokine storm for COVID-19 patients. Early HP is recommended as it is correlated with shorter duration of ventilatory support, shorter hospital stay and decreased mortality.

#5657
FRAILTY AND VASCULAR ACCESS IN HEMODIALYSIS PATIENTS
Eleni Intzevidou1, Charalampos Louradis1, Ourania Kougioumtzidou1 and Georgios Pitoulias2
1Dialysis Center Evangelismos, Veria, Greece and 22nd Department of Surgery, Gennimatas Hospital, Aristotle University of Thessaloniki, Division of Vascular Surgery, THESSALONIKI, Greece

Background and Aims: Frailty is a geriatric syndrome characterized by increased vulnerability to stressors. The elderly become vulnerable and susceptible to adverse outcomes for their health and to functional restrictions. Previous guidelines suggested fistula creation as first choice for vascular access. Current guidelines suggest a more tailored approach to the patient’s needs. Despite the high prevalence of frailty in hemodialysis patients, there is paucity of work investigating the relationship between frailty and vascular access failure. The aim of the study was the estimation of frailty with different scores and relationship with the choice of first vascular access, the current vascular access and vascular failures.

Method: 67 patients in hemodialysis participated to the study (observational cross-sectional study). Frailty was assessed with 6 different scores, Clinical Frailty Scale (CFS), Frailty Phenotype (FP), Edmonton Frailty Scale (EFS), Groningen Frailty Index (GFI), Short Physical Performance Battery (SPPB), PRISMA-7 and ankle-brachial index (ABI) and hand grip were also estimated. The current vascular access, the first vascular access, the vascular access failures and the mean duration of the vascular accesses were also recorded. Finally, the levels of the hemoglobin, albumin, C reactive protein, cholesterol were measured for all patients and the hemodialysis adequacy (URR, sp Kt/V) was calculated from the levels of urea before and after the hemodialysis session. Finally, the levels of the hemoglobin, albumin, C reactive protein, cholesterol were measured for all patients and the hemodialysis adequacy was calculated from the levels of urea before and after the hemodialysis session.

Results: The first vascular access of hemodialysis presents statistically significant relation between frail and robust patients that start hemodialysis with central venus catheter and AVF-AVG respectively. (SPPB- tunneled CVC 85, 7%, non tunneled CVC 46,2% p=0,032, PRISMA-7- frail tunnelled CVC 100%, non tunnelled CVC 76,9% p=0,018, Groningen FI -frail tunnelled CVC 100%, non tunnelled CVC 65,7% p=0,011, Edmonton FS -AVF-AVG not frail 64,7%, vulnerable 20,6% p=0,042) (Table 1-4). ABI presented a statistically

### Table 1: First vascular access and frailty (SPPB).

<table>
<thead>
<tr>
<th>First Vascular Access</th>
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### Table 2: First vascular access and frailty (PRISMA-7).

<table>
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<th>FRAIL</th>
<th>p</th>
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<tbody>
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<tr>
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<td>25%</td>
<td></td>
</tr>
<tr>
<td>TrnCVC</td>
<td>0%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>nTnCVC</td>
<td>23,1%</td>
<td>76,9%</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3: First vascular access and frailty (Groningen FI).

<table>
<thead>
<tr>
<th>First Vascular Access</th>
<th>NOT FRAIL</th>
<th>FRAIL</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVF</td>
<td>60%</td>
<td>40%</td>
<td>0,011</td>
</tr>
<tr>
<td>AVG</td>
<td>75%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>TrnCVC</td>
<td>0%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>nTnCVC</td>
<td>34,6%</td>
<td>65,4%</td>
<td></td>
</tr>
</tbody>
</table>
significant relationship with the current vascular access. 68.18% of the patients with normal ABI have AVF-AVG and 60.87% of patients with abnormal ABI have tunneled CVC (p=0.022). In addition, the number of vascular accesses per patient, the mean duration of the accesses and the premature failures (3 months after creation) don’t present statistically significant relation with frailty. Conclusion: The frailty score could be used as a tool for the choice of vascular access in hemodialysis patients. Further studies, in a larger number of patients, are required to define a reliable and easy to use frailty tool, which is best suited to dialysis access selection.

#6282
MAKING DECISION OF VASCULAR ACCESS TYPE BASED ON UPPER ARM DOPPLER PARAMETERS AMONG INCIDENT HEMODIALYSIS PATIENTS: A SINGLE CENTER EXPERIENCE
Aleksandar Jankovic1, Sofija Rajić2, Zeljko Davidovic1, Bojan Stopić1, Petar Djuric1, Snezana Pešić1, Radomir Naumovic1,2
1University Medical Center Zvezdara, Nephrology Department, Belgrade, Serbia and 2Belgrade University, Medical Faculty, Belgrade, Serbia

Background and Aims: Functional vascular access (VA) remains one of the most important problems related to successful hemodialysis (HD) treatments. Pivotal issue related to inadequate vascular access is decision making process of which type of VA should be created at start. Therefore, the aim of our study is to examine possible impact of Doppler examination of upper arm on decision of VA type creation.

Method: During 5 year period (January 2018th- December 2022th), 260 patients started hemodialysis in our department. Among them, 18 died during the first three months after HD was started, 3 were transferred to other hospitals for chronic HD program and 5 have created vascular access in other hospitals. So, we analyzed data for 234 patients (No. hospitals for chronic HD program and 5 have created vascular access in other hospitals. So, we analyzed data for 234 patients (No=150, 63.6% males, mean age 62.6±13.8) which vascular access were created in our Center. We have divided them into two groups (Group A-patients with arterio-venous fistula (AVF) as first created VA and group B-patients with arterio-venous graft (AVG) or permanent central venous catheter (pCVC) as first created VA. From medical records, we have collected demographic data, type of created vascular access, Doppler parameters of upper arm and laboratory findings.

Results: Out of 234 patients, in Group A were 167 patients (male No=109, 65.2%, mean age 61.0 years±13.8), while in group B were 67 patients(male No=40, 59.7% mean age 66.8 years±13.2). In table 1, demographic, laboratory and Doppler data is presented. We found that in Group A patients are statistically younger (61.0 years±13.8 vs 66.8 years±13.2, P = 0.004) and their vena cephalica (2.9mm± 2.5 vs 1.9mm±0.1, P = 0.000) and artery radialis (2.2mm±0.4 vs 1.9mm±0.1, P = 0.002) are with better diameters. Also, their protein levels were statistically lower (69±9 vs 78±3, P = .036) and CRP levels higher (21.2±35.3 vs 8.1±2.1, P = 0.000) compared to Group B. Binary logistic regression revealed that there are no statistically significant variables that could impact decision to create AVF, but larger diameter of vena cephalica increase this decision over 13 fold (OR 13.497, CI 0.706-257.868, P = .084), and diameter of artery radialis 17 fold (OR 17.073, CI 0.372-784.182, P = .146).

Conclusion: Diameters of vena cephalica and artery radialis could be the main variables in the planning of type of vascular access.

#5111
HEMODIALYSIS TUNNELED CATHETERS LOCK WITH TAUROLOCKTM VERSUS A COMBINATION OF GENTAMYCINE AND HEPARINE
Biser Borisov and Vanya Vasileva
Medical Universiti, Nephrology and Dialysis, Pleven, Bulgaria

Background and Aims: Catheter-associated infections (CAIs) and thrombosis (CAT) are the most common complications, associated with the use of tunneled catheters for hemodialysis. The incidence of infections is about 1.8-6.5/1000 catheter-days, and thromboses are the main cause of catheter dysfunction and loss of vascular access in 30-40% of patients. The aim of our study was to determine the incidence of these complications in patients in whom we used prophylactic "locking" of their tunneled catheters.

Method: The patients included in the study signed an Informed Consent (№29.06.2021) approved by the Research Ethics Committee at MU-Pleven. The study was conducted in the period of 01.03.2021 - 31.03.2022, a total of six months. The study included 23 men and 22 women with an average age of 60.82 (+/-13.629) years, and the age difference between the three groups can be considered insignificant (P = .046). All patients had tunneled catheters placed >3 months ago (mean duration was 714 +/- 247 catheter-days) as the only vascular access for hemodialysis treatment. After a clinical examination and a negative result of two blood cultures, the patients were randomly divided into three groups of 15 (fifteen) people each, a total of 45 (forty-five) participants: group A – locking the catheter only with TauroLockTM (Taupropharm, Waldbüttelbrunn, Germany), group B – locking with gentamicin (10 mg/ml) and heparin (1250 IU/ml) and group C – locking with TauroLockTM for three months, then – with heparin and gentamicin for the next three months of the study. Patients were monitored for the major complications of catheter-related infection (CRI) and catheter-related thrombosis (CRT). All data was statistically processed with Statgraphics 19.

Results: The median duration for tunneled catheters was 8,105 catheter-days (CD). One complication was reported in each of the three groups: group A – one case of CRI, groups B and C – one case of CRI each. No cases of catheter-associated bloodstream infection, requiring prolonged treatment and catheter thrombosis, requiring replacement of the tunneled catheter were reported. Reported costs for patients treated with TauroLockTM were calculated at 3 EUR/each dialysis session, and for patients treated with gentamicin and heparin – 0.88 EUR/dialysis session.

Conclusion: The data from our study unequivocally support the thesis that locking the catheter with a solution containing TauroLockTM is comparable to the effect of blocking the catheter with a solution containing an antibiotic and anticoagulant. In the short term, the difference in the price of medicines is significant, but it does not exceed the potential losses of public funds in the medium and long term. We recommend the use of a similar prophylactic regimen in all patients with tunneled catheters as the only possible vascular access for hemodialysis or with an expected duration of use greater than ninety days.
#2867

**EARLY DETECTION OF VASCULAR ACCESS STENOSIS USING NEPHROFLOW**

Soledad Pizarro Sanchez¹, Alejandra Elizabeth Collantes Toaza¹,², María López Picasso⁵, Eleno Burgos García¹, Saul Pampa Saico¹, Simona Alexandru⁵ and Laura García-Puente Suarez²

¹Hospital Rey Juan Carlos, Nephrology, Mostoles, Spain and ²Fundación Renal Íñigo Alvarez de Toledo, Nephrology, Spain

**Background and Aims:** The monitoring programs for vascular access make it possible to detect access dysfunction and indicate the need to perform an imaging test to confirm the presence of stenosis and proceed with its treatment. Measurement of arteriovenous fistula (AVF) flow using biosensors is a simple and reproducible method of vascular access assessment. AVF flow (QA) drops below 500 ml/min or a reduction of more than 25% in previous flow are considered predictors of stenosis and/or thrombosis. A stenosis with a high risk of thrombosis is defined as that which presents a decrease of more than 50% in the vascular lumen and a stenosis/prestenosis Peak Systolic Velocity ratio > 2, with additional criteria (residual diameter < 2 mm and/or QA (ml/min) < 500 (native AVF) or and/or decrease in QA > 25% if QA < 1,000 ml/min.

**Method:** We performed AVF flow measurement using the NephroFlow biosensor in prevalent hemodialysis patients.

**Results:** Sixty-one patients were studied, all with native or prosthetic AVF. Of which 42 men and 19 women. The distribution of AVFs was: 38 brachiocephalic (62%), 16 radiocephalic (26%) and 6 brachial-axillary (10%). The data was collected for 24 months. The mean follow-up time for the AVF was 16 months. In 17 patients (30%), flow was detected below 25% compared to previous controls or a decrease in QA < 500 ml/min. In these patients, echo-doppler was performed, showing in 15 cases stenosis with a high risk of thrombosis that was treated with angioplasty. In 1 patient, echo-doppler detected only insufficiency of the artery, and no stenosis was observed in fistulography. In 1 patient, there was a significant drop in flow (from 830 to 451 ml/min), which later recovered 650 ml/min with ultrasound without significant alterations, so an endovascular procedure was not performed. During the study period, 1 fistula thrombosis occurred in a patient who had already detected a drop in flow but could not repair it in time. At the end of the study, of the 61 patients analyzed, 51 patients continued with the technique and the flows remained stable or even increased. In the other 10 patients, 9 left due to transplantation or death and 1 patient had a new thrombosis and the AVF could not be repaired.

**Conclusion:** In hemodialysis units, the measurement of AVF flow using biosensors should be protocolized together with Doppler ultrasound to achieve better monitoring of vascular access, managing to detect and treat early stenosis with a high risk of thrombosis.

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#3736

**SACUBITRIL/VALSARTAN IMPROVES THE VASCULAR ACCESS FLOW OF HEMODIALYSIS PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION**

Chih-Ching Lin

Taipei Veterans General Hospital, Division of Nephrology, Department of Medicine, Taipei, Taiwan, Rep. of China

**Background and Aims:** Sacubitril/valsartan improved left ventricular systolic and diastolic function in patients with heart failure with reduced ejection fraction ≤40% (HFrEF) and end-stage kidney disease. However, there was no report concerning the effect of sacubitril/valsartan on access flow (Qa) of vascular access in maintenance hemodialysis (HD) patients with HFrEF. We aimed to investigate the effect of sacubitril/valsartan on Qa of vascular access in HD patients with HFrEF.

**Method:** We retrospectively screened the HD patients who received echocardiography and Qa measurement in Taipei Veterans General Hospital and Cheng Hsin General Hospital from Jan. 2019 to Dec. 2021. Patients with HFrEF received twice of both echocardiography and Qa at 1 year apart were enrolled and divided into two groups, including those with or without the treatment of sacubitril/valsartan. The difference of Qa at baseline and 1 year later was preferred. One previous study [2] identified physical concerns regarding fistulas as the predominant barrier preventing patients with a CVC from switching to an AVF. Here we provide an expansion on these barriers, alongside novel exploration of nursing opinion on access choice.

**Methods:** Data was collected through individually administered patient surveys across 4 regional dialysis sites in East Anglia (n = 380), and anonymised online survey requests to nursing staff at the sites. Deductive and inductive strategies were employed for analysis of the qualitative data. The aim of the thematic analysis was to determine the preferred access modality of patients and nurses, and the drivers for the preferences.

**Results:** 63% (n = 238) of patients responded to the questionnaire. Patient responses fell into one of four categories; drivers toward, or barriers against AVFs or CVCs. The largest of these categories was the barriers for AVFs, within which four main themes were identified: ‘Fear’, ‘difficult AVF surgery’, ‘patient preference for lines’ or ‘patients awaiting AVF surgery or transplant’. A smaller theme of ‘insufficient information’ regarding access choice was also identified. ‘Fear’ was the largest theme, within which five subthemes were identified: fear of needles, pain, bleeding, fistula appearance, or fear of complications heard from other patients on the dialysis unit. ‘Difficult AVF surgery’ encompassed two subthemes; those who have had previous failed traumatic attempts or those whose current vascular architecture was not amenable to fistula surgery. The other three categories received far fewer responses. The AVF driver category focused on fistulas being preferred medically with reduced infection risk, whilst drivers for lines included it being ‘comfortable’ and patients saying that the line works for them. The one comment in the CVC barrier category cited difficulties experienced with lines like blockages and infections. 13 responses were received from dialysis nurses. All respondents were aware of the medical preference for patients to have a fistula, and the reasons why. Nurses themselves also preferred their patients to have fistulas, referencing the same reasons. However, most nurses thought patients preferred CVCs, and were able to cite the same reasons as the patients themselves. Lastly, nurses reported that they convey the benefits and risks of different access types correctly when asked by patients at the dialysis units.

**Conclusion:** These findings highlight that, whilst doctors and nurses focus on long-term health benefits of AVF when discussing vascular access choices, patients are focussed on the immediate potential risks of an AVF. We hypothesise that, whilst dialysing, patients share stories of fistula-related complications that drive short-term fear of AVFs, with such impact that the messages conveyed by health professionals are often negated. This difference in agendas is essential to acknowledge. The relationship between clinician, nurse and patient in the haemodialysis setting is unique given its longevity, frequency of contact, and holistic nature. Implementing a strategy to bridge this agenda gap could strengthen this relationship and provide a basis for optimum, evidence-based treatment. We therefore suggest the use of positive patient AVF experiences, delivered via peer education sessions, as a tool to introduce drivers for, and uptake of, AVF for dialysis patients in the future.

**REFERENCES**


Figure 1: Sacubitril/valsartan group.

Figure 2: Control group.

compared by Wilcoxon signed-rank test, with a statistical significance of P<0.05.

Results: A total of 33 HD patients with HFrEF were analyzed with a mean HD vintage of 4.7 years. Sixteen patients received sacubitril/valsartan and the other 17 patients received conventional treatment. The mean Qa increased significantly from 633.8 to 948.8 mL/min (P<0.001) and the Qa change correlated with LVEF change [Fig. 1, correlation coefficient (r) =0.70, P=0.006] after 1-year treatment of sacubitril/valsartan; however, there was neither significant change of Qa (from 637.7 to 621.8 mL/min, P=0.44) nor correlation with LVEF change (Fig. 2, r=0.41, P=0.13) for controls after one year.

Conclusion: Sacubitril/Valsartan improves Qa in HD patients with HFrEF possibly related to the increase of LVEF.

#4376
THE ASSOCIATION AMONG CAROTID IMT, PWV AND VASCULAR ACCESS FAILURE IN HEMODIALYSIS PATIENTS
Jong-Woo Yoon1, Hyunsuk Kim2, Seokhyung Kim2, Gwangho Choi2, Jin-Up Kim2 and Youn-Ki Lee3
1Hallym University Medical center, Chuncheon Sacred Heart Hospital, Division of Nephrology, Department of Internal Medicine, Chuncheon, Rep. of South Korea, 2Hallym University Medical center, Chuncheon Sacred Heart Hospital, Division of Nephrology, Department of Internal Medicine, Rep. of South Korea and 3Hallym University Medical center, Kangnam Sacred Heart Hospital, Division of Nephrology, Department of Internal Medicine, Rep. of South Korea

Background and Aims: Patients with chronic kidney disease (CKD) or end stage renal disease (ESRD) have an increased risk of cardiovascular mortality and morbidity. We aimed to compare the value of IMT with tests such as coronary CT and Pulse wave velocity(PWV) as predictors of cardiovascular risk in ESRD patients undergoing maintenance dialysis and examine their association with cardiovascular disease.

Method: We reviewed the patients’ medical records, including height, body weight, smoking status, alcohol intake, medication history, etiology of ESRD, HD vintage, and blood pressure which were measured during hemodialysis. Carotid dopplerwas performed by an skilledsonographer who are unaware of the aims of the study and blinded to the laboratory findings. For PWV measurement, Patients lie down, rest for at least 5 minutes, and prohibit smoking and coffee for 3 hours before the measurement. BaPWV is measured by recording pulse waves of both arm and both ankles from the pressure signal obtained by measuring 4-extremity blood pressure.

Results: One hundred patients were included, of whom 51 (50.5%) were men. The median age was 66 years (interquartile range 58-76 years). The median vintage of hemodialysis was 47.5 months (range 31.3-89.1 months). There were no significant differences between high IMT groupand low IMT group in sex, hemodialysis vintage, end-stage renal disease etiology, and type of vascular access. However, age was significantly older in the high IMT group. IMT was significantly associated with PWV (hazard ratio [HR] 2.109, 95% CI 1.037-4.291, P = 0.039). After adjusting for age, sex and presence of diabetes, IMT was independently associated with PWV (HR 2.110, 95% CI 1.036-4.298, P = 0.040). The risk of recurrent vascular access failure was higher in the high IMT group (HR 1.615, 95% CI 1.460-5.669, P = 0.034).

Conclusion: IMT was associated with PWV and recurrent access failure. Thus IMT may be suggested as a potential predictor of vascular access failure.

#5245
SUCCESSFUL THROMBOLYSIS OF AN ATRIAL TUNNELED DIALYSIS CATHETER AS A LAST RESORT VASCULAR ACCESS
Salah Saïd1, Najjar Mariem1, Meriem Mbarek1, Ilhem Ben Othman1, Imane Gorsane2, Yassine Khadhar2, Tasnim Ben Ayed3, Hayet Kaaroud1, Fethi Ben Hmida1, Jaleleddine Zidi2 and Ezzeddine Abderrahim1
1Charles Nicolle Hospital, Department of Internal Medicine A, Tunis, Tunisia, 2La Rabta Hospital, Department of Cardiac and Vascular surgery, Tunis, Tunisia and 3Charles Nicolle Hospital, Kidney Pathology Laboratory LR005P01, Tunis, Tunisia

Background and Aims: The prolonged survival of patients on dialysis has resulted in a higher frequency of complications and failure related to vascular access. As a result, the situation of depleted vasculature in hemodialysis is becoming increasingly prevalent. The use of an atrial tunneled dialysis catheter (ATDC) has been reported as an effective solution for vascular access in these patients, but limited data is available on the associated complications, particularly thrombosis.

Method: This study reports the experience of a single nephrology center in Tunis with thrombosis of an ATDC as a last resort vascular access for dialysis.

Results: A 32-year-old patient with undetermined tubulo-interstitial nephropathy receiving dialysis presented in November 2022 with depleted vasculature. An ATDC was inserted as a final solution for vascular access. One month later, dialysis could not be initiated through the ATDC. Catheter thrombosis was diagnosed as a guidewire was unable to pass through the catheter's lumen. The patient was successfully treated with thrombolysis using 50 mg of Alteplase, allowing dialysis to be resumed with a blood flow of 300 mL/min.

Conclusion: ATDC is a lifesaving and safe option for patients with depleted vasculature, with only 51 cases reported since 1999 [1]. The treatment of catheter thrombosis is not well defined, and to the best of our knowledge, no thrombolysis protocol has been established. This successful case may contribute to filling the knowledge gap in this field.

REFERENCE

#3194
THE IMPACT OF COVID-19 PANDEMIC ON PSYCHOLOGICAL AND SOCIOECONOMIC WELL-BEING OF HEMODIALYSIS PATIENTS: AN ANALYTICAL CROSS-SECTIONAL STUDY
Jane Angele Pasamante
Makati Medical Center, Internal Medicine, Section of Nephrology, Makati, The Philippines

Background and Aims: This study aimed to determine and assess the prevalence of depression, anxiety, and stress of the COVID-19 pandemic among...
outpatient hemodialysis patients and the relationship to sociodemographic and clinical factors, and to assess the economic impact of the COVID-19 pandemic.

**Method:** In this analytical, cross-sectional study, purposive sampling was used and a total of 69 subjects were enrolled. Sociodemographic data were collected using researcher-administered questionnaires and recent laboratory parameters were collected by reviewing medical records. Patients completed 4 sets of questionnaires including Patient Health Questionnaire 9 (PHQ-9), Generalized Anxiety Disorder 7 (GAD-7), Perceived Stress Scale 4 (PSS-4), and CoRonavirus Health Impact Survey (CRISIS). Quantitative variables were presented using mean and standard deviation, median, and Interquartile Range (IQR). Qualitative variables were presented using frequency and percentages. Pearson's correlation was used to determine the relationship of laboratory parameters with anxiety, depression, and stress scores. The Chi-Square test was used to determine the relationship of sociodemographic profile with anxiety, depression, and stress scores. P values <0.05 were considered statistically significant.

**Results:** Our study showed that the prevalence of anxiety, depression, and stress were 39%, 16%, and 51% respectively. There was an association between age and stress level, with older subjects reporting higher stress scores. Hemoglobin levels had a weak negative correlation with anxiety, depression and stress. The distribution of anxiety scores was significantly different between patients with normal phosphorus levels and elevated phosphorus levels. Financial worries were less of a concern since almost two-thirds of our subjects were retired and unemployed.

**Conclusion:** Hemodialysis patients belong to high-risk populations with a high prevalence of psychological distress hence they are subjected to more severe psychological stress, depression, and anxiety. Our findings suggest that psychological intervention may be necessary for some patients during this pandemic.

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**Table 1: Prevalence and Relationship between Sociodemographic Profile and Anxiety, Depression and Stress Among Maintenance Hemodialysis in Kidney Unit.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64 (63)</td>
<td>64 (63)</td>
<td>64 (63)</td>
</tr>
<tr>
<td>Sex</td>
<td>64 (63)</td>
<td>64 (63)</td>
<td>64 (63)</td>
</tr>
<tr>
<td>Marital status</td>
<td>64 (63)</td>
<td>64 (63)</td>
<td>64 (63)</td>
</tr>
<tr>
<td>Education</td>
<td>64 (63)</td>
<td>64 (63)</td>
<td>64 (63)</td>
</tr>
<tr>
<td>Delay of treatment</td>
<td>64 (63)</td>
<td>64 (63)</td>
<td>64 (63)</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>64 (63)</td>
<td>64 (63)</td>
<td>64 (63)</td>
</tr>
</tbody>
</table>

**Table 2: Effect of Pandemic on Patient's Health and Socioeconomic Well-Being.**

<table>
<thead>
<tr>
<th>Health Concern</th>
<th>Not at all S/None (%)</th>
<th>Moderate (%)</th>
<th>Very/Extremely (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being infected</td>
<td>44 (17.4)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>Friends and family being infected</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>Physical health influenced by COVID-19</td>
<td>18 (7.5)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>Mental and emotional health influenced by COVID-19</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>How stressful the restrictions on leaving home been for you</td>
<td>34 (15.2)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>To what degree have changes related to the COVID-19 crisis in your area created financial problems</td>
<td>49 (20.3)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>To what degree are you concerned about your living situation</td>
<td>51 (21.9)</td>
<td>49 (20.3)</td>
<td>25 (10.2)</td>
</tr>
<tr>
<td>How hopeful are you that the COVID-19 crisis in your area will end soon</td>
<td>14 (6.1)</td>
<td>25 (10.2)</td>
<td>25 (10.2)</td>
</tr>
</tbody>
</table>

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**#3249**

**BLOOD UREA NITROGEN TO CREATININE RATIO IS ASSOCIATED WITH HIGH MORTALITY IN ELDERLY PATIENTS STARTING HEMODIALYSIS: A KSGN RETROSPECTIVE COHORT**

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**Background and Aims:** Previous studies have shown that increased blood urea nitrogen to creatinine ratio (BCR) is a poor prognostic marker in patients with some chronic diseases or in the general population. However, the clinical implication of BCR in elderly dialysis patients is unknown. The purpose of
this study was to verify the association of BCR with the risk of death in elderly patients starting hemodialysis.

Method: The Korean Society of Geriatric Nephropathy Retrospective Cohort consists of patients who started maintenance hemodialysis from January 1, 2010 to December 31, 2017 at 17 nephrology centers in Korea. After excluding patients with malignancy or estimated glomerular filtration rate 30 ml/min/1.73 m2 or greater, we retrospectively analyzed 2183 patients. The main predictor was patients BCR at the time of hemodialysis initiation and subjects were divided into four groups according to their BCR quartile. The main outcome was all-cause mortality.

Results: During 7,545 person-years of follow-up, 1,382 (63.3%) patients died. Patients in the high BCR group died more (60.9%, 59.3%, 62.5% and 70.5% for the 1st to 4th BCR quartiles, respectively, P=0.001). In multivariable Cox proportional hazard model, BCR increase by one was associated with increased risk of death (HR 1.01; 95% CI, 1.01-1.02). This model was adjusted for age, sex, body mass index, cause of renal disease, hypertension, diabetes, ischemic heart disease, cerebrovascular disease, congestive heart failure, eGFR, hemoglobin, albumin, calcium and phosphorus. Compared to 3rd quartile of BCR group, 4th quartile group was associated with increased risk of death (HR; 1.30; 95% CI, 1.12-1.51).

Conclusion: High BCR is a predictor of high mortality in elderly patients starting hemodialysis. This result suggests that more attention should be paid to elderly patients starting hemodialysis with high BCR.

#5177
COVID-19 IN ELDERLY CHRONIC HEMODIALYSIS PATIENTS: PREDICTORS OF MORTALITY

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Background and Aims: Studies have shown that the incidence of severe COVID-19 pneumonia is higher in elderly patients and especially those with comorbidities including chronic kidney disease. The aim of our study was to determine risk factors for mortality in elderly chronic hemodialysis (HD) patients.

Method: We conducted a cross-sectional, observational, and analytical study, in the dialysis unit of the internal medicine department at Charles Nicolle Hospital over an 11-month period from September 2020 to August 2021. We studied the correlation between mortality and the different epidemiological, clinical and biological data via the SPSS software.

Results: We included 59 patients, with a mean age of 73 years [65-93] and a gender ratio of 1. All patients had confirmed COVID-19 infection, chronic kidney failure and required regular HD session at least 3 months. One on four patients had a coronary artery disease, 55% were diabetics and 72% had hypertension. From the 19 patients who underwent chest scan, 68% had severe lesions. Emergency HD had to be conducted for 25% of the patients, mainly because of hyperkalemia. At least one ongoing HD session was interrupted for neurologic, hemodynamic or respiratory instability in 26% of the patients. Mortality rate was 58%. Data that were associated with mortality in the univariate study were oxygen needs (p<0.001), COVID-19 infection severity (p=0.007), and interruption of HD session (p<0.003). Low blood pH levels and high pCO2 levels were also correlated to mortality (p=0.032 and p=0.020). Predictors of mortality in multivariate analysis were high oxygen needs (OR=1.368; 95% CI [1.081-1.732]; P=0.009), interruption of HD session (OR=1.426; 95% CI [1.070-1.846]; P=0.014) and severe form of COVID-19 infection (OR=1.770 95% CI [1.062-2.980]; P=0.029).

Conclusion: According to these results, high oxygen needs, severity of COVID-19 infection and interruption of HD session represented risk factors of death in elderly patients undergoing chronic hemodialysis. As highlighted in previous studies, mortality rate in COVID-19 seems to be higher among elderly patients. However, diabetes and cardiovascular diseases were not identified as predictors of mortality in this sample of patients.
SAFETY OF RAMADAN FASTING IN DIALYSIS PATIENTS: A TUNISIAN PROSPECTIVE MULTICENTER STUDY

Sirine Bchir1, Amel Ayed1, Nouha Ben Mahmoud1, Lazhar Jaballah1, Fadoua Hassine1, Sasssen Chouchen4, Samir Nouira3, Meriem Ben Salem1, Manel Ben Salah1, Hadj Brahim Mayssa2, Ahmed Latief1, Fawzi Hawala1, Mouna Hammouda1, Habib Skhiri1, Zohra Elati2 and Aloui Sabra1

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Background and Aims: Hemodialysis patients are generally exempt from Ramadan Fasting (RF) because they are more vulnerable to the risk of malnutrition as well as fluid and electrolyte imbalance. In addition, many muslim hemodialysis patients feel the spiritual need to fast during Ramadan, even when they are not compelled to do so. Moreover, there are no medical recommendations that specify who should and should not fast. The aim of our study is to explore the experiences of Muslim Hemodialysis patients fasting Ramadan in Hemodialysis centers.

Method: This prospective multicenter study involved patients from eight different hemodialysis centers in Monastir and Mahdia cities. Biochemical, clinical parameters and bioimpedance monitoring were performed before, during and after Ramadan with a group of Fasting Ramadan patients (RFG) and a group of Ramadan non-fasting hemodialysis patients (RNFG). Patients in RFG did so as a personal choice and they wouldn’t skip fasting on dialysis days due to fear of the side effects of fasting. Oral consent was taken from all the patients included in the study.

Results: One hundred and four (104) patients were enrolled in this study. Among them, 44 were in the RFG, and the remaining sixty (60) patients were in the RNFG. The mean age of RFG and RNFG was 47.13 +/− 12 years and 54.7 +/− 15 years, respectively. 32 patients (52.3%) were males in RFG and 38 were males (63.3%) in RNFG.

In RFG, about 6.8% (n = 3) and 43.2% (n = 19) had diabetes and hypertension, respectively. The mean duration on hemodialysis was 7 +/− 6.27 years. There were no significant differences between RFG and RNFG except in diabetic and hypertension status. Comparing biological findings pre, during and post-fasting in RFG, no significant differences were noted in serum sodium (135.9 +/− 4; 135.8 +/− 2.5 and 136.3 +/− 2.4 mmol/l respectively) and there were no drop in serum albumin during fasting (40.4 +/− 3.4; 40.8 +/− 3.7 and 40.6 +/− 4.34 g/l respectively). However, mean serum potassium was higher during RF (5.59 +/− 0.8 ; 5.6 +/− 1 and 5.2 +/− 0.88 mmol/l respectively) and, mean serum Phosphorus was also higher during RF (1.54 +/− 0.57; 1.73 +/− 0.52 and 1.69 +/− 0.7 mmol/l respectively).

Furthermore, with bioimpedance monitoring, comparing pre, during and post Fasting, more fluid retention in patients was observed during fasting (51.67 +/− 7; 54.3 +/− 7, 4 and 53.2 +/− 6 % respectively). But the mean of the inter dialytic weight gain (IDWG) remained the same (2.57 +/− 0.8 ; 2.53 +/− 1.1192 Abstract
0.82 and 2.61 \( \pm \) 0.7 Kg respectively), and none presented with pulmonary oedema or other emergency that might need hospitalization. However, there was positive change to body composition between pre and during fasting, shown as lower body fat mass (FM) percentage during fasting (29.4 and 28.2\%) respectively and also, lower body mass index (BMI) (26.5 and 25.9 respectively).

Nevertheless, when comparing findings between RFG and RNFG, there was no significant difference in any parameters.

Conclusion: The overall conclusions suggest that fasting is relatively well tolerated by hemodialysis patients and does not affect the morbidity and mortality rates. However, careful monitoring of fluid balance, serum electrolytes, and albumin is advisable.

#5153
CHARACTERISTICS AND MORTALITY OF PATIENTS STARTING HAEMODIALYSIS IN A PORTUGUESE TERTIARY HOSPITAL: A DESCRIPTIVE ANALYSIS
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\(^1\)Centro Hospitalar Universitário Lisboa Norte, Nephrology and Renal Transplantation, Lisboa, Portugal and \(^2\)Faculdade de Medicina de Lisboa, Lisboa, Portugal

Background and Aims: Portugal has one of the highest incidences and prevalence of end-stage kidney disease in Europe, with haemodialysis (HD) being the most common modality of renal replacement therapy. The aim of our study was to analyse a cohort of patients who started HD in a large tertiary care hospital in Lisbon and describe the evolution of the patient characteristics throughout the studied years.

Method: This study was a retrospective analysis of all adult individuals who started HD between January of 2014 and December of 2019 in tertiary care hospital in Lisbon. Data was attained from individual electronic clinical records. The primary outcome was mortality. Statistical significance was defined as a P-value lower than 0.05.

Results: We included 1122 patients (mean age 64.9 \( \pm \) 16.8 years, 21.2\% at least 80 years old; 60.9\% male and 79.7\% caucasian). At HD start, mean eGFR was 8.98 \( \pm \)5.66mL/min/1.73 m\(^2\) and the vascular access was a central venous catheter in 56.0\%, an arteriovenous fistula in 40.6\% and an arteriovenous graft in 3.4\%. The number of patients that started HD per year was variable between 169-204 and the percentage of elderly patients increased throughout the years. There was a trend of initiating dialysis with progressively lower eGFR. The percentage of patients with central venous catheter increased. In total 392 patients died (7.5\% within the first 90 days of starting HD). Mortality rate within the first 90 days and first year declined from 2015 to 2019. As expected mortality was higher in older patients (Fig. 1), as well as in patients that started HD with a central venous catheter (Fig. 2).

Conclusion: We describe a large cohort of Portuguese patients that started HD between 2014-2019 that correlates well with the available recent data from the national and european registries. There was a greater percentage of patients initiating HD by catheter, which was associated with higher mortality. Although, considering the increase in elderly patients starting HD, their underlying comorbidities might impair vascular access placement and also have an impact on mortality. Additionally, despite the increase in elderly patients, mortality within the first 90 days and first year declined, highlighting the quality of care provided, in addition to a better acknowledgment and referral to conservative care.

Figure 1: Survival according to age group.
Improvements in Quality of Life (QoL) of Hemodialysis Patients After the Pandemia; It Is Not What It Seems to Be

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Background and Aims: Patients on hemodialysis (HD), are a clinically vulnerable population. We analyzed changes in the results of the KDQOL™-36 questionnaire carried out in 2019 vs 2021, during Covid-19 pandemic. We have related the results to demographic and analytical parameters, BCM, modality and dose of dialysis, in addition to having suffered a COVID-19 infection.

Method: This is a retrospective, observational analysis performed in 47 clinics from Fresenius Medical Care (FMC) Spain. As part of our Healthcare Quality Improvement Program, HRQoL measurements were assessed using the KDQOL™-36 questionnaire. This questionnaire evaluates Physical and Mental Composite Scores (PCS and MCS, respectively) and three disease-specific scales: Effects, Burden and Symptoms dimensions (EKD, BKD, SKD). We focused our analysis in 1000 patients who completed both surveys in 2019 and 2021 in order to analyze differences. We compared results of both surveys by Wilcoxon test. Improvement between 2019 and 2021 was calculated for each QoL Score. We categorized patients based on QoL evolution (improvement vs worsening) and analyzed the relationship between QoL improvement and different variables by univariate and multivariate logistic regression. Non-normal variables were categorized.

Results: The results are presented in detail in the figures section.

Table 1: Comparison of results of different KDQOL-36 scales between 2019 and 2021. Median [Interquartile Range].

<table>
<thead>
<tr>
<th></th>
<th>2019</th>
<th>2021</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS</td>
<td>35.9 (28.5-45.2)</td>
<td>37 (29.8-45.4)</td>
<td>0.12</td>
</tr>
<tr>
<td>MCS</td>
<td>45.3 (36.7-53.5)</td>
<td>47.7 (39-55.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SKD</td>
<td>77.2 (64.6-87.5)</td>
<td>81.2 (70.8-89.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BKD</td>
<td>37.5 (18.7-56.2)</td>
<td>43.7 (25-62.5)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>EKD</td>
<td>60.71 (43.75-75)</td>
<td>71.43 (53.5-84.3)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Conclusion: Except for the PCS, there were an improvement in QoL results in 2021 vs 2019. Women presented a worse evolution in EKD, MCS and SKD scores. In our study, having COVID-19 infection did not seem to be a factor associated with changes in quality-of-life in 2021. Patients on OL-HDF presented an improvement on the SKD scale compared to those treated with conventional therapy. Higher lean tissue index was related with improvement in PCS scale. Age was related with better EKD scale evolution as CCI above 5 was related with MSC Improvement. BKD scale evolution was related with HD vintage.

Table 2: Comparison of results of improvements in different scales of KDQOL 36 between 2019 and 2021 and different factors. CCI: Charlson Comorbidity Index CRP: C Reactive Protein (mg/L), HD vintage: months.

<table>
<thead>
<tr>
<th></th>
<th>19% CI OR</th>
<th>95% CI OR</th>
<th>p</th>
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<tr>
<td>PCS Improvement</td>
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<tr>
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<td>1.01</td>
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<td>0.63</td>
<td>1.34</td>
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<td>0.99</td>
<td>0.69</td>
</tr>
<tr>
<td>(&gt;3-5)</td>
<td>0.86</td>
<td>0.54</td>
<td>1.36</td>
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<tr>
<td>CRP (ref.)</td>
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<td>1.11</td>
<td>0.74</td>
</tr>
<tr>
<td>(&gt;7)</td>
<td>1.18</td>
<td>0.78</td>
<td>1.77</td>
</tr>
<tr>
<td>Lean Tissue Index</td>
<td>1.13</td>
<td>1.06</td>
<td>1.21</td>
</tr>
<tr>
<td>Psychological assistance</td>
<td>0.52</td>
<td>0.37</td>
<td>0.74</td>
</tr>
<tr>
<td>PCS Score</td>
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<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(&lt;31.18)</td>
<td>11.93</td>
<td>7.61</td>
<td>18.68</td>
</tr>
<tr>
<td>(&gt;31.18 - 42.39)</td>
<td>4.47</td>
<td>2.99</td>
<td>6.69</td>
</tr>
<tr>
<td>COVID19</td>
<td>1.07</td>
<td>0.55</td>
<td>2.07</td>
</tr>
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</table>

MSC Improvement |           |           |       |
| Age    | 1.00      | 0.99      | 1.01  | 0.7   |
| Male   | 1.62      | 1.15      | 2.29  | 0.006 |
| CCI (ref.) | 0.1       | 0.82      | 0.57  | 1.17  | 0.2   |
| (>3)   | 0.63      | 0.41      | 0.98  | 0.04  |
| CRP (ref.) | 0.3       | 0.99      | 0.68  | 1.46  | 0.9   |
| (>7)   | 0.79      | 0.54      | 1.16  | 0.2   |
### Table 2: Continued

<table>
<thead>
<tr>
<th>Variable</th>
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<th>Inf</th>
<th>Sup</th>
<th>p</th>
</tr>
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<td>MSC</td>
<td>0.33 (0.21 - 0.49)</td>
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<tr>
<td>HD Vintage</td>
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<td>1.00</td>
<td>1.00</td>
<td>0.8</td>
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<tr>
<td>COVID 19</td>
<td>1.13 (0.61 - 2.10)</td>
<td>0.61</td>
<td>2.10</td>
<td>0.7</td>
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<tr>
<td><strong>SKD</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Improvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
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<td>1.01</td>
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<td>Male</td>
<td>1.44 (1.05 - 1.97)</td>
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<td>1.97</td>
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<td>(3-5)</td>
<td>1.01 (0.73 - 1.40)</td>
<td>0.73</td>
<td>1.40</td>
<td>0.9</td>
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<tr>
<td>(&gt;5)</td>
<td>0.74 (0.50 - 1.11)</td>
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<td>1.11</td>
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<td>HDF-OOL</td>
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<td>Calcium (mg/dL)</td>
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<tr>
<td>(2.1-7)</td>
<td>1.06 (0.74 - 1.50)</td>
<td>0.74</td>
<td>1.50</td>
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</tr>
<tr>
<td>(&gt;7)</td>
<td>1.09 (0.77 - 1.55)</td>
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<td>1.55</td>
<td>0.6</td>
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<td><strong>COVID</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>19</td>
<td>1.30 (0.52 - 2.11)</td>
<td>0.52</td>
<td>2.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>BKD</strong></td>
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<tr>
<td>Improvement</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td>1.00 (0.99 - 1.01)</td>
<td>0.99</td>
<td>1.01</td>
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<tr>
<td>Male</td>
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<td>1.79</td>
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<td>(3-5)</td>
<td>0.88 (0.64 - 1.22)</td>
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<tr>
<td>(&gt;5)</td>
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<td>0.54</td>
<td>1.20</td>
<td>0.2</td>
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<tr>
<td>HD Vintage</td>
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<td>1.00</td>
<td>0.008</td>
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<td>CRP (ref.)</td>
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<tr>
<td>(2.1-7)</td>
<td>0.90 (0.63 - 1.28)</td>
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<td>1.28</td>
<td>0.5</td>
</tr>
<tr>
<td>(&gt;7)</td>
<td>1.02 (0.72 - 1.45)</td>
<td>0.72</td>
<td>1.45</td>
<td>0.8</td>
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<tr>
<td><strong>COVID</strong></td>
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<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>19</td>
<td>1.27 (0.70 - 2.33)</td>
<td>0.70</td>
<td>2.33</td>
<td>0.4</td>
</tr>
</tbody>
</table>

### Background and Aims:
Acute kidney injury (AKI) diagnosis, management, the optimal prescription and delivery of renal replacement therapy (RRT) standards for best practice are lacking. The aim of this study was to explore the clinical approach to AKI and RRT in a broad population of Brazilian nephrologists.

### Method:
A cross-sectional survey was distributed to all nephrologists from multiple centres of a Brazilian private hospital group. The responses of the participants on several aspects of AKI management and renal replacement therapy were analysed and detailed.

### Results:
97 (66%) nephrologists from 8 Brazilian states responded. 45% referred KDIGO 2 as the stage usually present at time of nephrologist consultation, and mean time for nephrology consultation after AKI diagnosis was 24-48h for 51% of answers. 85% reported creatinine as the only biomarker available for diagnosis, and only 24% reported any AKI alert system. Sepsis was reported as the most frequent etiology by 95%; kidney biopsy indication was considered in less than 10% of the evaluations by 94%. Fluid status assessment is described in Figure 1. The most common criteria for starting RRT was fluid overload (30%) followed by urine output reduction (26%), hyperkalemia (14%) and acidosis (17%). 62% of them usually use furosemide stress test before RRT indication. Seventy-seven percent of participants said that never use peritoneal dialysis in AKI patients, although its available for 44% of responders. Hypotension was the most frequent RRT complication for 91% responders, followed by coagulation of the system for 42% and catheter dysfunction for 33%. CRRT was available for 92% of participants and for 88% this is the RRT for patients using vasoactive drugs. 77% usually use regional anticoagulation with citrate. The most common starting dose is 26 to 30ml/Kg/h and the net ultrafiltration rate is 1.01-1.75 ml/Kg/h. There is no weaning protocol of RRT for 81%, but 90% use the urine output as a weaning tool. Thirty- nine percent said that RRT patients’ mortality stayed between 20 to 50%, and 36% had no information about mortality.

### Conclusion:
In our survey, Nephrology consultation occurred after 24h and at KDIGO 2 stage. Early recognition of AKI is impeded by the use of serum creatinine as the only biomarker and the unavailability of AKI alerts. Fluid overload is the main reason for indicating RRT and nephrologists have expanded the use of non-invasive fluid status assessment methods others than physical examination. CRRT is the method of choice for unstable patients in this sample from private medical facilities, where almost all responders have access to CRRT. Effluent doses and net ultrafiltration rate were in accordance with the established in literature. Optimal timing for discontinuing RRT is still defined according to the physician's discretion. Standardization of AKI management and continuing education seem to be a fundamental aspect to anticipate the diagnosis, improve the therapeutic approach and bring better results for AKI patients.
Conclusion: After the massive vaccination, the higher number of patients and without memory bias are needed to prove an incidence of post-COVID-19 syndrome is due to the vaccination. Even so, more studies with a higher number of patients and without memory bias are needed to prove a lower incidence of this syndrome after the massive vaccination. Therefore, the higher number of patients and without memory bias are needed to prove a lower incidence of this syndrome after the massive vaccination.
Abstract

Objective: To study the mortality risk among incident hemodialysis (HD) patients in the presence of intradialytic exercise (IDE).

Method: A single-center, prospective study in adult HD patients eligible for IDE (cycling 3 times a week) was performed. After 1 year of IDE introduction, patients were followed up for up to 3 years. Three groups were created based on the IDE minutes per week: no exercise (patients who refused IDE), low load (≤87 min/week), and high load (>87 min/week). Kaplan-Meier models (unadjusted analysis) and Cox proportional hazard models (adjusted for age, dialysis experience, vascular access, comorbidity index, CVD, muscle tissue, overhydration, and hospitalizations) were used with a non-exercise group as a reference. In addition, a sub-analysis was conducted, limited to IDE participants, with exposure as a continuous variable.

Results: 106 patients (no exercise: 58; low exercise: 26; high exercise: 22) were followed for an average of 24.5 months. Uncorrected mortality differed between the three groups: (no exercise: 24.1%; low load: 23.0%; high load: 9.0%; p < 0.01). In the adjusted analysis, the high load group had a lower risk of mortality than the no exercise group (HR = 0.42, 95% CI 0.23–0.76, p < 0.05), while in the low load group this was not observed (HR = 1.07, 95% CI 0.66–1.52, p = 0.568). In addition, mortality risk decreased for every 55 minutes of exercise per week in unadjusted (HR = 0.46, 95% CI 0.29–0.76, p = 0.01) and adjusted analyzes (HR = 0.54, 95% CI 0.32–0.91, p < 0.05).

Conclusion: Our findings show that IDE is associated with a reduced risk of mortality in HD patients, but a significant amount of exercise is required. Thus,

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**Table 1: Factors associated with mortality among incident HD patients.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
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<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>31–60</td>
<td>1.16 (0.51–2.65)</td>
<td>.720</td>
</tr>
<tr>
<td>&gt;60</td>
<td>2.75 (1.24–6.11)</td>
<td>.013</td>
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<tr>
<td>Male</td>
<td>Reference</td>
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<tr>
<td>Female</td>
<td>0.97 (0.65–1.46)</td>
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<tr>
<td>Etiology of CKD</td>
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<tr>
<td>Diabetes</td>
<td>1.37 (0.91–2.06)</td>
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<tr>
<td>Hypertension</td>
<td>0.77 (0.47–1.27)</td>
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<td>CGN</td>
<td>0.80 (0.49–1.50)</td>
<td>.369</td>
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<td>Mode of dialysis</td>
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<tr>
<td>HDF</td>
<td>0.72 (0.37–1.39)</td>
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<tr>
<td>Frequency of hemodialysis</td>
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<td>CVC</td>
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<td>AVF/AVG</td>
<td>0.77 (0.51–1.16)</td>
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<tr>
<td>Negative</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Hepa B+</td>
<td>0.29 (0.04–2.05)</td>
<td>.213</td>
</tr>
<tr>
<td>Hepa C+</td>
<td>3.92 (1.23–12.49)</td>
<td>.021</td>
</tr>
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<td>Laboratory parameters</td>
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<td>Hemoglobin (mg/dl)</td>
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<tr>
<td>11–12</td>
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<td></td>
</tr>
<tr>
<td>&lt;11</td>
<td>1.61 (0.83–3.11)</td>
<td>.159</td>
</tr>
<tr>
<td>&gt;12</td>
<td>1.12 (0.44–2.83)</td>
<td>.817</td>
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<tr>
<td>Leukocyte count</td>
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<tr>
<td>&lt;5.8</td>
<td>1.23 (0.67–2.29)</td>
<td>.504</td>
</tr>
<tr>
<td>&gt;7.7</td>
<td>1.31 (0.81–2.12)</td>
<td>.264</td>
</tr>
<tr>
<td>Phosphorus</td>
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<td>3.5–5.5</td>
<td>Reference</td>
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<tr>
<td>&lt;3.5</td>
<td>1.86 (1.13–3.07)</td>
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<tr>
<td>&gt;5.5</td>
<td>0.81 (0.48–1.35)</td>
<td>.419</td>
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<tr>
<td>Calcium (g/dl)</td>
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<td>Reference</td>
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<tr>
<td>&lt;8.4</td>
<td>1.34 (0.87–2.06)</td>
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</tr>
<tr>
<td>&gt;9.5</td>
<td>1.01 (0.45–2.24)</td>
<td>.984</td>
</tr>
</tbody>
</table>

---

**Figure 1:** Graph of overall survival probabilities over time. Shaded areas represent the 95% confidence interval for survival estimates.
patients who achieve low load doses may require non-clinical approaches to PA in addition to IDE. These findings complement those of earlier studies and highlight the need for a tailored approach to the exercise.

#6715
COGNITIVE IMPAIRMENT IS ASSOCIATED WITH INCREASED MORTALITY IN HEMODIALYSIS PATIENTS
Evgeniy Shcherbakov¹ and Mikhail Pyatchenkov²
¹Military-medical Academy, Department of Nephrology and Blood Purification, Saint Petersburg, Russia and ²Military-medical Academy, Department of Nephrology and Blood Purification, Saint Petersburg, Russia

Background and Aims: Patients on dialysis are at substantially higher risk for developing cognitive impairment compared with the general population. At the same time cognitive impairment is a strong and independent risk factor for all-cause mortality. Given that the approaches used to access the prevalence of cognitive dysfunction widely vary in different patient populations, their true burden in hemodialysis patients remains poorly understood. The aim of our study was to determine the association between cognitive impairment and overall survival and mortality in patients undergoing hemodialysis treatment.

Method: A total of 69 chronic hemodialysis patients (47 men and 22 women) were included. The median age of patients was 61 [47-69] years. The median duration of hemodialysis treatment was 32 [21-72] months. The study of cognitive status was conducted using the Montreal Cognitive Assessment (MoCA) questionnaire. The test results are between 0 and 30 points. A score of 26 points or more is considered the norm, less than 26 indicates the presence of cognitive impairment. The end point was a fatal outcome from acute pathology or progression of a chronic disease. The analysis of survival and mortality was evaluated using survival tables, the construction of Kaplan-Mayer curves with the Mantel-Cox log-rank criterion. The risks of the influence of cognitive impairment on mortality were assessed using Cox regression.

Results: During the 24-month follow-up period, 23 patients died. Structure of mortality over the observation period: acute coronary syndrome – 6 (26 %), COVID-19 – 6 (26 %), acute cerebrovascular accident – 2 (9%), thromboembolic complications – 3 (13%), another causes – 6 (26 %). In patients with cognitive impairment on hemodialysis, the average survival value was 16.33 months ± 1.70 months [CI 95% 12.99-19.66] and 20.48 months±1.32 months [CI 95% 17.88-23.07] in patients without cognitive impairment. In patients with cognitive impairment the average survival value was 16.33 months ± 1.70 months [CI 95% 12.99-19.66] and 20.48 months±1.32 months [CI 95% 17.88-23.07] in patients without cognitive impairment. According to the Mantel-Cox log-rank criterion, there was a statistically significant decrease in overall survival in patients with cognitive impairment, \( P = .02 \). The mortality rate of dialysis patients with cognitive impairment was 51%, without cognitive impairment – 19%. Relative risk of death in the group of patients with cognitive impairment using Cox regression: Hazard ratio (HR) = 2.90 [95% CI 1.11-7.37, \( P = .03 \)].

Conclusion: Our results support the notion that cognitive impairment may be an independent predictor of all-cause mortality in hemodialysis patients. There are limitations on the sample size of patients in our study. Further larger-scale observations a large cohort of patients are required.

Figure 1: Kaplan-Mayer curves characterizing overall survival depending on the presence or absence of cognitive disorders.
#6140

DEPENDENCE IN THE ELDERLY PATIENT ON HEMODIALYSIS

Monica Pereira¹, Paula Manso¹, Marina Burgos¹, Damian Carneiro¹, Sebastián Mas¹, Emilio Gonzalez-Parra³, Maria Dolores Arenas¹ and Maria Luz Sánchez-Tocino¹

¹Fundación Renal, Madrid, Spain, ²CIBERDEM / IIS-FJD, Madrid, Spain and ³Instituto de Investigación Sanitaria Fundación Jimenez Diaz, Madrid, Spain

Background and Aims: Frailty constitutes a syndrome, characterized by loss of lean body mass (sarcopenia), weakness, and decreased resistance to physical exercise, which leads to decreased activity and a poor response to stress. Reduced activity, in turn, worsens sarcopenia and weakness, leading to a vicious cycle toward functional decline and increased risk of death. Frail patients starting HD may lose independence, as their functional capacity deteriorates, with increased frailty and sarcopenia, especially in the elderly.

Aims: Observe the clinical differences in elderly patients on hemodialysis depending on whether they are dependent or not and observe if dependence has an impact on the dialysis regimen used.

Method: Observational descriptive study for 1 year in patients of the chronic hemodialysis program of four out-of-hospital centers and a hospital unit of the Fundación Renal Íñigo Álvarez de Toledo (Spain). Of the total number of patients receiving dialysis in the units, 107 over 75 years of age, who had been in the program for more than 3 months and who had signed the informed consent, were included in the study.

The variables considered for the study were: age, sex, height, weight, and body mass index (BMI), etiology of kidney disease, time on hemodialysis, residual diuresis > 500 mL/min, and type of vascular access. In relation to the hemodialysis regimen, the duration variables were collected in hours of the HD session at the beginning of the program and at the time of the study, weekly hours and days per week

Analytically determined: albumin, total iron binding capacity (TIBC) and creatinine. In addition, the measure of dialysis efficacy was established by eKt/V

Results: Association between dependency and the rest of the qualitative variables. Data expressed n(%) or mean ± SD.

Conclusion: Dependent patients have lower residual renal function, greater comorbidity, less ability to walk, and therefore need transportation to go to dialysis, live in residences, and are extremely tired at the end of dialysis.

<table>
<thead>
<tr>
<th>Independent (normal), n=85 (79%)</th>
<th>Dependent (Altered), n=22 (21%)</th>
<th>P</th>
</tr>
</thead>
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<td><strong>Sex</strong></td>
<td><strong>Dialysis hours per week</strong></td>
<td><strong>Residual Diuresis</strong></td>
</tr>
<tr>
<td>Men, n=61</td>
<td>Less than 12 hours, n=49</td>
<td>YES, n=68</td>
</tr>
<tr>
<td>Women, n=46</td>
<td>More than de 12 hours, n=58</td>
<td>NO, n=39</td>
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<td><strong>Vascular Access</strong></td>
<td><strong>Arteriovenous fistula, n=57</strong></td>
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<td>YES, n=68</td>
<td><strong>Permanent Catheter, n=50</strong></td>
<td>45/85 (53%)</td>
</tr>
<tr>
<td>NO, n=39</td>
<td><strong>Malnutrition-inflammation score (MIS)</strong></td>
<td>45/85 (53%)</td>
</tr>
<tr>
<td><strong>Malnutrition-inflammation score (MIS)</strong></td>
<td><strong>Assessment scales</strong></td>
<td><strong>Fried Frailty Index</strong></td>
</tr>
<tr>
<td>Low comorbidity, n=44</td>
<td><strong>No Frailty, n=58</strong></td>
<td>41/85 (48%)</td>
</tr>
<tr>
<td>High comorbidity, n=63</td>
<td><strong>Frailty, n=49</strong></td>
<td>44/85 (52%)</td>
</tr>
<tr>
<td><strong>Fried Frailty Index</strong></td>
<td><strong>Charlson Comorbidity Index</strong></td>
<td><strong>Normal Nourished, n=48</strong></td>
</tr>
<tr>
<td>Normal Nourished, n=48</td>
<td>Low comorbidity, n=44</td>
<td>47/85 (55%)</td>
</tr>
<tr>
<td>Undernourished, n=59</td>
<td>High comorbidity, n=63</td>
<td>38/85 (45%)</td>
</tr>
<tr>
<td>Fried Frailty Index</td>
<td><strong>Ability to walk</strong></td>
<td><strong>NO, n=98</strong></td>
</tr>
<tr>
<td>No Frailty, n=58</td>
<td>55/85 (65%)</td>
<td>47/85 (55%)</td>
</tr>
<tr>
<td>Frailty, n=49</td>
<td><strong>NO, n=20</strong></td>
<td>30/85 (35%)</td>
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<td><strong>Transport to HD</strong></td>
<td><strong>Institutionalized</strong></td>
<td><strong>Ambulance sitting, n=82</strong></td>
</tr>
<tr>
<td>Ambulance lying down, n=3</td>
<td>Yes, n=9</td>
<td>0/85 (0%)</td>
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<tr>
<td>Ambulance sitting, n=82</td>
<td>NO, n=20</td>
<td>65/85 (77%)</td>
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<tr>
<td>Own media, n=22</td>
<td><strong>Ambulance lying down, n=3</strong></td>
<td>20/85 (23%)</td>
</tr>
<tr>
<td><strong>Extreme fatigue after treatment</strong></td>
<td><strong>Ambulance sitting, n=82</strong></td>
<td>43/85 (51%)</td>
</tr>
<tr>
<td>YES, n=60</td>
<td><strong>Own media, n=22</strong></td>
<td>42/85 (49%)</td>
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<tr>
<td>NO, n=47</td>
<td><strong>Extreme fatigue after treatment</strong></td>
<td>17/22 (77%)</td>
</tr>
</tbody>
</table>
Implementation of alternative therapy practices does not influence dietary compliance in chronic kidney disease: a cross-sectional study

Dimitra Prokopiou, Themistoklis Defteros, Pinelopi Papadopoulou, Christina Pouliantii, Theodoros Eleftheriadis, Ioannis Stefanidis

University of Thessaly, Nephrology, Larissa, Greece

Background and Aims: Implementation of alternative therapies is a common practice in patients with chronic disease. Frequency in different countries is varying, highly dependent on local cultural habits. Furthermore, alternative therapy, especially if taken seriously, might be associated with reduced compliance to conventional interventions. Chronic kidney disease (CKD) is a progressive chronic illness with a really high mortality, which ends up with renal replacement treatment. In CKD certain dietary restrictions are central part of conventional treatment. The scope of the presented study was to determine prevalence of self implementation of alternative therapies and its relationship with compliance to dietary restrictions in CKD patients in Greece. Respectively epidemiological data are still totally missing.

Method: Consecutive patients of the Outpatient Nephrology Wards and all patients of the Peritoneal Dialysis (PD) and Haemodialysis (HD) Units of the University Hospital of Larissa, the General Hospital of Veria and the University Hospital Attikon in Athens (Greece) were studied after informed consent from June to December 2019. The international Complementary and Alternative Medicine questionnaire (I-CAM-Q), was applied. The questionnaire registers all visits to complementary or alternative health-care providers, the respective treatments, the use of herbs, of dietary supplements, and self-help practices. Patients’ 24h recollection data were used to calculate dietary intake of protein, sodium, potassium and phosphorus. Albumin, phosphate, sodium, potassium, creatinine and urea were determined with routine methods in the central Laboratory of the University Hospital of Larissa.

Results: Overall 261 patients (165 males, aged 66.1 ± 13 years) with CKD were included. Among them 102 were on chronic haemodialysis and 59 on peritoneal dialysis treatment. The prevalence of alternative treatment practices was overall 45%, significantly higher in female patients (OR 1.494, ci 1.085-2.057, $P = 0.015$). The frequency in PD patients and in CKD patients was significantly higher than in HD patients (PD 69.5%, CKD 55% and HD 21.6%; $P < 0.01$). There was no significant variation due to profession or education. The prayers and confession (31.1%) as well as the use of herbs (25.3%) were the most frequent alternative practices applied. In HD prayers (prevalence 8.9%) and the use of herbs (8.9%) are less frequently practiced than in the other groups. The dietary compliance was for phosphorus about 24% and when all relevant diet parameters were considered 18%. Compliance to dietary restrictions was better in females ($P = .024$) but was independent of the patient’s profession ($P = .42$) and educational status ($P = .89$). No significant influence of the alternative treatment practices application was determined on the compliance to diet of either CKD, PD or HD patients.

Conclusion: The autonomous implementation of alternative medical and other treatment and self-help practices is common among patients with CKD with a predominance of females. In Greece the most commonly applied practices are herbs and prayers or the confession. There is overall a lower prevalence of alternative practices in HD patients than CKD and PD patients. The initial hypothesis, namely that alternative therapy implementation might combine with reduced compliance of patients to conventional interventions was not confirmed at least as far as the dietary restrictions prescribed for CKD patients are concerned. The role alternative treatment practices in CKD and its relationship to the patients’ physical and mental health deserves further investigation.

Epidemiological and clinical characteristics of migrants on chronic hemodialysis treatment

Gaetano Alfano, Francesco Fontana, Riccardo Magistroni, Gabriele Donati

Modena, Italy

Background and Aims: The rate of migrants with end-stage kidney disease is rising in Italy. Migrants often present to nephrologists with advanced kidney disease, a condition that limits the choice to perform a diagnosis and prevent the progression of the disease. Low literacy, language barriers, lack of medical insurance, illiteracy and cultural diversity are the main factors limiting the referral to physicians. Data about the prevalence and clinical characteristics of migrants in dialysis units are scarce in the literature. Our study aimed to evaluate and characterize the epidemiological profile of migrants on chronic hemodialysis (HD) treatment. Data about demographics, clinical characteristics health-related quality of life (HRQoL) were compared with the Italian population.

Method: A retrospective cross-sectional observational study was conducted on patients who underwent HD at the University Hospital of Modena from December 2021 to August 2022. All patients on chronic HD treatment aged > 18 years were enrolled in the study. Data were collected from electronic health databases and interviews with a selected number of patients. HRQoL was evaluated by “EQ-5D” questionnaire. Overall, it ranged between a score from level 5 (no problem) to 25 (extreme problems). A scale (EQ VAS), numbered from 0 (worst imaginable health) to 100 (best imaginable health) was used to assess global assessment of own health. Patients have been subdivided based on their origin into ‘migrants’ and ‘non-migrants’ (or Italians). According to the International Organization for Migrations (IOM), we considered migrants all patients that were born in a foreign country and came to Italy for work, family reunification, economic or political reasons.

Results: In our hemodialysis center, 302 patients underwent hemodialysis for kidney failure. Migrants accounted for 18.2% (n. 55) of the HD population. They moved to Italy from Africa (62%), Europe (20%), Asia (16%) and Latin America (2%) for seeking work (84.3%) and family reconciliation (15.7%). A consistent percentage of migrants (37.5%) crossed the national border as undocumented migrants. Migrants started hemodialysis at a younger age than non-migrants (48.1 [IQR, 39.7-56.7] vs 70.7 [IQR, 70.7-78.5]) years ($P = .001$) (Fig. 1). Most of them were male (69%). Migrant starter HD after 12.3 (IQR 6.5-20) years from their arrival in Italy. The age of migrants varied according to the geographic area: Subsaharian Africa (44.7 years), Asia (46 years), Europe (53.9 years) and northern Africa (54.5 years), although there was no statistically significant difference between groups ($P = .67$). The etiology of kidney disease was unknown in 40% of patients. Most of the patients (54.5%) started HD with a central vein catheter (CVC) and 33% of them were not referred to a nephrologist before HD. After a follow-up of 1.8 years, the rate of CVC decreased to 26.3%. Only 14.5% of the interviewed patients declared to be informed about home dialysis. Although, 87.2% of the patients were potentially eligible for kidney transplantation (age criteria) only a few of them (18.7%) was active on the waiting list.

Migrants have a better perception of health-related quality of life than non-migrants. In the migrants and non-migrant groups, median “EQ-5D” score was 5 (IQR, 5-6) and 7 (IQR, 5-10), respectively ($p = <.0001$). Global health assessment in migrants and non-migrant accounted for 90 (IQR, 80-91.5) and 80 (IQR, 70-90), respectively ($P = .028$). It is worth noting that these differences became not statistically significant when EQ-5D ($P = .45$) score and EQ VAS scale ($P = .52$) were adjusted for the age of participants.

Conclusion: Migrants were a consistent percentage of patients in our Dialysis Unit. This group of patients was formed by young people often unaware of their kidney disease. Late referral to the nephrologist had a profound implication on vascular access for HD. The language barrier and cultural diversity were the major limitations to entry into the kidney transplant waiting list.
COMPARISON OF TRACE ELEMENT CONCENTRATIONS IN PREDIALYSIS, HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS

Suleyman Koz¹, Esin Oğuz² and Cagla Sayın³

¹Sivas Cumhuriyet University Faculty of Medicine, Nephrology, Turkey, ²Sivas Cumhuriyet University Faculty of Medicine, Internal Medicine, Sivas, Turkey and ³Sivas Cumhuriyet University Faculty of Medicine, Internal Medicine, Turkey

Background and Aims: Regulation of many trace elements (TE) is critically dependent on kidney functions. Dialysis modality, duration of dialysis, equipment, purity of water and nutrition also impacts TE balance. There are inadequate data on comparison of TE in patients with different stages of kidney disease.

We aimed to compare TE levels in a restricted geographical area across a wide range of glomerular filtration rate (GFR) including end stage kidney disease. We assumed that this kind of design might be beneficial for understanding TE balance and impact of dialysis.

Method: Hemodialysis (HD), peritoneal dialysis (PD) and chronic kidney disease (CKD) patients with reduced GFR were included in this cross-sectional study. A sample of plasma was analyzed by inductively coupled plasma mass spectrometry (ICP-MS) (Thermo Scientific™ iCAP Q ICP-MS, USA). Sensitivity was on the order of ppb (μg/L). A control group (CG) with glomerular filtration rate ≥ 90 ml/min were used for comparison of plasma levels of TE.

Results: Results of TE are presented in the Table 1. Significant number of both patients and controls lack a valid TE measurement because of the concentrations below limit of the detection (LoD). Copper, in CKD patients, is negatively correlated with hospitalization within the last six months (r = -0.315, p= 0.005).

Conclusion: Our data suggest that TE levels except Zn and Mn deviate from that of CG in a statistically significant manner in renal patients. Existing data on TE in renal patients are inconsistent and there is some confusion. Similarly, our results are consistent with some data and conflicting with others. In future studies, this confusion could be eliminated by evaluating each trace element separately and minimizing methodological problems.

(This study is realized with support of Cumhuriyet University CUBAP)
Background & aims: The study recruited 202 eligible ESRD patients undergoing haemodialysis. Baseline characteristics of the study participants with and without Sudden Cardiac Arrest (SCA) were recorded using self-reported questionnaires. SCA and SCD events were identified by reviewing medical records and death certificates. Results: Out of 202 patients, 37 (18.3%) suffered from the episode of SCA, 18 (48.6%) of which succumbed to death. ESRD patients who endured SCA were statistically older in comparison with their non-SCA counterparts (58.2 ± 11.4 vs. 52.3 ± 9.3 years, P < 0.001). The HTN (67.6% versus 64.8%, P = 0.01), DM (62.2% versus 59.4%, P = 0.004), CAD (45.9% versus 41.8%, P = 0.001) and Congestive Heart Failure (CHF) (35.1% versus 34.5%, P = 0.002) were significantly prevalent in ESRD cohort with SCA in contrast to non-SCA. We also found LVH (62.2% versus 48.5%, P < 0.001), ventricular tachycardia (51.4% versus 30.9%, P < 0.001) and ventricular fibrillation/flutter (56.8% versus 25.5%, P < 0.001) to be statistically higher in ESRD patients on haemodialysis with SCA event. Through multivariate logistic regression analysis, we evidenced hypokalemia (OR 1.565, CI 1.469–2.342, P < 0.001); LVH (OR 1.861, CI 1.392–1.953, P < 0.001); CAD (OR 1.253, CI 1.012 – 1.386, P < 0.001); and ventricular fibrillation/flutter (OR = 0.547, CI 0.518 – 0.773, P < 0.001) to be significantly and independently associated with SCD in ESRD patients on haemodialysis.

Conclusion: The prevalence of SCD among ESRD patients on haemodialysis with SCA episode is very high. CAD and ventricular tachyarrhythmias were statistically significant among ESRD patients on haemodialysis with SCA in comparison with non-SCA and were independently associated with the prevalence of in-patient SCD among ESRD patients on haemodialysis.

D4 - CO-MORBIDITIES (ANAEMIA, CARDIOVASCULAR, CKD-MBD, PROTEIN WASTING, ETC.)

INCIDENCE AND RISK FACTORS OF SUDDEN CARDIAC DEATH IN END STAGE RENAL DISEASE PATIENTS UNDERGOING HAEMODIALYSIS: A RETROSPECTIVE STUDY
Muhammad Tassaduq Khan
Dow University Hospital, Renal Transplant Unit, Karachi, Pakistan

Background & aims: End Stage Renal Disease (ESRD) patients undergoing haemodialysis are prone to suffer from Sudden Cardiac Death (SCD). The present study was sought to evaluate the incidence and risk factors of SCD in ESRD patients on haemodialysis in Pakistani population.

Methods: The study recruited 202 eligible ESRD patients undergoing haemodialysis. Baseline characteristics of the study participants with and without Sudden Cardiac Arrest (SCA) were recorded using self-reported questionnaires. SCA and SCD events were identified by reviewing medical records and death certificates.

Results: Out of 202 patients, 37 (18.3%) suffered from the episode of SCA, 18 (48.6%) of which succumbed to death. ESRD patients who endured SCA were statistically older in comparison with their non-SCA counterparts (58.2 ± 11.4 vs. 52.3 ± 9.3 years, P < 0.001). The HTN (67.6% versus 64.8%, P = 0.001), DM (62.2% versus 59.4%, P = 0.004), CAD (45.9% versus 41.8%, P = 0.001) and Congestive Heart Failure (CHF) (35.1% versus 34.5%, P = 0.002) were significantly prevalent in ESRD cohort with SCA in contrast to non-SCA. We also found LVH (62.2% versus 48.5%, P < 0.001), ventricular tachycardia (51.4% versus 30.9%, P < 0.001) and ventricular fibrillation/flutter (56.8% versus 25.5%, P < 0.001) to be statistically higher in ESRD patients on haemodialysis with SCA event. Through multivariate logistic regression analysis, we evidenced hypokalemia (OR = 1.565, CI 1.469 – 2.342, P < 0.001); LVH (OR 1.861, CI 1.392 – 1.953, P < 0.001); CAD (OR 1.253, CI 1.012 – 1.386, P < 0.001); and ventricular fibrillation/flutter (OR = 0.547, CI 0.518 – 0.773, P < 0.001) to be significantly and independently associated with SCD in ESRD patients on haemodialysis.

Conclusion: The prevalence of SCD among ESRD patients on haemodialysis with SCA episode is very high. CAD and ventricular tachyarrhythmias were statistically significant among ESRD patients on haemodialysis with SCA in comparison with non-SCA and were independently associated with the prevalence of in-patient SCD among ESRD patients on haemodialysis.

TREATMENT OUTCOMES FOR IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS IN DIALYSIS PATIENTS
Seonju Kim 1, Dong Kyu Lee 1, Hae-Rim Kim 1, Jung Mee Park 1 and Hoon Yu 1
1ASAN Medical Center, Division of Nephrology, Department of Internal Medicine, University of Ulsan, College of Medicine, Seoul, Rep. of South Korea, 2ASAN Medical Center, Department of Otorhinolaryngology Head & Neck Surgery, University of Ulsan, College of Medicine, Seoul, Rep. of South Korea, 3University of Seoul, College of Natural Science, School of Statistics, Seoul, Rep. of South Korea, 4Gangneung Asan Hospital, Department of Otolaryngology, University of Ulsan, College of Medicine, Gangneung, Rep. of South Korea and 5Gangneung Asan Hospital, Division of Nephrology.
**Table 1: Characteristics of dialysis and non-dialysis pts with ISSNHL before and after PSM.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Before PSM</th>
<th>After PSM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-dialysis group (n = 653)</td>
<td>Dialysis group (n = 47)</td>
<td>Dialysis group (n = 47)</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>Female</td>
<td>329 (50.4)</td>
<td>21 (44.7)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>324 (49.6)</td>
<td>26 (55.3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td>58.41 ± 12.67</td>
<td>53.57 ± 10.77</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>24.45 ± 3.86</td>
<td>23.41 ± 4.03</td>
</tr>
<tr>
<td>Treatment delay (days)</td>
<td></td>
<td>3.36 ± 3.07</td>
<td>3.23 ± 3.32</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td></td>
<td>159 (24.3)</td>
<td>28 (59.6)</td>
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<tr>
<td>Hypertension (%)</td>
<td></td>
<td>229 (35.1)</td>
<td>39 (83.0)</td>
</tr>
<tr>
<td>Treatment strategy (%)</td>
<td>systemic steroid only</td>
<td>33.66 57.77</td>
<td>0.025</td>
</tr>
<tr>
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<td>combined systemic and IT steroid</td>
<td>29.77 53.21</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>IT steroid only</td>
<td>35.44 57.05</td>
<td>0.04</td>
</tr>
<tr>
<td>Initial PTA at 500 Hz (dB)</td>
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<td>64.72 ± 29.07</td>
<td>81.70 ± 27.51</td>
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<td>67.30 ± 29.97</td>
<td>83.40 ± 29.71</td>
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<td></td>
<td>65.20 ± 30.62</td>
<td>83.40 ± 25.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68.51 ± 30.26</td>
<td>89.47 ± 21.22</td>
</tr>
<tr>
<td>PTA average (threshold, dB)</td>
<td></td>
<td>56.93 ± 33.66</td>
<td>68.96 ± 29.77</td>
</tr>
</tbody>
</table>

**Table 2: Hearing improvement according to the Siegel's criteria at 2 weeks and 2 months after treatment.**

<table>
<thead>
<tr>
<th>Two-week follow-up</th>
<th>Two-month follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-dialysis group (n = 235)</td>
</tr>
<tr>
<td></td>
<td>Non-dialysis group (n = 235)</td>
</tr>
<tr>
<td>Complete response (%)</td>
<td>52 (22.1)</td>
</tr>
<tr>
<td>Partial response (%)</td>
<td>33 (14.0)</td>
</tr>
<tr>
<td>Slight response (%)</td>
<td>34 (14.5)</td>
</tr>
<tr>
<td>No improvement (%)</td>
<td>116 (49.4)</td>
</tr>
<tr>
<td>Complete/partial response (%)</td>
<td>85 (36.2)</td>
</tr>
<tr>
<td>Complete/partial/slight response (%)</td>
<td>119 (50.6)</td>
</tr>
<tr>
<td>PTA average (threshold, dB)</td>
<td>56.93 ± 33.66</td>
</tr>
</tbody>
</table>

#4637

**IS THE NEUTROPHIL/LYMPHOCYTE RATIO USEFUL IN PREDICTING THE OCCURRENCE OF DEPRESSION IN CHRONIC HEMODIALYSIS PATIENTS?**

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\(^1\)University Hospital Mohammed VI, Marrakech, Morocco, Nephrology Department, Marrakech, Morocco and \(^2\)University Hospital Mohammed VI, Marrakech, Morocco, Nephrology Department, Morocco

**Background and Aims:** Depression is one of the most described psychiatric disorders in chronic hemodialysis patients. Previous studies have shown that the chronic inflammatory state is involved in the progression of depressive symptoms. The neutrophil/lymphocyte ratio (NLR) is an inexpensive and easily measured inflammatory marker. To date, the association between NLR and depression in this population in Morocco has never been described.

**Method:** In this multicenter cross-sectional study, we included a population of chronic hemodialysis patients over a period of 3 months (September-December 2023). The Patient Health Questionnaire-9 (PHQ-9) translated into Arabic (validated version) was used to assess depressive symptoms. NLR was calculated as the ratio of neutrophils to lymphocytes. An N/L ratio greater than 2.5 was considered high. We also used the patients' medical records to collect data on their biological tests and medical history.

**Results:** A total of 69 patients with a M/F sex ratio 1.2. The mean duration of HD was 7 ± 3.5 years, with a mean age of 53 ± 13.2 years. 28% were diabetic and 32% hypertensive. Depressive symptoms were detected in 20% of the 69 patients, and 72% of our patients had an NLR >2.5. In univariate analysis, PHQ-9 scores were positively correlated with NLR and negatively correlated with albumin. There was no correlation between PHQ-9 score and sex, age, duration of dialysis, diabetes, hypertension, ferritin. NLR was a significant predictor of mild (p = 0.06) and moderate or moderately severe (p = 0.04)
#5586

Efficacy of Ablation of Parathyroid Autografts for Recurrent Hyperparathyroidism After Total Parathyroidectomy and Deltoid Auto Transplantation

Julia G Andres, Guanqi Hang, Sum Leong, Chow Wei Too, Jiunn Wong

**Background and Aims:** TPDI is the treatment of choice for patients with severe hyperparathyroidism who have failed medical therapy in our centre. The auto-transplantation of parathyroid tissue in the deltoid reduces the risk of permanent hypoparathyroidism. However, there is a risk of recurrent hyperparathyroidism from the implanted parathyroid tissue. Traditionally, these autografts are removed surgically in the event of recurrent hyperparathyroidism exposing the patients to the risk of permanent hypoparathyroidism. We attempted radiologically guided ablation of the implanted tissue to allow near but not complete ablation of the tissue. We aim to report our experience in using this technique to treat patients with recurrent hyperparathyroidism following TPDI.

**Method:** This is a single centre retrospective study of 9 patients who are on regular dialysis and underwent ablation of their deltoid parathyroid implants at Singapore General Hospital between May 2020 to July 2022. Baseline demographic data, as well as biochemical results including intact parathyroid hormone (iPTH), serum calcium, phosphorus and alkaline phosphatase (ALP) levels were retrieved from electronic medical records and analysed. We define success of the procedure as achieving 2 out of the following 3 criteria: 1. >50% drop in iPTH level at 3 months, ii. correction of hypercalcemia at 3 months, iii. off calcimimetic at 3 months

**Results:** A total of 9 patients underwent ablation of their parathyroid deltoid implants, of which 8 (89%) had thermal ablation and 1 (11%) had cryoablation. 1 patient required a repeat procedure within 3 months as only 50% of the implanted tissue was targeted instead of the intended 80% and another patient had a repeat procedure >3 month after initial unsuccessful procedure. The median age of patients undergoing this procedure was 60 years (IQR 60, 66) and majority were female (5/9, 55.5%). 8 out of 9 patients were on haemodialysis. 7 out of 9 patients (78%) had a successful procedure based on our definition. 6 patients (67%) had a >50% reduction of iPTH at 3 month, 6 patients (67%) were off calcimimetic at 3 months and out of the 5 patients who were hypercalcaemic pre procedure, 4(80%) patients had normalisation of hypercalcemia at 3 months. 3 patients (33%) had iPTH < 2x upper limit of normal with only 1 out of the 3 patient requiring high dose oral calcium replacement at 3 months.

Pre ablation levels of PTH decreased from 191.87 ± 93.52 pmol/L to 98.77 ± 111.007 pmol/L (P = 0.773) 1 day after ablation and 92.450 ± 70.235 pmol/L (P = 0.0450) at 1 month and 91.25 ± 81.25 (P = 0.024) pmol/L at 3 months. Serum calcium levels decreased from 2.48 mmol/L ± 0.286 pre ablation to 2.11 mmol/L ± 0.322 1 day post ablation (P = 0.007) and remained 2.28 mmol/L ± 0.403 (P = 0.122) at 3 months post ablation. Serum ALP levels decreased from 478 ± 292.00 pre ablation to 238 ± 157 at 3 months post ablation.

There were no re-admissions and no immediate post procedure complications in all patients. 4 out of 9 patients (44%) required intravenous calcium replacement post- procedure during the same admission.

Limitations of this study are the relatively short follow-up duration and the small number of patients. 2 out of the 9 patients were lost to follow up at 3 months.

**Conclusion:** Ablation of deltoid parathyroid autografts may be a safe and effective minimally invasive procedure to manage recurrent hyperparathyroidism and minimising the risk of permanent hypoparathyroidism. However, further studies with larger sample sizes and longer follow up duration would be prudent to confirm our findings

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#6113

Scratching the Surface? A Longitudinal Observational Study on Pruritus and its Current Treatment in Incident Dialysis Patients

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1Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Nephrology, Amsterdam, The Netherlands, 2North West Clinic, Department of Internal Medicine, Alkmaar, Netherlands, 3University Medical Center Utrecht, Department of Nephrology and Hypertension, Utrecht, Netherlands, 4University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands, 5Amsterdam UMC location AMC, Department of Dermatology, Amsterdam, Netherlands, 6Diapriva Dialysis Center, Amsterdam, Netherlands and 7Amsterdam Cardiovascular Sciences, Diabetes and Metabolism, Amsterdam, Netherlands

**Background and Aims:** Chronic kidney disease-associated pruritus (CKD-p) is a common condition in dialysis patients. It is associated with impaired health-related quality of life (HRQoL) and sleep disturbances. The pathophysiology remains unclear resulting in limited treatment options and lack of treatment guidelines. The exact course of CKD-p after dialysis initiation has not been identified nor the state of current medical treatment. Therefore, the aim of this study was to assess presence and severity of CKD-p during the first year of dialysis, and to assess how it is currently medically managed.

**Method:** Data were used from the ongoing multicentre, prospective, observational Dutch nOcturnal and hoME dialysis Study To Improve Clinical Outcomes (DOMESTICO). This study longitudinally compares HRQoL between different dialysis modalities. Incident dialysis patients (> 18 years) were included, if they completed a HRQoL questionnaire around initiation. Pruritus was assessed using the Dialysis Symptom Index (DSI), using a point Likert scale. Medication data were retrieved from electronic patient files. Outcome parameters were prevalence, severity of pruritus and the use of antipruritic medication, both systemic and topical, all measured at dialysis initiation and after 3.6 and 12 months. The association between pruritus and treatment was studied using logistic regression analysis and adjusted for potential confounders.

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#5759

Association Between Physical Activity Level Questionnaires and Daily Step Counts in Patients on Hemodialysis

Maycon Moura Reboredo1, Bárbara Alvarenga1, Luciana de Jesus1, Gabriela Paticcio1, Carlos Miguel Da Silva1, Amanda Amorim1, Camila de Souza1, Eva Segura-Ortí2, Bruno Pinheiro1, Leda Lucinda1,2

1Federal University of Juiz de Fora, Juiz de Fora, Brazil, 2Universidade Cardenal Herrera-CEU, Valencia, Spain and 3Barbacena School of Medicine, Barbacena, Brazil

**Background and Aims:** In patients on hemodialysis, sedentary lifestyle is high and prevalent and associated with a worse health-related quality of life (HRQoL) and disturbed sleep. The physical activity level of these patients can be confirmed by assessing the physical activity level (PAL) evaluated by accelerometers and questionnaires. Considering that the PAL questionnaires are quick to perform and inexpensive, the aim of this study was to evaluate the association of three PAL questionnaires with daily step counts measured by an accelerometer in patients on hemodialysis.

**Method:** A cross-sectional study was conducted with patients aged ≥18 years on regular dialysis treatment for at least three months. Patients were excluded if presented severe and unstable comorbidities, psychiatric or cognitive disorders, and hospitalization in the past three months. The daily step counts were recorded in the ActiGraph accelerometer (wGT3X-BT) during seven days, and analyzed by excluding the first and last day of recording and calculating the mean among the valid days (≥ 8 hours of wear time). Subsequently, the Human Activity Profile (HAP) questionnaire, the International Physical Activity Questionnaire (IPAQ) and the physical functioning domain of the 36-Item Short Form Survey (PF SF-36) were applied. The normality of the data was analyzed using the Shapiro–Wilk test. The associations between each PAL questionnaire score and daily step counts were tested using Spearman’s correlation coefficients. Three, three linear regression models were constructed with daily step counts as the dependent variable and PAL questionnaire score and potential confounders (age, gender, educational level, time on dialysis, hemoglobin, and body mass index) as independent variables. A p value < 0.05 was considered as statistically significant.

**Results:** This study included 105 patients (59.2 ± 12.5 years, 60.0% male). Daily step counts correlated significantly with the questionnaires scores (HAP, ρ = 0.552, p < 0.001; IPAQ, ρ = 0.386, p < 0.001; PF SF-36, ρ = 0.337, p < 0.001). After adjusting for potential confounders, the multiple linear regression models showed an association between daily step counts with the HAP questionnaire score (R² = 0.31; adjusted R² = 0.26; p < 0.001) and PF SF-36 score (R² = 0.23; adjusted R² = 0.18; p < 0.001).

**Conclusion:** The PAL questionnaires were associated with daily step counts measured by an accelerometer in patients on hemodialysis. However, our results suggest that the HAP was the best questionnaire to evaluate PAL in these patients.
Results: A total of 643 patients were included, 70.8% started with hemodialysis and 29.2% with peritoneal dialysis. The mean (SD) age was 64.0 years (13.8) and 68.3% were men. At dialysis initiation 53.5% of all patients suffered from pruritus with a fluctuation in prevalence following the first year of dialysis (Fig. 1). During the first year 35.7% of the patients had persistent itching, 35.5% had fluctuating itching and 28.8% never experienced itching. There was a small increase in number of patients without itching at 3 months followed by an increase in number of patients with ‘quite some itch’ to ‘severe itch’ over the next months (Fig. 2). At 6 months after start dialysis 10.8% of the dialysis patients received topical antipruritic treatment, 17.2% received systemic antipruritic treatment and 3.3% received both topical and systemic treatment. The majority of patients with topical antipruritic treatment received emollients (58.9%) followed by cutaneous steroids (37.6%). Systemic steroids were the most used systemic antipruritic treatment (58.7%), followed by antihistamines (20.4%) and gabapentinoids (17.4%). Patients treated with topical agents at 6 months showed an odds ratio of 3.48 (95% CI: 1.11 – 10.91) on severe itching compared to patients without treatment. Furthermore, patients with systemic antipruritic treatment and with both systemic and topical treatment showed an odds ratio of 1.40 (95% CI: 0.48 – 4.03) and 1.52 (95% CI: 0.41 – 5.70) compared to patients without treatment respectively.

Conclusion: CKD-aP is highly prevalent in incident dialysis patients. The presence of CKD-aP is fluctuating during the first year of dialysis, with a third of patients experiencing intermittent itching. Starting dialysis may have a small beneficial effect on presence and severity of CKD-aP, but this is lost over time with moderate to severe CKD-aP increasing over the following months. Approximately a third of the patients received treatment for CKD-aP, predominantly as systemic treatment. The use of topical antipruritic treatment is associated with more severe CKD-aP at six months after start dialysis. These findings emphasize the need for further research on the pathophysiology and optimal treatment in dialysis patients.

Background and Aims: People with advanced stages of chronic kidney disease (CKD) undergoing hemodialysis often suffer from comorbidities that together with malnutrition and frailty contribute to a sedentary lifestyle, and cognitive and emotional impairments. Intradialytic non-immersive virtual reality exercise programs may improve the health-related quality of life and physical function of people undertaking hemodialysis. The aim of the GoodRENAI project was to test the feasibility of an intradialytic holistic virtual-reality platform designed to combine exercise with efforts to improve nutrition and psychological well-being as well as cognitive functioning and to assess the impact on physical, nutritional and psychological variables.

Method: People undergoing hemodialysis for at least 3 months who were medically stable, from Spain (Hospital de Manises), Sweden (Skane University Hospital and Karolinska Institutet), and Greece (Aristotle University of Thessaloniki) were selected and randomized into the GoodRENAI intradialysis intervention group and a control group (usual care). The GoodRENAI group
was exposed to a platform that consisted of several Virtual Scenarios (games) for each one of the targeted treatment areas: Physical Activity, Nutritional Information, Psychological Well-being and Cognitive Functionality. Specifically, these scenarios (‘games’) are aimed to make participants move (Physical Activity), learn aspects related to nutrition that they must follow (Nutritional Information), improve their psychological state (Psychological Well-being), and practice their cognitive abilities (Cognitive Functionality). The interaction with the Virtual Scenarios was designed to minimize ‘invasive’ and ‘annoying’ features by using a depth camera (AZURE Kinect), so that the patient, through the movement of their lower extremities (legs) was able to carry out the interaction. The control group carried out the usual care in the unit. The test battery included physical variables (lower-limb muscle strength, sit-to-stand to sit test 10 repetitions, 4-meters gait speed, and 6-minute walking test), nutritional variables (short-form food question, 7-point subjective global assessment, body weight, and handgrip strength), psychological variables (depression and anxiety), and cognitive variables. Differences between groups (GoodRENal vs usual care) will be analyzed with a mixed ANOVA model for repeated measures.

Results: The study so far includes 55 participants (mean age 65.4 ± 13 years), 17 females, median time on hemodialysis 48 months). The program, which starts in 2023, will last 12 weeks, until the middle of May 2023.

Conclusion: The evaluation of the GoodRENal platform will show if this is a feasible holistic treatment for improving the physical, nutritional, psychological and cognitive condition of people undertaking hemodialysis.

#5686
CANCER STATUS AND MORTALITY IN ELDERLY INCIDENT HEMODIALYSIS PATIENTS
Hyunjeong Cho1, Miran Park2, In O Sun3, Woo Yeong Park4, Jang-Hee Cho5, Soon Hye Kwon6, Won Min Hwang7, Yu Ah Hong8, Sung Joon Shin9, Sungjin Chung10 and Kyung Don Yoo10
1Chungbuk National University Hospital, Internal Medicine, Cheongju, Rep. of South Korea, 2Presbyterian Medical Center, Internal Medicine, Jeonju-si, Rep. of South Korea, 3Keimyung University Dongsan Hospital, Internal Medicine, Daegu, Rep. of South Korea, 4Kyungpook National University Hospital, Internal Medicine, Rep. of South Korea, 5Soochunhyang University Seoul Hospital, Internal Medicine, Seoul, Rep. of South Korea, 6Konyang University hospital, Internal Medicine, Daejeon, Rep. of South Korea, 7The Catholic University of Korea Daejeon St. Mary’s Hospital, Internal Medicine, Daejeon, Rep. of South Korea, 8Dongguk University Ilsan Hospital, Internal Medicine, Goyang-si, Rep. of South Korea, 9The Catholic University of Korea Yeouido St. Mary’s Hospital, Internal Medicine, Seoul, Rep. of South Korea, 10Ulsan University Hospital, Internal Medicine, Ulsan, Rep. of South Korea

Background and Aims: Chronic kidney disease and elderly people are associated with an increased risk of malignancy. But it remains unclear whether older patients with active cancer or a history of previous cancer and those without a cancer history carry the same mortality risk after initiation of hemodialysis (HD). Hence, we investigated the prognosis according to cancer status in elderly patients who started HD.

Method: Using a retrospective cohort of the Korean Society of Geriatric Nephrology, in this analysis, we included 2,085 patients older than 70 years who initiated hemodialysis between 2010 and 2017. Primary outcome of all-cause mortality was assessed using the Kaplan-Meier survival estimator and Cox proportional hazards regression analysis.

Results: At recruitment, 262 (12.6%) had a history of previous cancer and 55 (2.6%) had active cancer. During a median follow-up of 3.2 years, 1357 (65.1%) died. All-cause mortality was significantly higher in the active cancer group than in the previous cancer group and the no cancer group (85.5% vs 68.3% vs 64.0%, p < 0.002). Kaplan-Meier analysis revealed that all-cause mortality was significantly different among the 3 groups (p < 0.001, by log-rank test). After adjustment for various clinical factors, multivariate Cox regression analysis showed a strong association of active cancer with all-cause mortality (HR:1.89; 95%CI: 1.36–2.64; p < 0.001). However, previous cancer was not related to an increased risk of overall mortality (HR:1.07; 95%CI: 0.90–1.28; p = 0.448)

Conclusion: Active cancer was associated with high mortality in incident older hemodialysis patients. But patients with a history of previous cancer had a similar mortality risk compared to patients without a cancer history. Therefore, our study suggests that older cancer survivors may be able to maintain dialysis successfully.

Figure 1: Kaplan-Meier survival curve according to cancer status. All between-group comparisons were significant by pairwise log rank test.
BRAIN NATRIURETIC PEPTIDE LEVEL IN CHRONIC EGYPTIAN HEMODIALYSIS PATIENTS: ITS RELATION TO VENTRICULAR FUNCTION AND VOLUME STATUS

Alaa Sabry, Rana Elsaeed, Shaahat Ali and Zakariaf Lotfy
Mansoura, Mansoura, Egypt

Background and Aims: Volume overload is major problem in chronic hemodialysis patient and BNP level is related to volume status of the patient.

Aims: To assess BNP level in hemodialysis patient before and after HD session and to study its role as a marker for volume overload in hemodialysis patient depending on clinical findings and echocardiography parameters hemodialysis.

Method: The study was conducted on 50 patients of Nephrology and hemodialysis unit, Mansoura University Hospital. Our patients were classified according to left ventricular mass index (LVMI) into patients with left ventricular hypertrophy (LVH) (35 patients) and patients without LVH (15 patients). We classified our patients into another two groups according to predialysis BNP level to group with BNP level $>$ 100 pg/ml (33 patients) which was associated with cardiac dysfunction and group with BNP level $<$ 100 pg/ml (17 patients).

Results: In the present study, the median of pre-dialysis BNP level was 126 pg/ml and the median of post-dialysis BNP was 25 pg/ml, this demonstrate that BNP plasma level decline after the hemodialysis session.

<table>
<thead>
<tr>
<th>Table 1: Comparison between BP, weight and BNP pre and post dialysis.</th>
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<tbody>
<tr>
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<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
</tr>
<tr>
<td>BNP (pg/ml)</td>
</tr>
</tbody>
</table>

P value $\leq$ 0.05: significant difference

There is significant difference between pre and post BP, weight and BNP pre and post dialysis in pre and post dialysis patients.

BNP pre dialysis as a predictor of LL edema, basal crepitations, congested neck veins and HTN

Among the studied patients, the mean of predialysis systolic BP in patients with high BNP level $>$ 100 pg/ml is (155.65) higher than patients with low BNP level $<$ 100 pg/ml.

The incidence of lower limb edema, congested neck veins and chest crepitations was high in the group with BNP level $>$ 100 pg/ml when compared with BNP level $<$ 100 pg/ml. In the present study, according to ROC curve, predialysis BNP level may be a marker for lower limb edema with cutoff point (140.8) pg/ml with (85%) sensitivity and (77%) specificity and shows that the best cutoff point of predialysis BNP level in prediction of neck veins is (40.4) pg/ml with (94%) sensitivity and (28%) specificity and shows that the best cutoff point of predialysis BNP level in prediction of chest crepitation is (42.8) with (82%) sensitivity and (30%) specificity.

Conclusion: In Egyptian hemodialysis patients, there is a negative correlation between BNP predialysis and weight pre and post dialysis. There is significant correlation between BNP postdialysis and systolic BP predialysis, RVD and COP. There is significant correlation between delta BNP and systolic BP predialysis and ultrafiltration volume.

Figure 1: BNP levels pre and post dialysis among the studied patients.
#6869
CARDIAC ALTERATIONS FOUND IN PATIENTS WHO START DIALYSIS

Maria Iraola Legarra, Jose Jesus Broseta Monzo, Pedro Caravaca, Diana Rodriguez, Elena Cuadrado, Marta Farrero and Francisco Maduell
Hospital Clinic de Barcelona, Barcelona, Spain

Background and Aims: The presence of cardiac structural alterations in patients with chronic kidney disease who start renal replacement therapy is frequent. In fact, the real prevalence of heart failure is not well known due to the masking of symptoms by frequent ultrafiltration. Despite this, most deaths in these patients occur due to cardiovascular events, especially non-atheroembolic events, which are closely related to heart failure and ventricular remodeling. This study aimed to describe the echocardiographic alterations present in patients who start renal replacement therapy.

Method: Cross-sectional study to evaluate the prevalence of structural abnormalities in transthoracic echocardiography performed in patients at the time of initiating renal replacement therapy in the prevalent group of patients in kidney replacement therapy program at Hospital Clinic de Barcelona. Demographic variables and baseline drugs for heart failure were also collected.

Results: We included 170 patients of 67.84 ± 15.92 years. 115 (67.6%) were men, and 55 were women (32.4%). Of these, 124 (72.9%) were on hemodialysis, 11 (6.5%) on home hemodialysis, and 35 (20.6%) on peritoneal dialysis. Transthoracic echocardiogram findings at the beginning of dialysis showed a left ventricular ejection fraction of 47.5 ± 10.6%. It was reduced in 21 (12.4%), slightly reduced in 9 (5.3%) and preserved in 125 (73.5%) of the patients. The estimated pulmonary artery systolic pressure was 28.5 ± 3.53 mmHg. The telediastolic diameter of the left ventricle was 5.5 ± 0.71 cm, that of the interventricular septum was 1.15 ± 0.27 cm, the diameter of the left atrium was 4.5 ± 1.27 cm, its volume was 95.05 ± 56.5 mL in the biplane section and 54.3 ± 28.28 mL in the four-chamber section. There were no significant differences between groups when analyzed by type of renal replacement therapy.

Regarding valvulopathies, 47 (21.8%) had some degree of aortic stenosis, 68 (40%) had some degree of aortic insufficiency, 104 (62.2%) had some degree of tricuspid insufficiency, 118 (69.4%) some degree of mitral insufficiency. Regarding treatment, 50 (29.4%) of the patients had some RAASi, 60 (35.3%) had beta-blockers, and 2 (1.2%) had MRA.

Conclusion: The presence of structural alterations in the heart of patients initiating renal replacement therapy is practically universal and independent of the type of technique initiated. Nephrologists should become aware of these findings and seek ways to prevent and reverse these alterations as far as possible to achieve better clinical results in dialysis.

Table 2:

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>P value</th>
<th>Lower border</th>
<th>Upper border</th>
<th>Cut off point of pre BNP</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema LL</td>
<td>0.827</td>
<td>&gt;0.006*</td>
<td>0.66</td>
<td>0.99</td>
<td>140.8</td>
<td>85%</td>
<td>77%</td>
</tr>
<tr>
<td>Congested Neck veins</td>
<td>0.58</td>
<td>0.35</td>
<td>0.4</td>
<td>0.75</td>
<td>40.4</td>
<td>94%</td>
<td>28%</td>
</tr>
<tr>
<td>Basal crepitation</td>
<td>0.57</td>
<td>0.4</td>
<td>0.39</td>
<td>0.74</td>
<td>42.8</td>
<td>82%</td>
<td>30%</td>
</tr>
<tr>
<td>HTN</td>
<td>0.645</td>
<td>0.14</td>
<td>0.42</td>
<td>0.86</td>
<td>131</td>
<td>63%</td>
<td>62%</td>
</tr>
</tbody>
</table>

AUC area under curve. delta BNP as a predictor of LL edema, basal crepitations, congested neck veins and HTN.

Table 3:

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>P value</th>
<th>Lower border</th>
<th>Upper border</th>
<th>Cut off point of delta BNP</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema LL</td>
<td>0.925</td>
<td>&lt;0.001</td>
<td>0.846</td>
<td>1</td>
<td>17.12</td>
<td>95%</td>
<td>71%</td>
</tr>
<tr>
<td>Basal crepitation</td>
<td>0.982</td>
<td>&lt;0.001</td>
<td>0.946</td>
<td>1</td>
<td>80.6</td>
<td>97%</td>
<td>94%</td>
</tr>
<tr>
<td>HTN</td>
<td>0.965</td>
<td>&lt;0.001</td>
<td>0.919</td>
<td>1</td>
<td>18.7</td>
<td>97%</td>
<td>72%</td>
</tr>
</tbody>
</table>

This table shows that the best cutoff point of delta BNP (predialysis BNP - postdialysis BNP) in prediction of LL edema was 17.12 pg/ml with 95% sensitivity and 71% specificity and shows that the best cutoff point of delta BNP in prediction of crepitation was 80.6 pg/ml with 97% sensitivity and 94% specificity and shows that the best cutoff point of delta BNP in prediction of HTN was 18.7 pg/ml with 97% sensitivity and 72% specificity.

#3930
EFFECT OF TWO PHOSPHATE BINDERS ON VITAMIN D LEVELS IN HEMODIALYSIS PATIENTS

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General Hospital of Thessaloniki Agios Pavlos, Nephrology Unit, Thessaloniki, Greece

Background and Aims: A recent meta-analysis highlighted the impact of different types of phosphate binders on vitamin D metabolism in patients with stage 3 CKD. Sevelamer was associated with lower serum 25(OH) vitamin D levels probably due to reduced intestinal absorption of D3 (cholecalceforol). Corresponding effects of different phosphate binders in hemodialysis patients have not been studied.

Method: We performed an observational prospective study in which 55 stable hemodialysis patients were followed for 28 months. Patients’ age was 42-91 years old and duration of hemodialysis was 2-312 months. Patients received as phosphate binders sevelamer, sucroferric oxyhydroxide or combination. The type of binders, the administration of D3 supplements, paricalcitol or etecalcetide as well as the biochemical control of the patients were recorded every two months. Serum 25(OH) vitamin D levels and the proportion of patients who required D3 supplementation to maintain 25(OH) vitamin D levels >20ng/mL were assessed.

Results: At baseline, 66% of patients used sevelamer as phosphate binder, 22% sucroferric oxyhydroxide and 18% combination, while 36% were on D3 supplements. Levels of 25(OH) vitamin D showed a significant increase after the first year of follow-up. (Dstart:16±6ng/mL vs D12months:26±10ng/mL, P = .001). After one year D3 supplementation ratio increased to 48% and remained at these levels until the end of follow-up. Taking paricalcitol or etecalcetide did not affect the results. No differences in 25(OH) vitamin D and D3 supplementation rate levels were observed between those receiving the different binders or the co administration group. No differences were observed in the biochemical markers tested as well as in dialysis adequacy.

Conclusion: In context of daily clinical practice, no differences were observed in the levels of 25(OH) vitamin D in either patients receiving sevelamer, sucroferric oxyhydroxide or combination of both as phosphate binders. Half of hemodialysis patients require cholecalciferol supplementation to maintain adequate 25(OH) vitamin D levels.
Patients were excluded if present physical or cognitive incapable to perform the proposed tests, assisted gait, uncorrected visual impairments, severe and unstable comorbidities, and hospitalization in the past three months. Postural balance was evaluated by the Mini-BESTest and posturography [a force plate recorded the center of pressure (COP) path length in a static position with eyes opened (EO) and eyes closed (EC) on a firm surface]. The normality of the data was analyzed using the Shapiro–Wilks test. The associations between Mini-BESTest score and COP path length in the EO and EC were tested using Spearman’s correlation coefficients. Then, two multiple linear regression models were constructed with COP path length in the EO and EC as the dependent variable and Mini-BESTest score and potential confounders (age, gender, diabetes mellitus, body index mass, hemodialysis efficiency index, and hemoglobin) as independent variables. A p value < 0.05 was considered as statistically significant.

**Results:** This study included 109 patients (58.4 ± 12.9 years, 57.8% male). The Mini-BESTest was correlated with COP path length in the EO (ρ = -0.365, p < 0.001) and EC (ρ = -0.279, p = 0.003). The multiple linear regression models showed an association of the Mini-BESTest with COP path length in the EO (R² = 0.28; adjusted R² = 0.23; p < 0.001) and EC (R² = 0.26; adjusted R² = 0.20; p < 0.001).

**Conclusion:** The Mini-BESTest was associated with posturography in patients on hemodialysis. Therefore, the Mini-BESTest is a feasible test to evaluate postural balance in clinical routine practice during the physical function evaluation of these patients.

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**Abstract**

**#2905 CLINICAL OUTCOMES OF ORAL ANTICOAGULATION AND NO ANTICOAGULATION AMONG HEMODIALYSIS PATIENTS WITH ATRIAL FIBRILLATION**

Eratosthenes Polito and Grecia Darunday
Perpetual Succour Hospital, Internal Medicine, Section of Adult Nephrology, Cebu, The Philippines

**Background and Aims:** The delicate balance of risk versus benefit of oral anticoagulation in the general population is well established but the decision to use these agents in end-stage renal disease (ESRD) remains complex and difficult owing to the paucity of clinical trials and lack of substantial evidence in literature for its safe and effective use in the haemodialysis population. This study aims to determine the difference in clinical outcomes between oral anticoagulation and no anticoagulation therapy among ESRD patients on maintenance haemodialysis with atrial fibrillation.

**Method:** This is a prospective, single-center, observational study conducted in Perpetual Succour Hospital that included all ESRD patients on maintenance haemodialysis for at least 3 months with atrial fibrillation. Out of the 188 identified patients, only 69 patients were included in the study and were grouped according to how the cardiac dysrhythmia was approached either with oral anticoagulation or no use of oral anticoagulation. Basic demographic information were obtained as well as the aetiology of ESRD, CHA2DS2-VASc Score and the HAS-BLED Score. Lastly, patients were prospectively followed for a period of 12 months and were then assessed for new onset of thromboembolic events, hemorrhagic events, calciphylaxis and all-cause mortality.

**Results:** At enrolment, 59 (85.5%) patients were identified to have no oral anticoagulation therapy and 10 (14.5%) were already receiving oral anticoagulation. Ischemic strokes was more prevalent among patients who were on oral anticoagulant (80%, p < 0.0001). Patient outcomes differ significantly in terms of intracranial hemorrhage (30%, p = 0.0004) and gastrointestinal bleeding (50%, p < 0.00001) which were noted among patients on oral anticoagulation. In relation to over-all mortality, acute myocardial infarction, peripheral arterial occlusive disease and calciphylaxis, there was no significant difference between the two groups.

**Conclusion:** This study suggests that the use of oral anticoagulation did not prevent ischemic strokes in ESRD patients on maintenance haemodialysis with atrial fibrillation and its use was associated with increased risk for intracranial haemorrhage and gastrointestinal bleeding. There was no significant difference in relation to all-cause mortality, acute myocardial infarction, peripheral arterial occlusive disease and calciphylaxis between the two study groups.
Figure 1: Flow diagram illustrating the details on how the study population were obtained.

Table 1: CHA2DS2-VASc and HAS-BLED Score profiles of the study population.

<table>
<thead>
<tr>
<th>Variables</th>
<th>With Anticoagulant (n=10)</th>
<th>No Anticoagulant (n=59)</th>
<th>Total (n=69)</th>
<th>p-value (z-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA2DS2-VASc Score</td>
<td></td>
<td></td>
<td></td>
<td>n.a</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>n.a</td>
</tr>
<tr>
<td>1</td>
<td>1[10%]</td>
<td>2[3%]</td>
<td>3</td>
<td>0.34</td>
</tr>
<tr>
<td>3</td>
<td>1[10%]</td>
<td>12[20%]</td>
<td>13</td>
<td>0.44</td>
</tr>
<tr>
<td>&gt;4</td>
<td>8[80%]</td>
<td>45[76%]</td>
<td>53</td>
<td>0.79</td>
</tr>
<tr>
<td>HAS-BLED Score</td>
<td></td>
<td></td>
<td></td>
<td>n.a</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>n.a</td>
</tr>
<tr>
<td>2</td>
<td>1[10%]</td>
<td>8[14%]</td>
<td>9</td>
<td>0.74</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>14[24%]</td>
<td>14</td>
<td>0.08</td>
</tr>
<tr>
<td>&gt;3</td>
<td>9[90%]</td>
<td>37[63%]</td>
<td>46</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Table 2: Comparison of Clinical Outcomes between patients on oral anticoagulation and no anticoagulation among End-stage renal disease patients on maintenance hemodialysis with atrial fibrillation.

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>With Anticoagulant (n=10)</th>
<th>%</th>
<th>No anticoagulant (n=59)</th>
<th>%</th>
<th>Total (n=69)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thromboembolic Events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic Strokes</td>
<td>8</td>
<td>80%</td>
<td>8</td>
<td>14%</td>
<td>16</td>
<td>&lt;.00001</td>
</tr>
<tr>
<td>Acute Myocardial Infarction</td>
<td>4</td>
<td>40%</td>
<td>33</td>
<td>56%</td>
<td>37</td>
<td>0.3500</td>
</tr>
<tr>
<td>Peripheral Arterial Disease</td>
<td>3</td>
<td>30%</td>
<td>20</td>
<td>34%</td>
<td>23</td>
<td>0.8100</td>
</tr>
<tr>
<td><strong>Hemorrhagic Events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial Hemorrhage</td>
<td>3</td>
<td>30%</td>
<td>1</td>
<td>2%</td>
<td>4</td>
<td>0.0004</td>
</tr>
<tr>
<td>Gastrointestinal Bleeding</td>
<td>5</td>
<td>50%</td>
<td>3</td>
<td>5%</td>
<td>8</td>
<td>&lt;.00001</td>
</tr>
<tr>
<td>Calciphylaxis</td>
<td>4</td>
<td>40%</td>
<td>8</td>
<td>14%</td>
<td>12</td>
<td>0.4136</td>
</tr>
<tr>
<td>Death</td>
<td>5</td>
<td>50%</td>
<td>25</td>
<td>42%</td>
<td>30</td>
<td>0.6500</td>
</tr>
</tbody>
</table>

Figure 2: Risk prediction scores for thrombotic and hemorrhagic events of the study population.

#3560

STATIN THERAPY IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HAEMODIALYSIS

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Background and Aims: In 2017, around 4 million people with end-stage renal disease worldwide were on renal replacement therapy. Haemodialysis is accounted as the most common therapy, accounting for 69% of all renal replacement therapies and 89% of all dialysis. Patients receiving haemodialysis present significantly higher risk for cardiovascular events which affect more than two-thirds of patients, making it the primary cause of morbidity (Bello et al., 2022). Statin therapy is used as primary prevention of cardiovascular risk amongst the general population; nonetheless, in patients with chronic kidney disease the benefits of statins are controversial (Fellström et al., 2009). The aim of this study is to analyze data of statins use in patients from different Latvian haemodialysis centers.

Method: A cross-sectional observational study included consecutive patients from four haemodialysis centers from June till October 2022. Patients were interviewed about disease anamnesis, comorbidities, statins and other drug usage. Data was analyzed with SPSS statistics.

Results: Among 113 included patients, 64.6% were man, mean age was 62.8±14.9 years, mean body-mass index was 26.66±5.3 kg/m². Current smokers were 14.2%. Most common primary cause for haemodialysis (47.2%) was glomerular diseases. Comorbidities as primary arterial hypertension and diabetes were diagnosed in 39.8% and 17.7% of patients, respectively. History of arterial vascular disease was present in 47 (41.6%) patients, 26 (23%) patients underwent revascularization. Anamnesis of kidney transplantation was present in 17.7%. Mean plasma concentration for total cholesterol, LDL cholesterol and triglycerides were 4.4±1.3 mmol/L, 2.5±1.1 mmol/L and 1.7±1.3 mmol/L, respectively. Mean haemodialysis period was 51.88 months ±1.7. The most common type and dosage was atorvastatin 20 mg in 21 (35%) patient, following by atorvastatin 40mg in 9 (15%) and rosuvastatin 20mg in 9 (15%) patients. Majority of statin users (49.2%) had unknown therapy starting date regarding haemodialysis, while 31.7% of patients were using statins before haemodialysis and only 19% of patients started statin therapy while undergoing haemodialysis. Patients who had transplantation were associated with 2.4 times increased usage of statins (P = .09). No significant lipid concentration difference was observed between patients who underwent transplantation and those who did not (p>0.05). LDL concentration with and without statin use was 1.97 and 2.73 (P = .03), respectively.

Conclusion: Statin therapy was related to history of cardiovascular events and revascularization, as well expressing significantly lower LDL concentration, that might be beneficial in secondary prophylaxis. History of transplantation was associated with increased statin administration.

#5622

DIALYSING THE ELDERLY: IMPACT ON THE PATIENTS’ HEALTH-RELATED QUALITY OF LIFE OUTCOME

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1International Islamic University Malaysia, Nephrology, Kuantan, Malaysia and 2International Islamic University Malaysia, Community Medicine, Kuantan, Malaysia

Background and Aims: The number of elderly who suffers from end stage renal disease (ESRD) is increasing and hence the dialysis therapy rate. Although dialysis increases life span, the overall benefits to elderly patients is arguably unpredictable due to the multiple comorbidities and functional impairment. Health-related quality of life (HRQOL) has been an important key outcome in the decision-making yet to date, there is no available local data of the dialysis implications on the elderly. Therefore, we aim to study on the impact of dialysis initiation on HRQOL among elderly ESRD patients.
Method: This is a prospective, multi-centered study conducted from 2021 to 2022 in 12 hospitals (aged ≥65) who started high-flux dialysis therapy. Health-related quality of life (QOL) were assessed using Kidney Disease Quality of Life-36 (KDQOL-36) questionnaire within the first month of initiation (baseline) with a follow-up review performed after six months.

Results: The study included 29 patients with the oldest was 95 years old. 27 patients underwent haemodialysis (HD) and another 2 had peritoneal dialysis. The average age of them was 62.12 and 12, respectively. 8 of them required catheterization for dialysis mobilization. All of the patients had underlying comorbidities with 25 of them had 3 and more comorbidities. Majority of the patients (n=24) were diabetic with 13 of them had an underlying ischemic heart disease. Their mean baseline haemoglobin and albumin were 8.1 g/dL (±0.3) and 34.2 mmol/L (±1.3) respectively. Only 1 of the study patients was initiated HD via a fistula which was in patients using temporary catheter. At 6 months of follow-up, 5 of the patients died due to cardiovascular events, catheter-related sepsis and one of them resorted to palliative care due to exhausted conventional vascular access. 13 patients out of 22 remained on cather for HD with 9 patients were still using temporary catheter. We observed improvement in all five domains of HRQOL assessed. The mean score of physical component summary was 33.00% (±10.58) at baseline and 41.22% (±9.54) after 6 months (P = .011). The mean scores for mental component at baseline and 6-month review were 45.53% (±14.78) and 52.95% (±10.57) respectively (P = .018). As for symptoms and problems domain, they initially scored 58.59% (±18.71) which increased to 76.61% (±16.05) after 6 months (P = .003). The scores for ‘burden of kidney disease’ and ‘effects of kidney disease’ domains were and 43.49% (±35.62) and 58.21% (±26.74) respectively at baseline with improvements to 58.85% (±31.81) (P = .026) and 76.04% (±24.65) (P = .008) after 6 months.

Conclusion: Our study showed that dialysis therapy results in significant improvement in HRQOL among elderly ESRD patients. The decision for dialysis among this group of patients is nonetheless a complex process with consideration made on individual basis followed by continuous evaluation of its effectiveness, incorporating HRQOL assessment tool in particular.

#5653
MEASURABLE IMPROVEMENT IN ABD WITH SMALL CHANGE IN HD SETTING
Nikolija Smokovska1, Nadica Misovska2, Suzana Stanojevska1, Ivica Nikolov1, Sredanka Kostadinoska1 and Marija Piperkoska1
1Diaverum North Macedonia, Skopje, Republic of North Macedonia and 2Diaverum North Macedonia, Skopje, Republic of North Macedonia

Background and Aims: Majority of the patients with chronic kidney disease on hemodialysis (CKD HD) have various bone-related pathologies covered under one clinical entity chronic kidney disease – mineral bone disorders (CKD-MBD). One of the most common is the adynamic bone disease (ABD).1 Published data are showing that changes of calcium level in HD fluid might improve the ABD.2,3 Our aim was to assess whether the lowering of the calcium level in dialysis fluid will improve the ABD in our HD patients.

Method: Prospective study was conducted in a single HD centre in a period of 12 months (01.10.2020 until 30.09.2021), with further 6 months follow up. One hundred thirty three HD patients were screened, 64 patients of them had ABD (iPTH <150 ng/ml). 53 patients were enrolled who met the inclusion criteria (age >18 years, and HD vintage >90 days) and 50 completed the study, during which the only phosphate binder used was calcium based. The calcium level content in the dialysis fluid was changed from various calcium concentration (1.5 mmol/L; 1.75 mmol/L and set to 1.25 mmol/L in the enrolled patients. Laboratory parameters were followed each month and the level of iPTH trimestally.

Results: Data from 50 patients was collected and analysed, 50.9% (n=27) males. The average age of the cohort was 69.31 years (±12.49), average HD vintage was 51.94 months (±43.82). Average HD time was 254.8 minutes (±14.71) with average blood pump 393.4 ml/min (±44.38). At study end, the iPTH level was significantly changed (p=.00001), from 67.48 ng/ml (±32.85) to 150.38 ng/ml (±92.96). 24 out of 50 patients (48%) had iPTH level >150 ng/ml, p=.0001. Calcium level changed slightly from 2.27 mmol/L (±0.15) to 2.25 mmol/L (±0.18), p=.25. The phosphate level changed from 1.29 mmol/L (±0.49) to 1.35 mmol/L (±0.48), p=.804. The alkaline phosphatase level significantly changed (p=.00002), from 82.61 IU/L (±49.5) to 118.71 IU/L (±50.23). Patients who had iPTH level >150 ng/ml at the study end had level of calcium of 2.2 mmol/L (±0.16), p=.17 compared to patients who had iPTH level <150 ng/ml (level of calcium of 2.31 mmol/L ±0.18, p=.43). There was improvement in the level of phosphate and alkaline phosphatase: 1.31 mmol/L (±0.46) vs. 1.6 mmol/L (±0.46), p=.002 and 82.57 IU/L (±57.22) vs. 130.83 IU/L (±60.24), p=.004, accordingly. Diabetes mellitus (DM) had insignificant impact on ABD in the patient cohort. 66.7% of the patients with DM (n=10) and 40% of the patients without DM (n=14) reached iPTH >150 ng/ml at study end. Intergroup comparison showed significance only in the level of calcium, DM group calcium=2.16 mmol/L (±0.1); non DM group calcium=2.29 mmol/L (±0.1), p=.01. Additionally, at study end, Karnovsky score was higher in patients with iPTH >150 ng/ml, 76.09% (±13.05); p=.009. Patients who did not reach iPTH >150 ng/ml (n=26) were further followed up for 6 months, and 10 of them reached iPTH >150 ng/ml.

Conclusion: Indirectly minor change in HD setting, as lowering the calcium level in dialysis fluid required a care of proportionate increase in phosphate binder and might improve the adynamic bone disease. Presence of diabetes did not show significant impact on ABD. However, Karnovsky score showed significant improvement, and exercise may also improve ABD in HD patients. These findings might be used as recommendation in low and middle-income countries in which pharmacological treatments for ABD are limited and/or unavailable.

#6696
COGNITIVE IMPAIRMENT IN PATIENTS ON HEMODIALYSIS EXPERIENCE FROM A CENTER IN SANTA ROSA GUATEMALA
Céselo Mazarriegos Campos1, María Palencia Pérez2, Herbert Ferrer Cuesta1, Carlos Avendaño1 and José Vicente Sánchez Polo2
1Corporación Integral de Diálisis, Guatemala, Guatemala and 2Instituto Guatemalteco de Seguridad Social, Guatemala, Guatemala

Background and Aims: Cognitive impairment in patients with chronic kidney disease (CKD) involves multiple factors such as inflammation, uremic toxins and endothelial dysfunction, having rates of up to 10.7 cases per 1000/patient year and that can increase in renal replacement therapy (RRT). The cognitive impairment can progress to dementia and this has adverse long-term outcomes such as mortality. The prevalence of cognitive impairment is 19% to 77% in patients with hemodialysis therapy. The aims of this study was determine the prevalence of cognitive impairment in hemodialysis patients and possible associated factors.

Method: A cohort study was conducted in a hemodialysis unit of Santa Rosa, Guatemala. Patients over 18 years of age were included with more than two months of having started hemodialysis and with 3 sessions per week. Patients with a previous diagnosis of dementia, with visual-hearing deficits, illiterate, a history of cerebrovascular events or psychiatric disorders and who did not agree to participate in the study were excluded. For cognitive assessment, the Montreal Cognitive Assessment tool (MoCA test) was used, taking a score of less or equal to 26 points as cognitive impairment. A value of p<0.05 was taken significant.

Results: 78 patients were screened, however 30 patients were discarded due to exclusion criteria. A total of 48 patients were analyzed. A mean age was of 51.14 years, the majority of whom were male, 40% had only a basic level of education and 38% did not know the cause of CKD. Arterial hypertension was the most frequent comorbidity and the most used antihypertensive were beta-blockers. As for medications for complications of CKD, vitamin D and erythropoietin are the most used. The patients had an average time on hemodialysis of 41.3 months, the last calculated Kt/V was of 1.73 (mean), the mean hemoglobin level was 9.9 g/dl and the mean MoCA test score performed for the study was 8.75 (±2.15).

Table 1: Association between Cognitive Domains and Cognitive Impairment.

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>Preserved</th>
<th>Altered</th>
<th>Value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visuospatial</td>
<td>54%</td>
<td>46%</td>
<td>NS</td>
</tr>
<tr>
<td>Executive</td>
<td>79%</td>
<td>21%</td>
<td>NS</td>
</tr>
<tr>
<td>Naming</td>
<td>58%</td>
<td>42%</td>
<td>0.004</td>
</tr>
<tr>
<td>Memory</td>
<td>27%</td>
<td>73%</td>
<td>NS</td>
</tr>
<tr>
<td>Attention</td>
<td>35%</td>
<td>65%</td>
<td>0.03</td>
</tr>
<tr>
<td>Language</td>
<td>58%</td>
<td>42%</td>
<td>0.023</td>
</tr>
<tr>
<td>Abstraction</td>
<td>63%</td>
<td>37%</td>
<td>NS</td>
</tr>
<tr>
<td>Delayed Recall</td>
<td>12%</td>
<td>88%</td>
<td>0.012</td>
</tr>
<tr>
<td>Orientation</td>
<td>71%</td>
<td>29%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2: Analysis of Correlation with the MOCA Test Score.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson correlation</th>
<th>Value of P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−0.46</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.01</td>
<td>0.9</td>
</tr>
<tr>
<td>Kt/V</td>
<td>0.1</td>
<td>0.49</td>
</tr>
<tr>
<td>Variable</td>
<td>Spearman correlation</td>
<td>Value of P</td>
</tr>
<tr>
<td>Time on Hemodialysis</td>
<td>−0.02</td>
<td>0.89</td>
</tr>
</tbody>
</table>
was 23.3 points. Regarding the primary objective, it was determined that the prevalence of cognitive impairment was 67% and when analyzing the variables it was found that age and level of education are associated with greater cognitive impairment, older patients (p: 0.002) and with lower level of education (p: 0.02). In analysis the cognitive domains, it is found that those patients who present alterations in the attention and delayed recall domain are those that are statistically more associated with cognitive impairment and their counterpart those who have conserved the naming and language domain are those that are associated with having a normal global cognitive practice (Table 1). A correlation analysis was performed where it was found that there is a negative correlation which is moderate and statistically significant between age and the MoCA test score (Table 2).

Conclusion: The prevalence of cognitive impairment was 67%, age and educational level seem to be influencing factors, with older patients and those with lower single-coat level being the most affected. Within the cognitive domains, attention and delayed recall are the most affected and most associated with cognitive impairment. It is important to conduct further studies evaluating other variables that have been shown to influence cognitive status such as vitamin B12, vitamin D and homocysteine. It is important to perform cognitive evaluation of patients on hemodialysis and other RRT to have an early diagnosis and intervene early considering that cognitive impairment can progress to dementia and this is a cause of abandonment in treatment and mortality.

### 3429 HIGHER INPATIENT COSTS FOR HEMODIALYSIS PATIENTS HOSPITALIZED FOR CEREBROVASCULAR DISEASE

Aki Kuroki1 and Satoru Shimura 1

1Yokohama General Hospital, Kidney Disease Center, Yokohama, Japan

**Background and Aims:** Dialysis patients often have comorbidities that result in frequent hospitalizations. Several studies showed that inpatient costs contributed largely to the medical costs of dialysis patients. In this study, to assess the impact of comorbidities on inpatient costs in dialysis patients, we examined the association between reasons for admission and the inpatient costs using electronic medical records.

**Methods:** This was a single-center, retrospective, observational study of dialysis patients admitted to Yokohama General Hospital (300 beds) between April 2020 and March 2022. Information on patient demographics, cause of end-stage kidney disease (ESKD), dialysis duration, number of complications, and reasons for admission were collected from electronic medical records. Inpatient costs were calculated from claims data and analyzed based on patient characteristics and reasons for admission. Inpatient costs for dialysis patients were compared with those for all hospitalized patients. Data were analyzed using the Kruskal-Wallis test.

**Results:** During the observation period, 172,160 patients were admitted to the hospital, of which 169 were maintenance dialysis patients. One hundred and twenty-three of them were male, with a mean age of 73.0 years. Diabetic kidney disease was the most common cause of ESKD (n=128), followed by chronic glomerulonephritis (n=21), nephrosclerosis (n=19), and autosomal poly cystic kidney disease (n=1). The median time on dialysis was 5 years. Seventy-three patients were admitted for peripheral vascular disease, 24 for cardiovascular disease, 24 for fractures, 16 for gastrointestinal disease, 13 for cerebrovascular disease, and remainder for other conditions. Inpatient costs ranged from €764 to €7,9743, with a mean of €1,4884, and a median of €9002. Inpatient costs did not differ significantly by age, sex, time on dialysis, number of complications, or cause of ESKD. There were significant differences in inpatient costs according to the reason for admission. Patients hospitalized for cerebrovascular disease had significantly higher inpatient costs with a mean of €11,7733 and a median of €14,6623 (p = .049). During the study period, dialysis patients accounted for 0.098% of all inpatient admissions, and their medical costs were 3% of the hospital's total inpatient medical costs.

**Conclusion:** Considering the number of dialysis patients as a percentage of all inpatients during the study period, it was clear that dialysis patients had a high cost burden. Among dialysis patients, hospitalization for cerebrovascular disease was associated with significantly higher costs.

### 4654 THROMBOEMBOLIC EVENTS AND THEIR RELATIONSHIP WITH COVID-19 IN HEMODIALYSIS PATIENTS: MYTH OR TRUE?

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**Background and Aims:** Since the beginning of COVID-19 pandemic, there has been more than 668 million of diagnosis and more than 6 million deaths worldwide. This pandemic also has had a dramatic impact on chronic patients, such as those with end stage renal disease (ESRD) on hemodialysis (HD). Many studies have hypothesized that COVID-19 could induce a hypercoagulability state, activating coagulation cascade. Post-mortem studies revealed vascular injuries in more than 60% of lung tissues and many patients diagnosed with COVID-19 have suffered neurological pathologies, as ischemic stroke. Patients with ESRD are also at higher risk of thromboembolic events than healthy subjects.

In this study, we analyze thromboembolic events in HD patients with or without COVID-19 diagnosis.

**Method:** We performed a retrospective observational study between March 2020 and December 2022 with 4679 HD patients (2635 COVID-19 positive patients (Group 1) and 2044 COVID-19 negative (Group 2)) from 50 Spanish clinics. The baseline dates of the non COVID-19 patients were randomly selected. Follow-up time was 1 year since COVID-19 diagnosis (Group 1) or since collection (Group 2). We identified patients who has suffered any thromboembolic event during follow-up time. We compared usual clinical parameters between groups using Chi2 and Mann-Whitney U tests. Survival analysis was performed by Kaplan-Meier and Cox regression. Continuous variables were categorized to perform the Cox analysis.

**Results:** Small differences between Group 1 and 2 were found in age (70.45 (62.81-82) vs 68.94 (61-80); p < 0.001), proportion of men (63% vs 67.2%; p < 0.05), HD vintage (34 (14-71) vs 30 (11-65); p < 0.05), preHD systolic blood pressure (SBP) (140.73 (126-155) vs 142.65 (128-157); p < 0.05), plasma hemoglobin (Hb) (11.19 (10.40-11.90) vs 11.31 (10.5-12); p < 0.05) and proportion of patients with antithrombic medication (60% (22.9%) vs 401 (19.6%); p < 0.05).

No statistically significant differences were found in time to first thromboembolic event between the two groups (Figure 1). In univariate Cox regression (Table 1) thromboembolic events showed significant relationship with gender, Charlson Index above 8, preHD relative overhydration (reLOH) above 13.4% and preHD SBP above 155 mmHg. In multivariate analysis (Table 1), Charlson Index and preHD SBP showed hazard ratio above 1.5 for thromboembolic event (p < 0.05). COVID-19 diagnosis did not show strong relationship with thromboembolic events.

**Conclusion:** Publications on thromboembolic events in HD patients who have suffered from COVID-19 are scarce and with small size samples. In our large HD sample, thromboembolic events were not related to COVID-19. Only Charlson Index and preHD SBP showed a significant relationship in the multivariate analysis.
**Table 1: Cox Regression to Thromboembolic Event in 1 year follow-up.**

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<tr>
<th></th>
<th>Univariate Cox Regression</th>
<th>Multivariate Cox Regression</th>
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<tr>
<td></td>
<td>HR</td>
<td>CI (95%)</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Age 66-78</td>
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<tr>
<td>Age &gt;78</td>
<td>1.210</td>
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<tr>
<td>Female</td>
<td>0.701</td>
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<td>Body Mass Index (kg/m²)</td>
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<tr>
<td>Body Mass Index 23.8-28.4</td>
<td>0.974</td>
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<tr>
<td>COVID-19 infection</td>
<td>0.987</td>
<td>0.735</td>
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<tr>
<td>Charlson Index 5-8</td>
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<tr>
<td>Charlson Index &gt;8</td>
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<tr>
<td>Dialysis Vintage (months)</td>
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<tr>
<td>Dialysis Vintage 18-52</td>
<td>0.842</td>
<td>0.608</td>
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<tr>
<td>Dialysis Vintage &gt;52</td>
<td>0.856</td>
<td>0.619</td>
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<tr>
<td>PreHD relOH (%)</td>
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<td>PreHD relOH 7.3-13.4</td>
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<td>Hb (g/dL)</td>
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<td>Hb &gt; 10.7-11.7</td>
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<td>Hb &gt; 11.7</td>
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<td>PreHD SBP (mmHg)</td>
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<tr>
<td>PreHD SBP &lt;133</td>
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<tr>
<td>PreHD SBP &gt;155</td>
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<td>Antiplatelet Medication</td>
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<td>0.826</td>
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**IMPLEMENTATION OF CLINICAL ALARM SYSTEM IS ASSOCIATED WITH REDUCTION OF THE RISK OF INTRADIALYTIC HYPOTENSION**

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**Background and Aims:** Intradialytic hypotension (IDH) plays an essential role in hemodialysis. IDH prevalence can be up to 8% to 40% [1], according to research. Furthermore, research shows that IDH positively correlates with severe complications such as non-occlusive mesenteric ischemia[2], critical limb ischemia[3] and tissue ischemia, which leads to irreversible damage, even increasing the chance of infection. Many causes and risk factors result in IDH, such as excessive weight gain during dialysis, cardiovascular dysfunction, and improper use of blood pressure-lowering drugs[1]. Therefore, it still relies
on experienced medical professionals to monitor patients' blood pressure to beware of the risk of developing IDH. However, this increases the workload on medical professionals and does not provide standard or more objective early warning indicators of hypotension for new medical professionals.

**Method:** Selection of experimental and control group: In this study, we included 81 subjects that received hemodialysis in Tainan City Municipal Annan Hospital from January 2021 to August 2022. The control group was retrospective data collected from January 2021 to August 2021. Then, from January 2022 to August 2022, we implemented our IDH predicting system and took subjects' data from this interval as the experimental group to compare the incidence of IDH with the control group.

**IDH prediction system monitoring interface:** After integrating with the hemodialysis dataset, our prediction system will predict patients' systolic pressure and the likelihood of IDH in the next 30 minutes. As soon as the system detects that the patient will encounter hypotension, it sends warning signals, blood pressure and IDH incidence probability predictions to the monitoring interface to alert medical professionals. Furthermore, our system also supports multi-bed monitoring, which can significantly increase the efficiency of monitoring during hemodialysis.

**Results:** After implementing the IDH prediction system, the outcome yielded an IDH incidence of 6.12% in August 2022. Compared to the control group, when the IDH system was not yet implemented, which yielded an IDH incidence of 9.34%, it showed a reduction of 34.5% in IDH cases. Furthermore, the average reduction in IDH rate each month was 12%.

**Conclusion:** The present study demonstrated that implementing the IDH predicting model may efficiently reduce the incidence of IDH. However, along with the IDH warning multi-bed monitoring interface, medical professionals must develop a standard procedure to deploy when noticing the warning signals. As a result, this may further reduce the incidence of IDH during hemodialysis sessions.

**REFERENCES**


**#6579**

**ANALYSIS OF RISK FACTORS FOR CUTANEOUS CALCIPHYLAXIS IN HEMODIALYSIS PATIENTS**

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**Background and Aims:** Risk factors with cutaneous calciphylaxis were analyzed in hemodialysis patients.

**Method:** Clinical data of hemodialysis patients who were diagnosed with cutaneous calciphylaxis and admitted to Sichuan University West China Hospital and hospitals in West China Nephrology Union were retrospectively collected. Noncalciphylaxis patients in hemodialysis center of West China Hospital Sichuan University were randomly selected as the controls. Group 1: The 1:1 matched cases and controls by age (year, within ±3) and duration of hemodialysis (month, within ±20%) as matching factors. Group 2: The controls were matched to cases in a 1:1 ratio by gender and duration of hemodialysis (month, within ±20%) as matching factors. Univariate and multivariate binary Logistic were used regression analysis model, screening for statistically significant variable factors.

**Results:** Most of cutaneous calciphylaxis patients were male and elderly. Group 1: The univariate regression analysis showed that gender, diabetes mellitus, coronary heart disease are significantly associated with calciphylaxis. Laboratory examination results showed that parathyriod hormone (PTH), serum albumin, serum phosphate, C reactive protein (CRP) were significantly with calciphylaxis. Diabetes mellitus, lower albumin, higher serum phosphate and higher CRP were independent risk factors after multivariate analysis. Group 2: The univariate logistic regression analysis showed that age, BMI, coronary heart disease, diabetes were significantly associated with calciphylaxis. Laboratory examination showed that alkaline phosphatase (ALP), PTH, serum albumin and CRP were all significantly associated with calciphylaxis. Diabetes mellitus, lower albumin, higher PTH, and higher CRP were independent risk factors after binary Logistic analysis.

**Conclusion:** Diabetes mellitus and higher CRP, higher PTH, higher serum phosphate, lower albumin, are important high risk factors.

**#6658**

**ORAL HEALTH STATUS IN DIABETIC AND NON-DIABETIC PATIENTS ON MAINTENANCE HEMODIALYSIS TREATMENT**

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**Background and Aims:** Uremic toxins and inflammation influence the oral health in patients on maintenance hemodialysis treatment. The presence of diabetes additionally aggravates the oral status. Aims: To compare the oral health status in diabetic and non-diabetic patients on different dialysis modality treatment.

**Method:** Observational, cross-section, monocentric study was conducted in 72 hemodialysis (HD) patients divided into two groups regarding the presence of Diabetes mellitus (DM). Patients were routinely designed to hemodialysis or hemodiafiltration (HDF) during the previous year of HD treatment. Demographic characteristics as patients age, dialysis vintage, laboratory inflammatory markers as C-reactive protein (CRP), albumin and Interleukin 6 (IL-6) were measured at the start of the study. Also, uremic small and middle molecules as blood urea nitrogen (BUN), creatinine, β2-microglobulin (β2M), myoglobin, albumin, free light chains kapp (FLC-k), and free light chains lambda (FLC-λ) were analyzed. Patients were examined by a dentist specialist scoring the oral hygiene index (OHI) by Greene Vermillion as good, fair and poor. Presence of tooth fillings and extractions, caries, hyperkeratosis, periodontal disease, erosions, ulceration, erythema, pigmementsations, saburral tonque and uremic fetor were notified. Gingival hyperplasia (GH) was scored (1-3) with 3 for worst score and the tooth color was scored 1-3, signing 1-
Results: The patients from group 1 - with DM (N=26) didn’t differ from the non-diabetic group (N=46) in respect of gender, age and dialysis modality but had significantly shorter dialysis vintage (48.68 ± 37.45 vs. 88.13 ± 63.29, \( P = .02 \), respectively). From the inflammatory markers only IL-6 was significantly higher in diabetics (\( P = .03 \)). All the analyzed uremic toxins – small and middle molecules also didn’t differ between the two groups. Diabetic patients were at 3 fold risk for manifestation of fissure, 4 fold risk for pigmentation and 7 fold risk for erythema (OR 3.58; CI:1.017-12.380, \( p = 0.003 \); OR 4.12; CI:0.684-22.870; \( p = 0.02 \), OR 4.84; CI:1.343-17.498, \( p = 0.000 \); OR 7.25; CI:1.123-46.880, \( p = 0.000 \), respectively). GIH was more likely to be present in diabetic patients (35%, 54%, 11% vs 83%, 15, 0%, \( p = 0.000 \), respectively). The presence of hyperkeratosis, periodontal disease erosions, caries, extractions, tooth fillings and the tooth colour didn’t differ between the groups. Diabetics were found with higher percentage of bad oral hygiene index (38% vs 20%), but the overall comparison of OHI showed no significant difference.

Conclusion: Oral health is significantly deteriorated in dialysis patients, especially in those with inflammation. Diabetic patients are at higher risk of developing changes in the oral health status.

Results: Among 70 patients maintained on regular hemodialysis, 42 patients have normal hemoglobin level (above 12 mg/dl with high serum ferritin > 300 ng/ml). They classified into two group: A 26 patients with high ferritin, high TSAT >20%, and normochromic red blood cells, A 16 patients with high ferritin level, low TSAT <20% and hypochromic red blood cells. Among the 26 patients, 17 male and 9 female, and among the 16 patients, 11 male and 5 female. The 26 patients have mean age of (41 +/- 13) and the 16 patients have mean age of (39 +/- 10). No significant difference between the two groups regarding sex and age with p value (0.5 and 0.1 respectively). Assessment of cognitive function by SLUM score revealed regarding normal group (4 have normal score, 18 have mild impairment of cognitive function and 4 have dementia score) and the iron deficient group (4 have normal score, 9 have mild impairment of cognitive function and 3 have dementia score) with no statistically different between the two group (\( P = .6 \)).Regarding quality of life, no statistically difference was found between the two groups regarding physical functioning (\( p = 0.18 \)), role physical (\( p = .11 \)), bodily pain (\( p = 0.33 \)), general health (\( p = 0.5 \)), vitality (\( p = .41 \)), social functioning (\( p = .2 \)), role emotional (\( p = .4 \)), and mental health (\( p = .21 \)).

Conclusion: Non-anemic hemodialysis Patients with Functional iron deficiency has no statistically different regarding neurocognitive function and quality of life from normal iron non-anemic patients.

### #6917

**IMPACT OF FUNCTIONAL IRON DEFICIENCY IN NON-ANEMIC HEMODIALYSIS PATIENT ON NEUROCOGNITIVE AND QUALITY OF LIFE: A SINGLE CENTER CROSS-SECTION STUDY**

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**Background and Aims:** The clinical paradox of high ferritin levels and low TSAT is a condition known as ‘functional iron deficiency.’ This occurs when the body has adequate iron stores, as indicated by high ferritin levels, but the iron is not available for use in the body, as indicated by low TSAT levels. This can be caused by inflammation, chronic disease, or other conditions that interfere with the body’s ability to absorb and utilize iron. Hemodialysis patients may suffer from both absolute and functional iron deficiency. Most studies were directed to study effect of absolute iron deficiency even patients may suffer from both absolute and functional iron deficiency. This paradox is encountered more often in those with inflammation. Diabetic patients are at higher risk of developing changes in the oral health status.

**Conclusion:** Oral health is significantly deteriorated in dialysis patients, especially in those with inflammation. Diabetic patients are at higher risk of developing changes in the oral health status.

### #2736

**THE PHASE ANGLE AS A PREDICTOR OF SARCOPENIA IN NORMOHYDRATED PATIENTS ON HEMODIALYSIS: A MULTICENTER STUDY**

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**Background and Aims:** The skeletal muscle index (SMI) is an impedance parameter that assesses muscle mass, and the phase angle (PA) is inversely related to strength and muscle mass in hemodialysis patients. Both parameters may represent useful and inexpensive tools to identify sarcopenic patients. The phase angle (PA) are evaluated as markers of muscle mass and strength, respectively.

**Method:** The presence of sarcopenia was analyzed in 348 normohydrated patients in 5 hemodialysis centers by means of vector bioimpedance using the BIA101 BIVA PRO equipment. To do this, the skeletal muscle index (SMI) and the phase angle (PA) are evaluated as markers of muscle mass and strength, respectively.

**Results:** Mean SMI and PA were 8.64 ± 1.5 and 5.2 ± 0.9. The mean PA was 5.6 ± 0.9 in those with SMI within normality (9.2 ± 1.9). In moderate and severe sarcopenics patients, the means of SMI (8.9 ± 1.2 vs 7.5 ± 0.9) and PA (5.3 ± 0.86 vs 4.7 ± 0.67) were significantly lower (\( p < 0.001 \)) (Table 1). In patients on standard hemodialysis, the PA (\( P = .02 \)) and the SMI (\( P = .004 \)) were significantly lower. The PA (\( P = .014 \)) and the SMI (\( p < 0.01 \)) were significantly lower in the female gender but the number of sarcopenic patients was higher among the men (\( p < 0.001 \)). The cut-off value of PA, which predicted a higher risk of sarcopenia, was 3.5 in all patients (95% CI, 0.60-0.71; \( P = .0001 \); 100% sensitivity, 96% specificity); 3.55 for men (95% CI, 0.57-0.78; \( P = .003 \); 100% sensitivity, 94% specificity) and 3.65 for women (95% CI, 0.60-0.73 ; \( P = .0001 \); 100% sensitivity, 96% specificity) (Fig. 1).

In the logistic regression analysis, male gender, standard hemodialysis technique, and PA were associated with a higher risk of sarcopenia (Table 2).

**Conclusion:** PA is a good predictor of sarcopenia in hemodialysis patients.
### Table 1:

<table>
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<tr>
<th>SARCOPENIA</th>
<th>N</th>
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<th>Std. Deviation</th>
<th>Std. Error</th>
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(p < 0.001)

### Figure 1:

**Table 2:**

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### #4430

**PREVALENCE OF AMPUTATION IN HD PATIENTS: A DIALYSIS PROGRAM WITHOUT SOCKS**

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1Spain

**Background and Aims:** Peripheral arterial disease affects very commonly CKD patients on dialysis. Frequently such injuries precede severe complications that lead to hospitalizations, amputations and even death.

**Objectives:** Study the prevalence of ulcers and amputation on dialysis, analyze related risk factors, post-surgical results and establish a prevention program.

**Method:** Descriptive, observational, retrospective (7 years), single-center study in patients with CKD on dialysis.

**Results:** 202 patients (12 PD 190 HD), 67 active and 135 off dialysis, 127 men 75 women. Average age 69 years. Average time on dialysis 47 months. Vascular access: 56%, native fistula 37%, catheter 7%, prosthesis. Cause CKD 30.2% ND, 22.8% NAS. 95.54% HBP, 46.53% DM 26.73% Ischemic heart disease, 31.19% chronic ischemia, 26.24% had intermittent claudication, 12.38% had all the comorbidities indicated. Higher comorbidity in males M:F 4:1. 53.47% ex-smokers or active habit.

Ulcers 29.7% (40 men 20 women), 76.67%, diabetics. Half of the patients with DM (48.94%) presented ulcers. The most frequent was vascular ulcer (43.67%) followed by that associated with diabetic foot (26.67%) and pressure ulcer 15%. Amputations (11 major and 13 minor) in 24 patients (16 men 8 women) with a prevalence: overall 12%, DM 22.34%, with ulcers 40% and 46% if they are diabetics. Analytics in amputees. Average: PTH 352 ng/dl, Phosphorus 4.4 mg/dl, Vitamin D 19 mg/dl, Albumin 3.3g/dl, hypercholesterolemia in 20%. 17 patients with chronic ischemia were revascularized (76.47% ended in amputation).

Mortality: 88 patients died (43.56%), of which 41 were patients with ulcers (68.33%) and 20 were amputees (83.33%, 3 early mortality and 17 late mortality).

**Conclusion:** The prevalence of amputations on dialysis is high. Most are male, DM with high cardiovascular comorbidity and a previous history of ulcers. Mortality increases in patients with CKD and ulcers and amputees. There is a need for 11 dialysis without socks® programs for early detection of dialysis ulcers to reduce the incidence of amputees.

### #4310

**DEVELOPMENT OF A HOME DIALYSIS PATIENT SUPPORT SYSTEM WITH EXERCISE FUNCTION PART 1 - SYSTEM DEVELOPMENT AND EVALUATION**

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**Background and Aims:** Although many people use communications infrastructure, direct connection of electronic medical records to the Internet is restricted at medical institutions in Japan. Therefore, patient information outside the medical institution cannot be viewed on systems inside the medical institution. We are developing a safe and secure dialysis support system that connects dialysis patients and medical institutions, which is separate from the system within medical institutions. We have developed a dialysis support system that can share vital data, dialysis records, meal records, etc., between patients and medical institutions.

In this study, to support dialysis patients’ exercise and its continuation, we created an ergo-storage device combining an ergometer and storage device for this research and added functions to the existing dialysis support system. This system with additional exercise function could encourage patients to exercise, store the amount of exercise as the amount of electricity used, this electricity represented a reward to the patient for exercising. These additional features allow the patient to exercise at home on both dialysis and non-dialysis days.
Method: An ergometer was used as exercise equipment for dialysis patients with a hub dynamo to convert the rotations of the ergometer through a belt into electricity. This allowed the dynamo to take over the rotation of the ergometer. In addition, we developed a new circuit that converts the power generated by the dynamo to USB voltage. A simple USB voltage and current checker was added to allow the integrated power to be displayed making it possible to visualize momentum as power generation. In addition, the generated power could be stored in the USB charger. To record the amount of exercise of the patient, the information from the ergometer was output to a tablet in CSV format. This CSV file was sent to the developed system and linked with the patient information in the existing system. This system made it possible to visualize and display the exercise information along with the patient’s daily dialysis information and meal information on the developed system.

Results: Momentum could be converted to electrical energy using the ergo-storage device. The patient could now see and store the amount of exercise they have done, enabling the patient to exercise on both dialysis and non-dialysis days. As the amount of exercise could be visualized at a glance, the patient was encouraged and prompted to exercise daily. In addition, as the amount of exercise could be stored as electricity, this electricity represented a reward to the patient for exercising. The patients reported that it was good to be able to exercise instead of having a quota, and that they were able to continue exercising. Patients began exercising voluntarily instead of being forced to exercise by health care workers. In addition, it was possible to link the system with the patient’s dialysis records and share the amount of exercise, making it easier for medical professionals to understand the patient’s physical condition.

Conclusion: A function that allows dialysis patients to exercise was added to the developed system. Using this system, patients and medical institutions could share dialysis records, such as the patient’s amount of exercise. The patients could exercise on both dialysis and non-dialysis days, and the amount of exercise and dialysis records could be shared with medical institutions. In addition, the amount of exercise was stored as electricity, which increased the patient’s motivation to exercise. The patients began to exercise voluntarily. This research was supported in part by Gakushin Kaken (JP20H03982).

ULTRASOUND EXAMINATION OF THE SUBCUTANEOUS PERITONEAL CATHETER TUNNEL IN CASES NOT RELATED TO INFECTION
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Background and Aims: According to the guidelines of the International Society of Peritoneal Dialysis possible indications of ultrasound (US) examination of the catheter tunnel are suspected tunnel infection, initial evaluation of exit-site infection without clinical signs of tunnel involvement, follow-up of exit-site and tunnel infection after treatment and relapsing peritonitis episodes. Other authors suggest US examination of the subcutaneous tunnel in every case of peritonitis. We analyzed the associations between US findings at the catheter
### Table 1: Association between ultrasound findings and their clinical impact.

<table>
<thead>
<tr>
<th>Ultrasound findings</th>
<th>Clinical impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance of the external cuff from exit site</td>
<td>Risk of cuff infection or cuff extrusion</td>
</tr>
<tr>
<td>Extend of leakage</td>
<td>Reduction of filling volume / need of dialysis interruption</td>
</tr>
<tr>
<td>Size of hematoma</td>
<td>Need of surgical reintervention</td>
</tr>
<tr>
<td>Proximity of the inferior epigastric artery</td>
<td>Risk of vascular lesion at catheter removal</td>
</tr>
<tr>
<td>Inclination of the catheter</td>
<td>Risk of catheter dislocation/malfunction</td>
</tr>
<tr>
<td>Direction of the catheter</td>
<td>Risk of catheter dislocation/malfunction</td>
</tr>
<tr>
<td>Position of the inner cuff</td>
<td>Risk of adhesion/malfunction in the case of intraabdominal position</td>
</tr>
</tbody>
</table>

### Method:
The subcutaneous tunnel of the peritoneal catheter was examined with a linear probe of 6.5-10 MHz having covered the exit site with a transparent adhesive film-dressing. For the retrospective investigation covering the last 10 years, we selected peritoneal dialysis patients who performed an US examination without clinical signs or suspect of exit site or tunnel infection. During the US examination, the distance of the external cuff from the exit site, the presence and extend of leakage or size of a hematoma (along the catheter and at the surgical site), the proximity of the inferior epigastric artery to the catheter, the configuration of the subcutaneous tunnel (including inclination and direction of the catheter at the entrance into the peritoneal cavity) and the position of the inner catheter cuff were documented.

### Results:
Several US findings were found to be associated with a specific risk or need of intervention in the follow up of the patient. The following table reassumes the US findings and the respective clinical impact.

### Conclusion:
US findings documented during the examination of the catheter tunnel in cases related to infection have a certain clinical impact due to their association to a specific risk or need of intervention, and therefore should not be overseen during the examination.

### #6746

**SAFETY OF ANGIOTENSIN RECEPTOR-NPRLISIN INHIBITOR IN PERITONEAL DIALYSIS PATIENTS WITH HEART FAILURE: A MULTI-CENTER COHORT STUDY**

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Pimenta, G. Afonso, R: both authors contributed equally

### Background and Aims:
Anxiety between the two groups considered prior to psychological support was significantly higher in patients on peritoneal dialysis than in patients on hemodialysis (P = .31). The decrease of State Anxiety was bigger in patients on peritoneal dialysis (P = .50) than in patients on hemodialysis (P = .38). There was no significant difference between patients supported by in-person or on-line therapy. Further randomized studies are warranted to confirm safety and clarify the benefit of this therapy in PD patients with HFrEF.

### Conclusion:
Our results suggest that ARNI can be used safely in patients under PD with major cardiovascular risk. Further randomized studies are warranted to confirm safety and clarify the benefit of this therapy in PD patients with HFrEF.

### #4650

**EVALUATION OF PSYCHOLOGICAL SUPPORT IN HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS**

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### Background and Aims:
Chronic kidney disease is one of the chronic diseases with the biggest social impact. The quality of life of the patients with chronic kidney disease stage V is strongly affected by the recommended therapies. The choice between hemodialysis, peritoneal dialysis, transplantation or conservative management of chronic kidney disease is shared between clinician and patient. Caring of chronic kidney disease and especially renal function replacement treatment involves a commitment to the patient and family tissue that have an important influence on patient anxiety. Such situation alters the State-Anxiety, that expresses a perception connected to a specific context and it overlaps with Trait Anxiety; that evaluates relatively stable aspects of being prone to anxiety. Anxiety can be split into two components, State Anxiety, expressing a context-related feeling, and Trait Anxiety, expressing an intrinsic personality condition.

The aim of this study was to investigate the presence of anxiety in patients on hemodialysis and peritoneal dialysis and the benefit that psychological support (either in-person or on line) could produce in these populations.

### Method:
The study group enrolled 24 patients: 13 were under haemodialysis and 11 were peritoneal dialysis patients. All patients were older than 18 years old and were followed at the Nephrology Hospital San Bortolo in Vicenza. Patients underwent eight sessions of psychological support. The first and the eighth sessions have been held in-person, while the others either in-person or on-line according to the patients’ preference. Nephrologists select patients to be treated according to their needs of psychological support. The State-Trait Anxiety Inventory (STAI), which evaluates Trait and State Anxiety, was submitted during the first and eighth sessions. Statistical analysis was performed by software SPSS.

### Results:
The two groups were homogeneous for age, sex and comorbidities. There was no significant difference in the components of Trait and State Anxiety between the two groups considered prior to psychological support therapy (P = .38 and P = .64, respectively). Trait and State Anxiety decreased significantly after treatment both in hemodialysis and peritoneal dialysis (both p < 0.001). Trait Anxiety had a greater decrease compared to State Anxiety in both groups. The decrease of Trait Anxiety was similar in the two groups (P = .31)(Fig. 1). The decrease of State Anxiety was bigger in patients on peritoneal dialysis compared to hemodialysis patients: these patients had a greater benefit from the psychological support (P = .05)(Fig. 1). Furthermore, there was no significant difference between patients supported by in-person or on-line treatments (P = .68).

### Conclusion:
Psychological support in patients with renal replacement treatment leads to a reduction in Trait Anxiety and State Anxiety, regardless if the replacement therapy is hemodialysis or peritoneal dialysis. This allows patients to better tolerate the burden that the disease entails and to improve compliance to treatment. Psychological support could also help physicians in order to obtain better results with a stronger therapeutic alliance.
**Figure 1:** Comparison in terms of Trait and State-Anxiety in Peritoneal dialysis (PD) and Hemodialysis (HD) patients. We analysed the difference (delta) in STAI results for Trait and State Anxiety between the first and at the and eighth sessions.

**#5941**

**SERUM LEPTIN AND MALNUTRITION IN PERITONEAL DIALYSIS PATIENTS: A CONNECTION YET TO BE FOUND**

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Torres Novas, Nephrology, Torres Novas, Portugal

**Background and Aims:** Leptin is a hormone responsible for the modulation of the satiety signals and that it is known for being increased in patients undergoing Peritoneal Dialysis (PD) treatment. Nevertheless, conclusions about its role in the malnutrition associated with this technique remains to be done. Our study aimed to characterize the nutritional state of a Portuguese program of PD and to establish the impact that leptin levels had on it.

**Method:** A cross-sectional study was performed involving 28 patients of a PD program. To characterize the patients nutritional status we collected the following data: anthropometric measurements (weight, body mass index (BMI), fat tissue index and lean tissue index using Fresenius® Body Composition Monitor), analytical values (albumin, total proteins, total cholesterol, high-density lipoprotein cholesterol, low-density cholesterol, triglycerides, leptin serum levels), protein metabolism (normalized protein catabolic rate (nPCR), normalized diastylate protein loss (nEPL), normalized urine protein loss (nUPL), normalized total protein loss (nTPL) and normalized dietary protein requirement (nDPR)) and peritoneal dialysis adequacy (total, renal and peritoneal kT/v; total, renal and peritoneal creatinine clearance). The collected data were statistically analyzed and correlations were made using Mann-Whitney U test and Spearman test, depending on the variable type.

**Results:** 7 (25%) patients were females, and the mean age was 59.5 years old (± 14.31). The mean dialysis vintage was 27.04 months (± 20.14) and the majority (n=23, 82.1%) preformed automated peritoneal dialysis (APD). Regarding the nutritional status, the mean BMI, FTI and LTI was 26.64 kg/m2 (±4.39), 14.24 kg/m2 (±5.47) and 11.62 kg/m2 (±2.52) respectively. 57.1% (n=16) had serum albumin below 3.5 mg/dL, with a mean phosphorus of 5.01 mg/dL (±0.72) and a mean leptin of 28.88ng/ml (±28.44). The serum leptin was 5.4 times higher than the adjusted value for BMI in the population without kidney disease. The adjusted serum leptin for BMI was different between sex (U=15, P = .001) and it was positively correlated with total (ρ=0.47, P = .012) and high-density lipoprotein (HDL) cholesterol (ρ=0.535, P = .003). It was not associated with the protein metabolism (nPCR, nEPL, nUPL, nTOL and nDPR), albumin or total proteins and PD adequacy.

**Conclusion:** Leptin values independent of BMI are significantly higher amongst patients on PD. Alike the healthy population, women on PD are also prone to have higher serum leptin values. Although studies are still controversial about the association between this hormone and cholesterol, in this population there is a positive correlation. As so, hyperleptinaemia cannot yet be associated with the malnutrition that is generally present amongst PD patients, but it must be considered as a contribute to the already known increased cardiovascular risk.

**#5992**

**PERITONEAL DIALYSIS-RELATED PERITONITIS: A SINGLE CENTER EXPERIENCE**

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1Zvezdara University Medical Center, Clinical Department for Nephrology and Dialysis, Belgrade, Serbia, 2University School of Medicine, Belgrade, Serbia and 3Medical Academy, Serbian Medical Association, Belgrade, Serbia

**Background and Aims:** Peritonitis is a common and severe complication in Continuous ambulatory peritoneal dialysis (CAPD). A high peritonitis rate affects PD patients' technique survival and mortality. The aim of this retrospective study is to assess epidemiological aspects, microbiology presentation with antibiotic resistance and clinical outcomes for patients with acute CAPD peritonitis during 5-year period.

**Method:** The study included all patients treated by CAPD between the 1st of January 2017 and 1st of January 2022 in the Clinical Hospital Center Zvezdara. We included prevalent patients on CAPD, and analyzed demographic, clinical and microbiological data, and patient’s outcomes during 5 year period. The data was collected from patient records, medical history and processed in SPSS.

**Results:** This study included 119 patients treated by PD of which 24 (8.13%) had one or more acute episodes of CAPD peritonitis in the designated period. The mean age of the population was 69±9 years, 54% were male, 20% had diabetes mellitus and 60% arterial hypertension as cause of end stage renal disease. During follow up it was diagnosed 41 episodes of CAPD peritonitis. The main characteristics of patients with peritonitis were turbid liquid (100%), abdominal pain (73%) and fever (43%). Gram staining revealed that 53% were gram-positive, and 10% were gram-negative. The most frequent bacterial specimen was Staphylococcus epidermidis (11) followed by Streptococcus viridans (6), sterile culture (9), Staphylococcus aureus (3) and other organisms less than 2 episodes. The peritonitis rate was 1 episode per 27.36 patient-months, or 0.44 episodes per patient year. Resistance to Ampicillin and Penicillin occurred most often. In 2 patients, PD peritonitis was present once each, with multi-resistant bacteria: Klebsiella pneumoniae which was treated with parental administration of Tigacycline and Methicillin-resistant Staphylococcus aureus (MRSA) which was treated with parenteral administration of Moixifloxacin and Clindamycin. Out of 24 patients, 2 (8.33%) had 4 episodes of peritonitis, 3 (12.5%) had 3 episodes of peritonitis, 25% had 2 episodes of peritonitis, and the rest (54.16%) were had only one each. Only one patient had an episode of relapsing peritonitis. During 5-year period, 1 (4%) patient died of acute CAPD peritonitis caused by Proteus mirabilis, 7 (29%) died of other causes, 11 (46%) were transferred to hemodialysis and 5 (21%) are still receiving treatment by CAPD modality. CAPD peritonitis was the reason for technical failure in 20 patients.

**Conclusion:** PD-associated peritonitis is serious infective complication which could influence the outcome of PD patients, including technique survival. The rate and outcomes of peritonitis in our patients were slightly above of current recommendations.
ANEMIA IN PERITONEAL DIALYSIS
Andrea Alelo Oltra, Diana Manzano, Adoración Martínez, Ines Llamas Sarria, Jose Luis Albero Dolon, Pedro Pablo Ortuño, Manuel Lanuza, Julian Navarro Martinez, Pablo Navarro Martínez and Juan Cabezuelo-Romero
Spain

Background and Aims: Anemia is one of the most frequent complications of chronic kidney disease (CKD), affects quality of life and increases morbidity and mortality. Prevalence of anemia in patients on peritoneal dialysis (PD) is 83% according to the RIKAS study. Diagnosis of anemia in CKD is set at a hemoglobin (Hb) below 13 g/dL in men and less than 12 g/dL in women. These values serve to define the diagnosis, but not to indicate treatment. Treatment is based on the use of erythropoiesis stimulating agents (ESA) and iron therapy. Absolute iron deficiency (ferritin less than 100 ng/ml and transferrin saturation index (TSAT) less than 20%) and functional iron deficiency (TSAT less than 20% with normal ferritin), require correction with oral or intravenous iron before the use of ESA. Treatment with ESA is indicated when Hb is below 20% with normal ferritin), require correction with oral or intravenous iron.

Results: N = 58 patients, 64% men and 36% women. The mean age was 61.3 +/- 15.54 years. 31% of patients were CKD secondary to glomerulonephritis (predominant etiology). 5% had no cardiovascular risk factors (CVRF), 48% between one and two and 47% more than three. 74% on continuous ambulatory peritoneal dialysis (CAPD). Mean time of dialysis 28.74 +/- 25.05 months. Mean residual diuresis in 24 hours 1199.22 +/- 703.14 cc.

Prevalence of anemia 74%. Mean Hb of 10.97 +/- 1.29 g/dL with 78% of patients with values between 10-12 g/dL. Mean ferritin of 356.79 +/- 226.84 mg/dL with 79% of patients between 100-500 mg/dL. 83% received treatment with ESA, 33% with intravenous iron. No patient received oral iron. 4 patients needed of blood transfusion and 3 of them due to bleeding (2 gastrointestinal bleeding and 1 urinary bleeding).

Conclusion: Despite having more patients on CAPD, the number of peritonitis episodes per patient-year were in a decreasing trend. This was the result of the implementation of empirical first line intra-peritoneal antibiotics as part of the CAPD Peritonitis Management Protocol in 2015 and Decontamination Protocol in 2016.

We observed a statistically significant association between higher residual diuresis volume and adequate anemia control (P = .042) and between lower creatinine values and target Hb values (P = .0005). No statistically significant association was observed between adequate anemia control and type of dialysis (r= 0.106), time on dialysis (P = .28), sex (P = .224) and DM (P= 0.139).

20 YEARS’ EXPERIENCE OF PERITONEAL DIALYSIS IN SARAWAK, MALAYSIA
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1Sarawak General Hospital, Nephrology, Kuching, Malaysia, 2Sarawak General Hospital, Kuching, Malaysia and 3Sarawak General Hospital, Nephrology, Kuching, Malaysia

Background and Aims: Peritoneal dialysis is a modality of renal replacement therapy first introduced in the 1960s. In the event of the recent COVID 19 pandemic, peritoneal dialysis is gaining popularity due to the increased preference of home dialysis. Sarawak is the largest state in Malaysia with a population of more than 2 million. Unfortunately, 13% of households in the state are living in poverty. We present our experience with continuous ambulatory peritoneal dialysis (CAPD) for the past 20 years in a geographically and socioeconomically challenging region.

Method: Sarawak General Hospital is the centre of referral for Tenckhoff catheter insertion from other districts in Sarawak. This is a retrospective record review of all CAPD patients who were under our clinic follow up from 2001 to 2022. Data examined included patient’s demographic data, incidence of peritoneal dialysis related peritonitis and their outcome.

Results: All of the patients on CAPD were recorded by December of each year since we started our service in 2001 which shows a rising trend of patients on CAPD, with the highest in December 2022 at 399 patients. The number of patients with dialysis related peritonitis was also collected. Despite having more patients on CAPD, the number of peritonitis episodes per patient-year were in a decreasing trend. This was the result of the implementation of empirical first line intra-peritoneal antibiotics as part of the CAPD Peritonitis Management Protocol in 2015 and Decontamination Protocol in 2016.

Conclusion: Despite the headwinds of geographic and socioeconomic challenges, the number of patients on CAPD is on the rise. Over the years, peritonitis rate declined approaching to 0.2 episodes per patient-year. This was made possible with the introduction of local decontamination protocol and CAPD peritonitis management protocol, which helped improve the life expectancy and health of renal patients in the region.
ESTIMATION OF RENAL KT/V FROM 24-HOUR URINE VOLUME AND UREA DISTRIBUTION VOLUME IN PERITONEAL DIALYSIS

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Background and Aims: Residual renal function is an important factor in peritoneal dialysis (PD) regarding technical survival and implementation of incremental therapy schemes. The aim of the retrospective study was to develop an estimation formula of renal KT/V urea in PD based on urine output and anthropometric data.

Method: In 235 adult PD patients (151 males, 84 females, median age 66 years, median BMI 26.0, diuresis > 100 ml/day) urine output was registered together with anthropometric and lab data during the first peritoneal equilibration test. The dose of furosemide therapy was noted. Urea distribution volume calculated using the formula of DuBois. Measurement of urea in blood and urine was performed by a standard kinetic test with urease.

Results: 24-hour urine volume ranged from 100 to 3800 ml (median 1150 ml), similar in both sexes. Renal KT/V urea showed a significant linear correlation to daily urine volume ($r=0.78$, $p<0.01$) independent from sex and diuretic dose: renal KT/V urea = $5.116 + 0.0221 \times$ 24-hour urine volume (renal KT/V urea in liters/week, 24-hour urine volume in ml). Urea distribution volume varied between 24 and 60 liters (median 36.4 liters), and calculated renal KT/V ranged from 0.05 to 2.57 (median 0.84). Estimated renal KT/V, based on the before mentioned equation divided by urea distribution volume, correlated significantly to calculated renal KT/V ($r=0.75$, $p<0.01$). The goodness of fit analysis showed a mean absolute error of 0.24. The Bland-Altman Plot confirmed a tendency of over-estimation for renal KT/V < 1.0 and under-estimation for higher renal KT/V. A restriction of the analysis to 24-hour urine volume up to 1500 ml ($n=142$ patients, median age 69 years, BMI 25) resulted in an improvement of renal KT/V estimation (goodness of fit analysis: mean absolute error 0.20).

Conclusion: The estimation of renal KT/V in PD patients seems to be feasible utilizing 24-hour urine volume and anthropometric data.
METABOLIC PROFILING IN CHILDREN WITH END STAGE RENAL DISEASE ON PERITONEAL DIALYSIS: PRELIMINARY RESULTS OF AN ONGOING PRESPECTIVE STUDY

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Background and Aims: Peritoneal dialysis (PD) is the main renal replacement treatment for children and adolescents with end stage kidney disease (ESRD). Peritoneal fibrosis is a major complication in long-term PD patients. Aim of the present study is to record the metabolic fingerprint of children on PD and to investigate its correlation with PD history and dialysis adequacy as well as the emergence of potential biomarkers that could detect early or predict peritoneal dysfunction.

Method: Serum samples from 15 patients undergoing peritoneal dialysis were analyzed. Two targeted LC-MS methodologies were used for the determination of 107 metabolites in total. The obtained results were compared based on demographic and clinical parameters, both before and after the dialysis procedure. Serum samples were further divided into subgroups, based on PD duration, creatinine clearance, sex, anuria. Regarding metabolic technologies used, all samples were analyzed by a hydrophilic interaction liquid chromatography coupled to mass spectrometry (HILIC-MS / MS) method previously developed and validated in our laboratory for the simultaneous determination of amino acids and their derivatives in biological fluids. Also, high flow analysis was carried out (LC-qTOF analysis – HPLC/MS). The evolution of this IP was favourable in 91.5% of cases with a response to antibiotics. 7% of episodes were relapsing of which five were during the first episode of IP. IP recurrence occurred in one patient. A catheter change was required over 16 episodes of IP, and hemodialysis sessions were necessary in 27 patients, temporary in 10 patients. The multivariate study identified the following predictive factors of IP: poor adherence to treatment (OR = 3.851; 95%CI: 1.369-10.837; P = .011) and weight less than 15 Kg (OR = 6.314; 95%CI: 1.333-29.897; P = .02).

Conclusion: Considering the high risk of peritonitis in children on PD, it is imperative to establish a primary prevention based on training of the caregivers.
Abstract

child’s caregivers and families. Continuous quality improvement program and PD technique are systematically reviewed in every peritonitis episode. Nutritional management of children prior to the start of PD is necessary to limit the risk of IP.

#5521
TENCKHOFF CATHERET EXIT-SITE INFECTION BY ACTINOMYCES ODONTOLYTICUS: A RARE CASE

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Background and Aims: Actinomyces odontolyticus is an anaerobic Gram-positive bacteria, which can be found among the commensal flora of the mouth and oropharynx. Diagnosis of infections due to this microorganism can be difficult because of its rarity, indolent course and lack of specific symptoms. Only one case of exit-site infection (ESI) due to Actinomyces odontolyticus in a patient on continuous ambulatory peritoneal dialysis (CAPD) has been reported. This work aims to report a case of ESI due to this rare agent.

Method: We present a case of Tenckhoff catheter ESI due to Actinomyces odontolyticus in a patient on CAPD.

Results: Case report: We report the case of a 26-year-old woman with a personal history of dyslipidemia, arterial hypertension and end-stage chronic kidney disease caused by Alport Syndrome in a CAPD program since April 2016. In June 2020, the patient presented an episode of refractory ESI due to methicillin-sensitive Staphylococcus aureus and was submitted to a shaving of the external cuff of the Tenckhoff catheter, with good subsequent evolution. The patient had no complications related to the catheter until April 2021, when she presented purulent drainage through the exit-site associated with erythema of the surrounding area. The consecutive exit-site swabs were negative. She underwent antibiotic therapy with ceftriaxone for 2 weeks with apparent resolution. However, in May 2021, the patient presents again erythema and purulent drainage and, at that time, a rare agent was isolated in the swab: Actinomyces odontolyticus with resistance to penicillin, amoxicillin, ceftriaxone and cefoxoxame. Given this isolation, the patient was treated with doxycycline 100mg every 12 hours for 4 weeks. The evolution was favorable with resolution of the infection and absence of recurrence for a 6-month follow-up. At the end of this follow-up time, the patient was transplanted.

Conclusion: Actinomyces odontolyticus is a bacteria of the commensal flora of the oral cavity and upper gastrointestinal tract, which can acquire pathogenicity in situations of impaired mucosal integrity and in immunosuppressed patients. Infections caused by this agent are rare and represent a diagnostic challenge due to its growth in an anaerobic environment and prolonged isolation time (5 days to 4 weeks). The immunosuppression conferred by chronic kidney disease and the history of external cuff shaving may have propitiated the infection by this rare opportunistic agent in our patient. The ESI presented for the patient in the previous month, which did not have an identified agent, was possibly caused by Actinomyces odontolyticus, but it was not isolated probably due to culture difficulties. The treatment of Actinomyces infections is generally conservative with 2 to 4 weeks of high-dose of intravenous penicillin, followed by 2 to 6 months of oral antibiotic therapy. In case of allergy, regimens with ceftriaxone, doxycycline, clindamycin or carbapenems are recommended. There is no consensus on the duration of treatment, with some authors recommending a minimum of 2 to 6 weeks. The mentioned patient was treated with 4 weeks of doxycycline according to the sensitivity test and the result was favorable, without the need to remove the catheter.

#6192
COGNITIVE DYSPUNCT ON AND ASSOCIATED RISK FACTORS IN PERITONEAL PATIENTS

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Background and Aims: Patients with cognitive dysfunction (CD) are at greater risk of having a poor quality of life, hospitalization and mortality. Although CD in chronic kidney disease is current, most of the studies performed are cross-sectional. The aim of this cross-sectional study was to determine the presence of CD in the patients on peritoneal dialysis (PD) and to identify possible risk factors associated with CD.

Table 1: MMSE in relation with WTKt/V in PD patients.

<table>
<thead>
<tr>
<th>WTKt/V</th>
<th>N</th>
<th>Mean±SD</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.25</td>
<td>10</td>
<td>22.6±0.4,115</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>&gt; 2.25</td>
<td>19</td>
<td>26.7±1,843</td>
<td>23</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>25.3±4.3,425</td>
<td>18</td>
<td>29</td>
</tr>
</tbody>
</table>

Method: We performed a study to evaluate the CD of 30 PD patients in our institution using the mini-mental state (MMSE), and a score of <25 was considered to indicate cognitive dysfunction. Demographic, clinical and laboratory parameters, adequacy of dialysis and drugs were analyzed. The statistical analysis included the chi-square test, t-test of independent samples, Mann-Whitney, and correlation.

Results: We evaluated 30 patients mean age of 57.27 years (SD=±12.086); 56.7% were male. About 66.7% of our patients were in marriage, 73.3% were not actively working. 13.3 had a lower level of education, and 56.7% lived in a city. The most prevalent comorbidities were glomerulonephritis and hypertension, both with 30.0%. 19 (57.6%) patients had average fast membrane characteristics. 15 of them (50%) had a daily dose of calcium phosphate binder >2g. MMSE test with a score lower than 25 was present in 36.7% of patients (IQR=4). Statistical analysis revealed a positive correlation between MMSE and weekly total Kt/V area index (WTKt/V), and the t-test of independent samples showed that patients with better MMSE score values have significantly higher average WTKt/V values (t=3.062, p<0.011).

Conclusion: MMSE test with a score less than 25 was present in 36.7% of patients and patients with better MMSE scores have significantly higher average WTKt/V values.

#3493
INCIDENCE, PREVALENCE, DEMOGRAPHIC PROFILE, AND CLINICAL OUTCOMES OF PERITONEAL DIALYSIS IN A TERTIARY MEDICAL CENTER IN THE PHILIPPINES

Keth Ivory Dela Cruz1 and Clarissa Arsolon2
1 Southern Philippines Medical Center, Department of Internal Medicine - Section of Nephrology, Davao City, The Philippines and 2 Southern Philippines Medical Center, Department of Internal Medicine - Section of Adult Nephrology, Davao City, The Philippines

Background and Aims: Chronic Kidney Disease (CKD) has emerged as a global public health burden. As one of the treatment options for CKD-5, peritoneal dialysis is underutilized, accounting for only 11% of the global distribution of renal replacement therapy (RRT). In the Philippines, PD accounts for only 4.2% [1] of all dialysis. This is perplexing because PD has several advantages over hemodialysis including better survival in the first few years of RRT, better survival of PD to HD than HD to PD [2], more cost-effective [3], can be done at home without sophisticated equipment, and feasible in remote areas. This study aims to characterize the incidence, prevalence, demographic profile, and clinical outcomes of the PD patients in our center to uncover strengths, weaknesses, and roadblocks for a stronger “PD First” program in the Philippines.

Method: Descriptive retrospective chart review of 146 PD patients of the Southern Philippines Medical Center from January 2018 to September 2022.

Results: There were a total of 146 adult patients enrolled to the PhilHealth PD Z-package from January 2018 to September 2022. Majority of the patients were aged 50-59 years old (20%), followed by 40-49 years old (19%), and 60-69 years old (19%), mostly male (57%). Predominant etiology of CKD-5 was Chronic Glomerulonephritis (41%), followed by Diabetic Nephropathy (30%), and Hypertensive Nephrosclerosis (19%). Incidence rate of PD was 44%, 22%, and 41% for 2019, 2020, and 2021 respectively. The prevalence rate of PD was 64%, 56%, and 59% for 2019, 2020, and 2021 respectively. The PD peritonitis rate was 1.25, 0.4, 0.24, and 0.3 episodes per patient year in 2018, 2019, 2020, and 2021 respectively. Out of the 146 PD patients, 41 (28%) are still on active PD, 1 (0.67%) underwent Kidney Transplantation, 38 (26%) had PD Technique Failure from peritonitis and catheter malfunction, and 66 (46%) expired due to death at home, sepsis, and acute coronary syndrome. Among those who expired, 22 (33%) were PD First and 44 (67%) were shifted from HD. There was a significant difference in the primary outcomes between those who were PD First and shifted from HD, with a p-value of 0.048.

Conclusion: PD First is infrequently practiced in our center. There is a significant difference in the number of those who were PD First, and those who were shifted from HD. There is a higher rate of mortality among those who were shifted from HD to PD compared to those who were PD First. PD- peritonitis is the number one cause of PD Technique Failure followed by issues
with the PD Catheter. To improve the mortality rate of our CKD-5 patients, it is recommended to do PD First, rather than HD to PD, while awaiting transplant.

REFERENCES

3. Bayani DBS, Almirol BJQ, Uy GDC. HCO3 after: 26.5 (24, 29) mEq/L. There was a statistically significant increase in the arterial HCO3- concentration between the values before and after the procedure [HCO3 before:25.4 (22, 28), HCO3 after:26.5 (24, 29) mEq/L; P = .023]. Likewise there was a statistically significant increase in BE with median values before the procedure 1 (-1.2, 2.9) and after the flushing 2 (-0.6, 3.8), P = .018. Even though there was a statistically significant increase in the bases expression of the acid base balance of the patients there wasn’t any statistically significant alterations in pH levels i.e. Alkalemia (pHbefore=7.41, pHafter=7.42 – P = .35) or pCO2 levels i.e. Compensatory Respiratory Acidosis (pCO2pH=40, pCO2pH+2=40 – P = .179) nor to the levels of ionized calcium.

Conclusion: Flushing of peritoneal cavity using peritoneal dialysis solution with bicarbonate as a buffer is safe and in this study was not correlated with the development of metabolic alkalosis.

KIDNEY TRANSPLANTATION

E1 - EXPERIMENTAL, IMMUNE-TOLERANCE & XENOGENIC TRANSPLANTS

#3853
THE EFFECT OF PERITONEAL CAVITY FLUSHING ON ACID BASE BALANCE OF PERITONEAL DIALYSIS PATIENTS
Marios Theodoridis, Stylianos Panagousou, Nikos Margaritis, Charalampos Dimitrakopoulos, Triantafyllia Bounta, Efthimia Mourvati, Evaggelia Charitaki, Konstantia Kantartzii and Elias Thodos
University Hospital of Alexandroupolis, Nephrology, Alexandroupolis, Greece

Background and Aims: Flushing peritoneal cavity with dialysis fluid with short time dwells it is a necessity in some cases for peritoneal dialysis patients. Such cases are overhydration with pulmonary congestion or peritonitis before the initiation of antibiotic treatment as an effort to reduce pain. The aim of this study was to investigate the effect of frequent exchanges with peritoneal dialysis (PD) fluid with bicarbonate as a buffer on acid base balance of peritoneal dialysis patients.

Method: This is a single center cohort study of 18 stable PD patients (m=10, f=8). Their median age was 57 (47, 71) years, their median PD duration was 33 (16, 89) months and they all fulfill the criteria for achieving adequacy targets [median Kt/V 2.17 (1.99, 3.3)] with good nutrition markers [median albumin levels 3.9 (3.6, 4) gr/dl]. A sample of arterial blood gas (ABG) was taken from the patients before the procedure and after full drainage of the peritoneal cavity. The procedure included 4 times flushing of 1000 ml of dialysis fluid with bicarbonate every 15 minutes. In the peritoneal cavity each time. At the end of the procedure a new blood sample for ABG was taken. We used PD solution with bicarbonate as a buffer (34 mmol/L). We estimated the alterations of pH, of bicarbonate (HCO3-), of pCO2, of Base Excess (BE), of ionized calcium ([Ca++]) and lactate (Lac) levels after the procedure [HCO3 before:25.4 (22, 28), HCO3 after:26.5 (24, 29) mEq/L; P = .023]. Likewise there was a statistically significant increase in BE with median values before the procedure 1 (-1.2, 2.9) and after the flushing 2 (-0.6, 3.8), P = .018. Even though there was a statistically significant increase in the bases expression of the acid base balance of the patients there wasn’t any statistically significant alterations in pH levels i.e. Alkalemia (pHbefore=7.41, pHafter=7.42 – P = .35) or pCO2 levels i.e. Compensatory Respiratory Acidosis (pCO2pH=40, pCO2pH+2=40 – P = .179) nor to the levels of ionized calcium.

Conclusion: Flushing of peritoneal cavity using peritoneal dialysis solution with bicarbonate as a buffer is safe and in this study was not correlated with the development of metabolic alkalosis.

#5189
THE ASSOCIATION BETWEEN CD86 +1057G>A POLYMORPHISM AND ACUTE KIDNEY ALLOGRAFT REJECTION AMONG EGYPTIAN PATIENTS
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Urology and Nephrology Center, Mansoura University, Mansoura, Egypt

Background and Aims: T-cell mediated immune response is crucial in kidney transplantation and plays an important role in allograft rejection. CD86 is a costimulatory molecule that participates in the regulation of T-cell lymphocytes activation. Single nucleotide polymorphisms (SNPs) located in this gene have been studied with inconsistent results. The aim of the study was to examine the association between (rs1129055:G/A) polymorphism in the CD86 gene and the development of acute renal allograft rejection among Egyptian patients.

Method: In this non-concurrent cohort study, we included a group of 50 kidney transplant recipients diagnosed by acute allograft rejection (AR) (which was defined by clinical diagnosis, elevated serum creatinine >30% of basal line in the absence of other pathology including infection, urinary tract obstruction, allograft artery stenosis or calcineurin toxicity and responded to treatment by immunosuppression and was confirmed by positive biopsy that was graded according to Banff classification) and another matched group of 50 kidney transplant recipients without AR and all of the 100 patients were genotyped by direct sequencing for CD 86 polymorphism (rs1129055:G/A) by TaqMan genotyping assay.

Results: The genotypic frequencies of CD 86 rs1129055 SNP in the acute rejection group were 72% GG, 28% AG and 0% AA while in the no rejection group it were 66% GG, 30% AG and 4% AA. The AA genotype and A allele at position +1057 in the CD86 gene were more frequent in patients without AR (4% and 23.4%, respectively) compared with those showing an AR (0% and 16.2%, respectively). The odds of acute rejection weren’t statistically significant either in dominant or recessive model (P = 0.665 and 0.475 respectively).

Conclusion: These results suggest that AA genotype and A allele of CD86 +1057G>A polymorphism may provide a nonsignificant protection against acute kidney allograft rejection among Egyptian patients.
Background and Aims: Young adulthood is a sensitive developmental period, and the psychosocial impact of kidney failure in this group is implicated in the observed high risk for transplant loss and death. In the Surveying People Experiencing young Adult Kidney failure (SPEAK) study we described differences in life-course outcomes, worse mental wellbeing and twice the likelihood of psychological disturbance among UK young adults with kidney failure (transplant or dialysis) compared to the general population. There have been no longitudinal studies investigating the natural history of these outcomes as young adults mature and get older. We undertook SPEAK-2 as a five-year follow-up study to address this.

Method: In this prospective observational study, respondents to SPEAK were invited to complete a revised online survey. PPI guided components of the original survey to amend. We analysed how psychosocial health had changed among respondents between studies using the paired t-test, Wilcoxon signed-rank test and McNemar’s test for continues parametric and non-parametric data, and binary data respectively. We compared responses to age-matched respondents of the Health Survey for England 2012 using regression. Responses were weighted to increase generalisability.

Results: We had 158 survey responses. The analysis of psychological health change over time is presented in Table 1. A greater proportion of participants had evidence of psychological morbidity (45% versus 24% in the original SPEAK study; p<0.001). They had inferior mental wellbeing (Warwick-Edinburgh Mental Wellbeing Scale [WEMWBS] β =-1.76; 95% CI, -3.27 to -0.25; P = .02). No differences were identified in domains including quality of life (EQ5D).

Key outcomes of the comparison to the age-matched general population are presented in Table 2. Respondents were less likely to be married or have children and were more likely to be living with their parents. They were almost 15 times more likely to report being unable to work due to health. Respondents had poorer quality of life and poorer mental wellbeing compared to the general population. They also five times greater odds of having psychological problems or mental ill health.

Conclusion: We report the first longitudinal study of the psychosocial health of a cohort of young adults with kidney failure as they age and mature. Over five years, we observed worse psychosocial health in terms of mental wellbeing and psychological morbidity. Respondents also lagged behind their peers in terms of life-course and psychosocial outcomes. Dedicated long-term follow-up is needed to clarify the extent and duration to which kidney failure in young adulthood impacts life participation and psychosocial health in the long term. Regardless, the degree of psychosocial ill health we have described warrants urgent increased support for this group.

Table 1: Changes in self-reported psychologic health outcomes among SPEAK-2 respondents between studies.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>Possible range</th>
<th>SPEAK-2 median (IQR)</th>
<th>proportion (n)</th>
<th>SPEAK median (IQR)</th>
<th>proportion (n)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EuroQol-5D-3L tariff</td>
<td>114</td>
<td>-0.59 - 1.00</td>
<td>0.85 (0.69 – 1)</td>
<td>–</td>
<td>0.85 (0.69 - 1)</td>
<td>–</td>
<td>0.62</td>
</tr>
<tr>
<td>Independence with Activities of Daily Living scale score 27/27</td>
<td>113</td>
<td>–</td>
<td>59% (67)</td>
<td>–</td>
<td>51% (58)</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>General Health Questionnaire-12 score &gt; =4</td>
<td>112</td>
<td>–</td>
<td>45% (50)</td>
<td>–</td>
<td>24% (27)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>WEMWBS Scale</td>
<td>113</td>
<td>14-70</td>
<td>46.9 (10.9)</td>
<td>–</td>
<td>48.7 (11.6)</td>
<td>–</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 2: Self-reported socioeconomic and psychological outcomes in SPEAK-2 respondents, and age and sex-adjusted regression analyses comparing to the age-matched general population.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>Proportion</th>
<th>OR/β (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household and employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married or in civil partnership</td>
<td>149</td>
<td>18%</td>
<td>0.36 (0.2 to 0.62)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Have own children</td>
<td>142</td>
<td>17%</td>
<td>0.21 (0.11 to 0.37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Living with parents</td>
<td>150</td>
<td>39%</td>
<td>3.95 (2.48 to 6.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unable to work due to health</td>
<td></td>
<td>21%</td>
<td>14.41 (7.97 to 26.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psychological and physical outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQ-5D-3L tariff</td>
<td>114</td>
<td>0.85 [0.66, 1.00]</td>
<td>0.17 (0.11 to 0.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WEMWBS Score</td>
<td>143</td>
<td>46.7 ± 10.8</td>
<td>-6.26 (-8.46 to -4.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GHQ-12 scale score ≥4</td>
<td>142</td>
<td>44%</td>
<td>5.37 (3.45 to 8.35)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
#5456
**IMPACT OF KIDNEY DONATION ON PREGNANCY OUTCOMES: A RETROSPECTIVE ANALYSIS**

Anupma Kaul, Narayan Prasad and Dharmendra Bhanduaria
Sanjay Gandhi Postgraduate Institute of Medical Sciences, Department of Nephrology, Lucknow, India

**Background and Aims:** More than 50% of living kidney donors are females with a significant proportion being in the childbearing age group. Recent data suggests risk of gestational hypertension, proteinuria and pre-eclampsia among pregnancies after kidney donation with a lower likelihood of full-term delivery.

**Method:** This retrospective study was conducted among females who donated kidney between (1997 - 2017) at a tertiary renal transplant centre in Northern India to assess for consequences of pregnancy outcomes among donors in terms of maternal and foetal outcomes.

Data of participants were collected using pre-tested semi structured questionnaire.

**Results:** 925 female kidney donors (1332 pregnancies) in the pre donation group while 45 females (48 pregnancies) in the post donation period were included. Mean age of first pregnancy, weight (kg) gain, proportion of history of pre-natal check-up and history of unrelated donation was statically significant among the post - donation group. The proportion of pre-eclampsia, gestational hypertension, gestational diabetes, post-partum hemorrhage was insignificantly higher among post donation group with higher preterm birth with low birth weight babies.

In Univariate analysis, Cesarean delivery, proteinuria and low birth weight <2500g were significantly associated with a decrease in CV events: Hazard Ratio (HR) [95% confidence interval (CI)]: 1.22 [0.73–2.03] (P = .435), HR: 1.12 [0.66–1.89] (P = .672), and HR: 2.78 [1.19–6.53] (P = .018), respectively. In the multivariable Cox model, diabetes mellitus was strongly associated with CV events (HR: 4.39 [2.79–6.90], p<0.001), and statin exposure was not (HR: 1.25 [0.78–2.03]). In a subgroup of KTRs exposed to statins after kidney transplantation but not before (n=314), the median [IQR] levels of LDL-c was 3.48 [2.89–4.08] mmol/L at starting statins and 2.74 [2.14–3.35] mmol/L after one year of statin exposure, i.e. a significant decrease of 0.74 [0.60–0.85] mmol/L (p<0.001). The median [IQR] levels of triglyceride was 1.99 [1.47–2.91] mmol/L when starting statins and 1.72 [1.20–2.50] mmol/L after one year of statin exposure, i.e. a significant decrease of 0.27 [0.17–0.42] mmol/L (p<0.001). There were no significant changes in HDL-c levels.

**Conclusion:** Despite an improvement in the lipid profile including a reduction of LDL-c and triglyceride levels, statin exposure was not associated with a decrease in CV events in a long-term KTR cohort. Other CV risk factors than dyslipidemia, such as diabetes mellitus, were more likely related to such events.

**Method:** 613 consecutive KTRs from a single-center cohort were retrospectively included between 2006 and 2019. Exposure to statins (indicated in primary or secondary CV prevention) and atherosclerotic CV events during the study period were comprehensively documented. The primary outcome was the incidence of CV events in all statin users compared to that of non-users, based on the Cardiovascular and Stroke Endpoint Definitions for Clinical Trials [2]. In this study, only atherosclerotic events were selected (peripheral vascular stenosis, stroke, myocardial infarction, angina pectoris and transitional ischemic attack). The secondary outcomes were the incidence of CV events (i) in KTRs using statins indicated in primary CV prevention and (ii) in KTRs using statins indicated in secondary CV prevention compared to that of non-users.

Cox proportional hazard models including statin exposure as a time-dependent covariate and fitted with inverse probability treatment weighting (IPTW) were used, as well as a multivariable Cox proportional hazard model.

**Results:** During a median [interquartile range (IQR)] follow-up period of 4.6 [2.7–10.0] years, CV events occurred in 88 KTRs: 48 (55.5%) KTRs had peripheral vascular stenosis, 24 (27.3%) had myocardial infarction, 12 (13.6%) had stroke, three (3.5%) had angina pectoris and one (1.1%) had a transitional ischemic attack. The incidence of CV events was 24.8 per 1000 person-years. In the Cox models fitted with IPTW, exposure to statins, regardless of the indication or indicated in primary and secondary CV prevention, was not associated with a decrease in CV events: Hazard Ratio (HR) [95% confidence interval (CI)]: 1.22 [0.73–2.03] (P = .435), HR: 1.12 [0.66–1.89] (P = .672), and HR: 2.78 [1.19–6.53] (P = .018), respectively. In the multivariable Cox model, diabetes mellitus was strongly associated with CV events (HR: 4.39 [2.79–6.90], p<0.001), and statin exposure was not (HR: 1.25 [0.78–2.03]). In a subgroup of KTRs exposed to statins after kidney transplantation but not before (n=314), the median [IQR] levels of LDL-c was 3.48 [2.89–4.08] mmol/L at starting statins and 2.74 [2.14–3.35] mmol/L after one year of statin exposure, i.e. a significant decrease of 0.74 [0.60–0.85] mmol/L (p<0.001). The median [IQR] levels of triglyceride was 1.99 [1.47–2.91] mmol/L when starting statins and 1.72 [1.20–2.50] mmol/L after one year of statin exposure, i.e. a significant decrease of 0.27 [0.17–0.42] mmol/L (p<0.001). There were no significant changes in HDL-c levels.

**Conclusion:** Despite an improvement in the lipid profile including a reduction of LDL-c and triglyceride levels, statin exposure was not associated with a decrease in CV events in a long-term KTR cohort. Other CV risk factors than dyslipidemia, such as diabetes mellitus, were more likely related to such events.

**Figure 1:** Association between statin exposure and cardiovascular events (Cox proportional hazard models with statin exposure used as time-dependent covariable).

**IPTW:** Inverse Probability of Treatment Weighting; **N:** number of patients exposed to statins.

* Variables included in the propensity score: age, BMI, sex, sedentarity, smoking, arterial hypertension, diabetes mellitus, prior statin exposure, immunological risk, preemptive transplantation, etiology of CKD, calcium, parathyroid hormone, LDL-c, HDL-c and triglyceride levels, use of corticoids, thyroglobulin, basiliximab, cyclosporine, MMF, everolimus, anticoagulants and antiplatelet agents.

Abstract
**REFERENCES**


**#6389**

**EARLY WEIGHT LOSS AFTER BARIATRIC SURGERY IN PATIENTS WITH ORGAN FAILURE OR TRANSPLANTATION**

Linda Moore1, Stephanie Yi1, Garth Davis1, Vadim Sherman1, Ashrith Guha2, David Victor3, Howard Huang4, Richard Knight1, A Gaber1, R Ghobrial1 and Nabil Tariq1

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**Background and Aims:** Obesity is an epidemic that complicates global health and economies. Surgery for obesity (OS) is one effective treatment that results in significant weight loss. Patients with chronic organ failure who are obese undergo OS but it is unknown whether they achieve similar weight loss response as patients who do not have organ failure.

**Method:** Patient records of OS cases between May 2016 and June 2022 from a large healthcare system were examined to review weight changes after OS by whether the patient was a transplant patient or not. The proportion of excess weight lost was determined for 1-month, 3-months, 6-months and 1-year post OS. Non-parametric analyses were performed; p < 0.05 was considered significant.

**Results:** of 1,673 OS cases, the mean (SD) age was 47.6 (12.5) years, the majority were female (1,276, 76.3%), and 58% identified as Caucasian. Within this number, 92 patients were transplant candidates (n=50, 3%) or recipients (n=42, 2.5%). The transplant patients were older [51.5 (10.8) years vs 47.3 (12.6) years, P = .0008], had similar body weight [124.4 (22.5) kg vs 126.0 (27.2) kg, P = .8271] but a lower body mass index [42.6 (5.7) kg/m2 vs 45.1 (8.1) kg/m2, P = .0046] compared to patients who were not having a transplant. Transplant patients experienced different weight loss in the early post-operative period but similar weight loss after OS as non-transplant patients (Table 1 and Table 2).

**Conclusion:** Though early post-operative differences were noted in this study, patients with organ failure responded similarly to OS as patients without organ failure.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>1 month, % (SD)</th>
<th>3 months, % (SD)</th>
<th>6 months, % (SD)</th>
<th>1 year, % (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1,671</td>
<td>14.0 (8.1)</td>
<td>26.9 (11.2)</td>
<td>41.6 (13.7)</td>
<td>54.6 (19.4)</td>
</tr>
<tr>
<td>No transplant</td>
<td>1,506</td>
<td>13.9 (7.9)</td>
<td>26.7 (11.0)</td>
<td>41.6 (13.4)</td>
<td>53.6 (19.3)</td>
</tr>
<tr>
<td>Heart</td>
<td>21</td>
<td>9.8 (8.9)</td>
<td>28.3 (15.5)</td>
<td>41.7 (22.5)</td>
<td>46.6 (22.0)</td>
</tr>
<tr>
<td>Kidney</td>
<td>39</td>
<td>17.4 (7.4)</td>
<td>29.9 (10.5)</td>
<td>40.8 (13.4)</td>
<td>54.7 (16.4)</td>
</tr>
<tr>
<td>Liver</td>
<td>28</td>
<td>14.8 (16.3)</td>
<td>31.8 (18.4)</td>
<td>41.3 (19.8)</td>
<td>56.4 (23.7)</td>
</tr>
<tr>
<td>Lung</td>
<td>4</td>
<td>6.3 (4.7)</td>
<td>23.1 (9.3)</td>
<td>37.9 (19.1)</td>
<td>51.4 (17.7)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0009</td>
<td>0.0194</td>
<td>0.763</td>
<td>0.3326</td>
<td></td>
</tr>
</tbody>
</table>

*Abstract*
Table 2: Proportion of excess weight lost by transplant patients according to timing of obesity surgery relative to transplant surgery.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>1 month, % (SD)</th>
<th>3 months, % (SD)</th>
<th>6 months, % (SD)</th>
<th>1 year, % (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before transplant</td>
<td>50</td>
<td>13.6 (8.6)</td>
<td>28.1 (12.8)</td>
<td>37.8 (17.0)</td>
<td>60.2 (20.3)</td>
</tr>
<tr>
<td>After transplant</td>
<td>32</td>
<td>16.1 (8.7)</td>
<td>31.2 (10.4)</td>
<td>44.4 (16.0)</td>
<td>52.7 (26.9)</td>
</tr>
<tr>
<td>During transplant</td>
<td>10</td>
<td>11.2 (28.4)</td>
<td>33.9 (27.9)</td>
<td>45.0 (24.4)</td>
<td>53.6 (19.3)</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>0.6497</td>
<td>0.0052</td>
<td>0.1039</td>
<td>0.1193</td>
</tr>
</tbody>
</table>

Transplant timing vs no transplant

### #6668

**PREDICTION OF REMAINING RENAL FUNCTION IN PATIENTS UNDERGOING RADICAL NEPHRECTOMY DUE TO RENAL TUMOUR MASS AND AFTER NEPHRECTOMY IN LIVING DONORS**

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**Background and Aims:** Accurate assessment of renal function is of great importance in clinical practise, in particular in patients undergoing nephrectomy due to tumor nephrectomy or in potential living kidney donors. In both cases, residual renal function is dependent on the remaining nephron number and their function. A reliable prediction of the post-nephrectomy kidney function would be of great help to identify the patient with an increased functional risk. The aim of this study was to assess if the short-term kidney function after nephrectomy can be reliably predicted.

**Method:** We performed a retrospective study in 68 living kidney donors (LD-Nx) and 43 patients undergoing nephrectomy due to a renal tumour (Tu-Nx) between 1st of January 2011 to 31st of December 2015 at the University Hospital Zurich. Baseline serum creatinine was defined as lowest observed serum creatinine value before LD-Nx and Tu-Nx and was used for calculation of estimated glomerular filtration rate (eGFR) by the Cockroft-Gault (CG) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulas. The expected post-nephrectomy kidney function was calculated based on the formula (expected eGFRpost = 0.6 * eGFRpre + 8.7) described in detail in: (Prediction of kidney function after nephrectomy was performed by using the formulas previously established by our group [1]). Expected eGFR was calculated for CG and CKD-EPI formulas and expected serum creatinine was calculated from the expected eGFR based on CG formula. The expected kidney function was then compared to the observed kidney function based on lowest observed serum creatinine (LoObsSCr) during the first year after nephrectomy and the corresponding eGFR values for CG and CKD-EPI were calculated.

**Results:** Patients with nephrectomy due to renal tumour had significantly higher baseline serum creatinine levels compared to living donors (100±50 umol/l vs. 70±12 umol/l, respectively) with 35% having proteinuria, 58% hypertension and 14% diabetes mellitus. In addition Tu-Nx patients were significantly older and had a higher body weight. Living donors had a higher percentage of smokers (31%) compared to the other group. Predonation eGFR CKD-EPI was 71±23 ml/min/1.73 m² for Tu-Nx and 94±12 ml/min/1.73 m² for LD-Nx patients. Both groups showed an adaptive increase in kidney function calculated by eGFR CKD-EPI: 29% for Tu-Nx and 14% for LD-Nx. LD-Nx patients had less bias in prediction of post-nephrectomy kidney function (Table 1). Lowest observed serum creatinine after nephrectomy did not significantly differ between the groups. A significant correlation between expected and observed serum creatinine values, as well as between expected and observed eGFR post-nephrectomy, was seen in both groups of patients.

**Conclusion:** Despite older age, higher body weight and more comorbidities, patients with tumor nephrectomy show an adaptive increase in kidney function. Prediction of kidney function after nephrectomy is possible for both groups, however more accurate for living donor patients.

Table 1: Descriptive statistics of Tu-Nx and LD-Nx patients.

<table>
<thead>
<tr>
<th></th>
<th>Tu-Nx</th>
<th>LD-Nx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed</td>
<td>Expected</td>
</tr>
<tr>
<td>LoObsSCr(μmol/l)</td>
<td>120±51</td>
<td>133±45</td>
</tr>
<tr>
<td>eGFR CG(ml/min)</td>
<td>67±29</td>
<td>58±23</td>
</tr>
<tr>
<td>eGFR CKD-EPI(ml/min/1.73 m²)</td>
<td>56±17</td>
<td>51±14</td>
</tr>
</tbody>
</table>

Legend: LoObsSCr – lowest observed serum creatinine, Tu-Nx – patients with nephrectomy due to renal tumour, LD-Nx – living kidney donors, CG - Cockroft-Gault, CKD-EPI - Chronic Kidney Disease Epidemiology Collaboration.
ANALYSIS OF IMMUNOSUPPRESSANT ADHERENCE, TREATMENT PREFERENCES AND NEEDS, AND MENTAL HEALTH DISORDERS IN THE POST-TRANSPLANTATION PERIOD

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Background and Aims: Medical treatment after kidney transplantation is not enough to assure optimal outcomes due to emotional factors that contribute on graft survival. To incorporate patient’s treatment preferences in clinical practice improves health outcomes. Few is known about treatment preferences and needs of kidney transplant population. The aims of the study were to quantify mental health disorders prevalence, immunosuppressive adherence, treatment preferences and needs of Spanish kidney transplant patients in post-transplantation period.

Method: Transversal-observational study in stable kidney transplant patients from one center in Madrid-Spain. Demographics, social-clinical variables, validated questionaries for anxiety, depression, stress, resilience, life satisfaction and quality of life related with health, and an ad-hoc survey of treatment preferences and needs were applied.

Results: A total of 116 patients were included, 25% had mental health pathology before transplant. Mental health disorders prevalence for depression, anxiety and stress were 26%, 27% and 23.3% respectively. Life satisfaction screening revealed only 29% of patients very satisfied with life. Patients with lower scores in mental health tests were significatively related with poor immunosuppressive adherence ($P = .004$). Treatment preferences and needs identified were how to improve physical condition (47%), information for anxiety and/or depression management (37%), and to receive psychological therapy from Nephrology Service (95%). See Table 1 and 2 for results.

Conclusion: Mental health disorders prevalence in Spanish kidney transplanted patients were high and had a negative impact in immunosuppressive adherence. This demands a biopsychosocial, interdisciplinary, focused on patient’s treatment preferences approach, individually and in groups from Nephrology Service.

Table 1: Baseline characteristics of studied population. (N = 116).

<table>
<thead>
<tr>
<th>Studied variables. (N = 116).</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender (%)</td>
<td>43</td>
</tr>
<tr>
<td>Age (years ± standard deviation)</td>
<td>53.2 ± 14.2</td>
</tr>
<tr>
<td>Married/Partnership marital status (%)</td>
<td>67</td>
</tr>
<tr>
<td>University education (%)</td>
<td>46</td>
</tr>
<tr>
<td>Active laboral status (%)</td>
<td>41</td>
</tr>
<tr>
<td>Graft survival (months ± standard deviation)</td>
<td>117.7 ± 96.4</td>
</tr>
<tr>
<td>CKD-EPI (ml/min ± standard deviation)</td>
<td>50.0 ± 20.1</td>
</tr>
<tr>
<td>Patients with previous kidney transplants (%)</td>
<td>26</td>
</tr>
</tbody>
</table>

Mental health past history:
- Previous mental health pathology (anxiety/depression) (%) 25
- Current treatment with psychotropics (%) 21

Table 2: Results of structured survey about psychological treatment preferences and needs of studied population. N = 116.

<table>
<thead>
<tr>
<th>Psychological treatment preferences and needs explored in structures survey in studied population. N = 116</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How to make decisions about my disease and treatments with help of others so I can maintain control of the situation?</td>
<td>42 (36.2)</td>
</tr>
<tr>
<td>How to face the impact of my disease and treatments.</td>
<td>41 (35.3)</td>
</tr>
<tr>
<td>How to communicate properly my ideas, feelings and worries about my disease to health professionals (doctors, nurses, psychologist)?</td>
<td>42 (36.2)</td>
</tr>
<tr>
<td>How can I adapt better to treatments and lifestyle modifications (Immunosuppressive pills, diet, etc)?</td>
<td>45 (38.8)</td>
</tr>
<tr>
<td>How can I adapt better to corporal image modifications due to medical treatments.?</td>
<td>45 (38.8)</td>
</tr>
<tr>
<td>How to face modification in personal and social relations after kidney transplant. ?</td>
<td>30 (25.9)</td>
</tr>
<tr>
<td>How to improve my physical condition?</td>
<td>54 (46.6)</td>
</tr>
<tr>
<td>How to manage anxiety and depression?</td>
<td>39 (33.6)</td>
</tr>
<tr>
<td>Hoy to manage changes in sexual life after kidney transplant?</td>
<td>23 (19.8)</td>
</tr>
<tr>
<td>How to prevent caregiver burnout?</td>
<td>20 (17.2)</td>
</tr>
<tr>
<td>How to ask and improve psychological services?</td>
<td>36 (31.0)</td>
</tr>
<tr>
<td>How to access to testimonial groups of help from other kidney transplant patients?</td>
<td>40 (35.5)</td>
</tr>
<tr>
<td>¿Do you consider important that psychological assessment should be provided directly from Nephrology service? POSITIVE ANSWERS</td>
<td>110 (94.9)</td>
</tr>
</tbody>
</table>

POSITIVE ANSWERS

Psychological treatment preferences
- Face-to-face individual/grupal therapies with specialized psychonephrologist 84 (72.4)
- Self-help guides/educative materials 32 (27.6)
- Medication, pills 26 (22.4)
- Teleconsultation 26 (22.4)
KIDNEY TRANSPLANT-RELATED KNOWLEDGE AMONG SOUTH ASIAN COMPARED TO WHITE CANADIAN PATIENTS

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Background and Aims: Kidney transplant (KT) is the best treatment for many patients with kidney failure. However, patients from racialized communities are less likely to receive KT. Gaps in transplant-related knowledge may be one of the potential reasons for the observed inequities in accessing KT. Here we compare patient characteristics and KT-related knowledge between South Asian (SA) versus white Canadians with kidney failure using the “Knowledge Assessment of Renal Transplantation” (KART) questionnaire.

Method: Secondary analysis of data from a cross-sectional convenience sample of white and SA adults with kidney failure. Sociodemographic data, self-reported information about racialized status and KART score were collected through electronic data capture. The association between racialized status and participant demographics were assessed using ANOVA, Kruskal–Wallis test or chi squared test, as appropriate. The independent association between racialized status and KART scores was assessed by multivariable adjusted linear or multinomial logistic regression, with adjustment for immigration status, racialized status and KART scores was assessed by multivariable adjusted linear model.

Results: Among 578 participants (mean [SD] age: 57 [14] years, 64% male), 43% were white and 16% were SA. 84% vs 27% of SA vs white participants were immigrants. The Charlson Comorbidity Index score was greater for SA (p = 0.001). The median (interquartile range) KART score of white vs SA participants was 17 [6] vs 14 [7] (p < 0.001). A univariable linear regression model the KART score was significantly associated with SA status (B: -3.27 [(95% CI): -4.76, -1.77, p < 0.001]. This association remained significant after adjustment for potential confounding (B: -3.36 (95% CI): -5.05, -1.67, p < 0.001) (Table 1). 26% of SA vs. 41% of white participants scored in the highest tertile for KART score (p < 0.001) (Fig. 1). The relative risk ratio to be in the lowest KART tertile was 3.09 [95% CI: 1.49, 6.43] for SA compared to white participants in our final, adjusted multinomial model.

Conclusion: SA participants with kidney failure are commonly immigrants who have poorer KT-related knowledge compared to white participants. Our findings indicate the need to develop culturally relevant KT-related patient education for South Asian Canadian communities.

RENAI L RESERVE IN LIVING KIDNEY DONORS: THE HIDDEN ROLE OF OVERWEIGHT

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1Fresenius Medical Care, Hemodialysis center, La Laguna, Spain, 2Hospital Universitario de Canarias, Department of Nephrology, La Laguna, Spain, 3Universidad de La Laguna, Laboratorio de Función Renal (LFR), La Laguna, Spain, 4Hospital Universitario de Canarias, Laboratorio de Función Renal (LFR), La Laguna, Spain, 5Unidad de Investigación Clínica y Ensayos Clínicos, Hospital Universitario de Canarias, Research Unit Department, La Laguna, Spain, 6Universidad de La Laguna, Faculty of Medicine, La Laguna, Spain, 7Universidad de La Laguna, Internal Medicine Department, Instituto de Tecnologías Biomédicas (ITB), La Laguna, Spain, 8Hospital Universitario de Canarias, Research Department, La Laguna, Spain, 9Hospital Universitario Insular, Nephrology Department, Las Palmas de Gran Canaria, Spain, 10Hospital General de Lanzarote, Nephrology Department, Arrecife, Spain, 11Hospital Universitario Doctor Negrín, Nephrology Department, Las Palmas de Gran Canaria, Spain, 12Hospital Universitario Nuestra Señora de Candelaria, Nephrology Department, Santa Cruz de Tenerife, Spain, 13Hospital General de La Palma, Nephrology Department, Santa Cruz de La Palma, Spain and 14Hospital Universitario de Canarias, Radiology Department, La Laguna, Spain

Background and Aims: Renal reserve (RR) is the capacity to increase glomerular filtration rate (GFR) under certain stimuli such as obesity, hyperglycaemia, metabolic syndrome, etc. The importance of the presence or absence of RR is unknown. We investigated the prevalence and factors associated with RR in a group of living donors for renal transplantation.

Method: We investigated RR before donation in 52 living kidney donors. GFR was measured by iohexol clearance before and after the stimulation of RR by endovenous amino acid infusion. The presence of RR was defined as an increase greater than 10% of basal GFR. According with the presence or absence of RR, subjects were grouped in those without RR; with RR and using RR. The latter was defined as the lack of increase in GFR after stimulation in patients with GFR > 100 mL/min. GFR was unadjusted to body surface area (BSA). The characteristics of these three groups were evaluated.

Results: 13 (25%) had no RR, 24 (46%) had RR and 15 (29%) were using RR. Subjects without RR was predominantly female (92%) with lower BSA and BMI than those with RR or using RR (BMI: 22 ± 3 vs 28 ± 3 and 29 ± 4, p < 0.005); also had a lower GFR than the other groups (84 ± 10 vs 95 ± 14 and 131 ± 5.05,-1.67

<table>
<thead>
<tr>
<th>Model</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>P value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.27</td>
<td>0.76</td>
<td>&lt;0.001</td>
<td>-4.76, -1.77</td>
</tr>
<tr>
<td>2</td>
<td>-2.35</td>
<td>0.84</td>
<td>0.006</td>
<td>-4.01, -0.70</td>
</tr>
<tr>
<td>3</td>
<td>-3.42</td>
<td>0.87</td>
<td>&lt;0.001</td>
<td>-5.12, -1.72</td>
</tr>
<tr>
<td>4</td>
<td>-3.36</td>
<td>0.86</td>
<td>&lt;0.001</td>
<td>-5.05, -1.67</td>
</tr>
</tbody>
</table>

Model 1: Racialized status (3 category: White, SA, Other) Model 2: 1 + Immigrant status (yes/no) Model 3: 2 + age, gender, marital status, education, employment status, OMI, Muslim/non-Muslim Model 4: 3 + transplant history, current modality, CCI
Survivals were compared between the two groups.

Data on demographics, comorbidities, immunologic properties and graft of pre-transplant dialysis treatment: Group A, Sina Hospital. KTRs were divided into two groups according to the duration of pre-transplant dialysis treatment (more than 10 years) on the outcomes of renal (KTRs) due to the donor shortage in Turkey. We assessed the effect of pre-transplant dialysis duration (more than 10 years) on the outcomes of renal (KTRs) due to the donor shortage in Turkey. We assessed the effect of pre-

Method: We retrospectively evaluated 480 KTRs who were grafted between 2000 and 2009 in Ankara University School of Medicine, Ibn Sina Hospital. KTRs were divided into two groups according to the duration of pre-transplant dialysis treatment: Group A, ≥10 years and Group B, <10 years. Data on demographics, comorbidities, immunologic properties and graft survivals were compared between the two groups.

Results: Group A included 60 patients and dialysis vintage was 288±60 months (Table 1). 420 patients in Group B had an average of 19 months period of dialysis treatment. While cadaveric transplantation was 78.3% in Group A, it was much lower in Group B (11.2%, p<0.001). Most of the patients were on hemodialysis treatment (95.0% vs. 58.3%, respectively, p = .001). Recipients’ age (P = .001), HLA mismatch number (P = .008) and PRA positivity (P = .001) were significantly higher in Group A. Although anti-human T-thymocyte globulin had been mostly chosen for induction therapy in Group A (p<0.001), almost all patients were under standard triple maintenance immunosuppression therapy. First year and late acute rejection rates were similar between two groups (p=1.000 and P = .407, respectively). Clinically important difference was demonstrated in graft loss, which was mostly seen in the ≥10 years dialysis group (Group A, 28.3% vs. Group B, 8.3%, P = .014). The 1-, and 5- years graft survival rates were 91.4%, and 81.3%, respectively, in Group A and 97.4%, and 93.4%, respectively, in Group B (P = .029 and P = .014, respectively). Patient loss was significantly higher in Group A (Group A, 28.3% vs. Group B, 14.3%, P = .018).

Conclusion: We demonstrated that pre-transplant dialysis duration for more than 10 years has adverse effects on post-transplant graft and patient outcomes, accompanied by high immunological risk. Updates of organ allocation system considering sensitized candidates and strategies to expand donor pool and donation rates are needed to reduce waiting times on dialysis.
Table 1: Clinical Characteristics and Outcomes in Kidney Transplant Recipients, According to Dialysis Vintage.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dialysis Vintage ≥10 years (n=60, 12.5%)</th>
<th>Dialysis Vintage &lt;10 years (n=420, 87.5%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean±SD)</td>
<td>50±10</td>
<td>47±13</td>
<td>0.049</td>
</tr>
<tr>
<td>Female gender n, (%)</td>
<td>24 (40.0)</td>
<td>168 (40.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Living donor n, (%)</td>
<td>13 (21.7)</td>
<td>373 (88.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Donor age (years) (mean±SD)</td>
<td>47±12</td>
<td>49±15</td>
<td>0.615</td>
</tr>
<tr>
<td>Donor female gender n, (%)</td>
<td>31 (52.5)</td>
<td>253 (61.4)</td>
<td>0.193</td>
</tr>
<tr>
<td>Etiology of ESRD</td>
<td></td>
<td></td>
<td>0.104</td>
</tr>
<tr>
<td>Chronic glomerulonephritis</td>
<td>12 (20.0)</td>
<td>112 (26.7)</td>
<td></td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>1 (1.7)</td>
<td>25 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Vescicoureteral reflux+ Pyelonephritis</td>
<td>13 (21.7)</td>
<td>41 (9.8)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (16.7)</td>
<td>42 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (6.7)</td>
<td>56 (13.3)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>5 (8.3)</td>
<td>53 (12.6)</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>15 (25.0)</td>
<td>91 (21.7)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus n, (%)</td>
<td>3 (5.0)</td>
<td>105 (25.0)</td>
<td>0.017</td>
</tr>
<tr>
<td>Hypertension n, (%)</td>
<td>36 (60.7)</td>
<td>244 (58.1)</td>
<td>0.783</td>
</tr>
<tr>
<td>Cardiovascular disease n, (%)</td>
<td>10 (17.2)</td>
<td>46 (11.1)</td>
<td>0.406</td>
</tr>
<tr>
<td>Renal replacement treatment n, (%)</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>57 (95.0)</td>
<td>245 (58.3)</td>
<td></td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>3 (5.0)</td>
<td>39 (9.3)</td>
<td></td>
</tr>
<tr>
<td>Preemptive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time of dialysis (months) (mean±SD)</td>
<td>288±60</td>
<td>19±29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HLA mismatch number(min-med-mx)</td>
<td>0-4-6</td>
<td>0-3-6</td>
<td>0.008</td>
</tr>
<tr>
<td>PRA status n,(%)</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Negative</td>
<td>32 (53.3)</td>
<td>305 (73.8)</td>
<td></td>
</tr>
<tr>
<td>Positive class I</td>
<td>6 (10.0)</td>
<td>27 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Positive class II</td>
<td>6 (10.0)</td>
<td>41 (9.9)</td>
<td></td>
</tr>
<tr>
<td>Positive class I-II</td>
<td>16 (26.7)</td>
<td>40 (9.7)</td>
<td></td>
</tr>
<tr>
<td>Induction therapy n,(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATG</td>
<td>29 (48.3)</td>
<td>78 (19.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-2R</td>
<td>28 (46.7)</td>
<td>174 (42.5)</td>
<td>0.547</td>
</tr>
<tr>
<td>First year AR n, (%)</td>
<td>9 (15.0)</td>
<td>64 (15.2)</td>
<td>1.000</td>
</tr>
<tr>
<td>Late AR n, (%)</td>
<td>2 (3.3)</td>
<td>30 (7.1)</td>
<td>0.407</td>
</tr>
<tr>
<td>Graft loss n, (%)</td>
<td>11 (18.3)</td>
<td>35 (8.3)</td>
<td>0.014</td>
</tr>
<tr>
<td>Time of graft loss (months) (mean±SD)</td>
<td>60±37</td>
<td>68±43</td>
<td>0.123</td>
</tr>
<tr>
<td>Patient loss n, (%)</td>
<td>17 (28.3)</td>
<td>60 (14.3)</td>
<td>0.018</td>
</tr>
<tr>
<td>Follow-up (months) (mean±SD)</td>
<td>64±35</td>
<td>70±44</td>
<td>0.188</td>
</tr>
</tbody>
</table>

Abbreviations: AR, acute rejection; ATG, anti-human T-thymocyte globulin; ESRD, end-stage renal disease; HLA, human leukocyte antigen; IL-2RA, interleukin-2 receptor antagonist; PRA, panel reactive antibody.

#5337

PHENOTYPIC CHANGES OF LYMPHOCYTES FOLLOWING RENAL TRANSPLANTATION

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Background and Aims: Phenotypic changes in lymphocytes have been described following renal transplantation (RT), including both CD4 and CD8 subpopulations. The present work aims to prospectively assess T lymphocyte phenotypic alterations, after RT and compare differences between deceased (DR) and living (LR) donor recipients.

Method: One hundred six RTRs were included in the study, 78/106 (74%) DR, age 52.5(15) yrs and 28/106 (26%) LD, 35(21) yrs. Lymphocytes, CD4, CD8, CD4CD28null, CD8CD28null, CD16+CD56+ (NK) and CD4+CD25+FoxP3+ (Tregs) were evaluated at peripheral blood, by flow cytometry, at certain time points: RT and 3, 6, 12 months (T0, T3, T6, T12, respectively).

Results: During follow up, at T3, T6, T12, eGFR was 61(23.6), 62.2(31.1), 63.5(23.9)ml/min/1.73 m2, p=NS and 91(24.8), 61(25.3), 62(22.7), p=NS, in DR and LR group, respectively. eGFR showed no significant difference between DR and LR at any time point. At any time point, T0, T3, T6, 12,

lymphocytes were significantly increased in DR compared to LR groups, P = .001, p <0.0001, P = .002, p <0.0001, similarly CD4, P = .001, p <0.0001, P = .001, p <0.0001, and CD8 cells, P = .002, p <0.0001, P = .005, P = .006, respectively. Tregs were increased at T0, T3, T6, not at T12, p <0.0001, p <0.0001, P = .001, p = .1, respectively. At this point, Tregs were increased in RTRs with eGFR>50ml/min/1.73 m2, 20.3(9.3) vs. 27.2(18.6), P = .03. CD4CD28null, CD8CD28null cells did not change during follow up, and there was no difference between two groups at any time point.

Conclusion: Immune profile was improved in both groups, DR or LR, however a significantly better effect managed in LR, although elimination of CD28 molecule could not be restored. Interestingly, Tregs were associated only by renal function one year following RT.

Abstract
Table 1:

<table>
<thead>
<tr>
<th>Cells/μL</th>
<th>T0</th>
<th>T3</th>
<th>T6</th>
<th>T12</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes</td>
<td>1100(300)</td>
<td>1308(800)</td>
<td>1600(918)</td>
<td>1508(800)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4 cells</td>
<td>414(249)</td>
<td>600(607)</td>
<td>729(615)</td>
<td>588(417)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD8 cells</td>
<td>266(163)</td>
<td>390(223)</td>
<td>455(275)</td>
<td>450(289)</td>
<td>= 0.02</td>
</tr>
<tr>
<td>NK cells</td>
<td>198(125)</td>
<td>125(131)</td>
<td>142(149)</td>
<td>149(158)</td>
<td>= 0.001</td>
</tr>
<tr>
<td>Tregs</td>
<td>20(13)</td>
<td>23.7(22.5)</td>
<td>27(24.5)</td>
<td>20(16.4)</td>
<td>= 0.001</td>
</tr>
</tbody>
</table>

Figure 1: Graft survival.
Figure 2: Patient survival.

#4437

ASSESSMENT OF THE PSYCHOLOGICAL EXPERIENCE OF KIDNEY TRANSPLANT PATIENTS DURING THE COVID-19 PANDEMIC

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Marrakesh, Nephrology, Hemodialysis, Marrakesh, Morocco

Background and Aims: The coronavirus (COVID 19) pandemic has caused a major health crisis, and quarantined half of the world's population, therefore it contributed to the appearance or aggravation of mental distress such as anxiety, depressive disorders and deterioration of the quality of sleep especially in the immunocompromised population and especially in the kidney transplant patients. Among the causes of these disorders are the risk of infection and the relatively high mortality rate associated with this virus. The aim of our study is to investigate anxiety and depression scores in renal transplant patients during the COVID 19 pandemic and compare them to those of the general population to highlight the impact that the pandemic has had on this vulnerable population.

Method: This is a descriptive and analytical case-control study of a group of 113 patients divided into 2 groups: group of kidney transplant patients and that of the general population. A questionnaire collecting sociodemographic data was used. Anxiety symptoms were assessed by the GAD anxiety scale. Depressive symptoms were assessed using the Beck's scale abbreviated.

Results: In our study, the rates of anxiety and depression in the general population group were around 33.3% and 18.3% respectively. This rate was significantly higher in subjects with previous psychiatric history. These rates were higher in women with an anxiety rate of 18.3% versus 15% in men and a depression rate of 11% in women versus 7% in men and were significantly higher in subjects with previous psychiatric history. In the group of kidney transplant patients the rates of anxiety and depression were high compared to the general population, with a rate of anxiety at 66% and depression at 26.4% (p<.001).

Conclusion: This study raised the major negative impact of the covid 19 pandemic on the increase of psychiatric disorders in this at-risk population compared to the general population. This requires a multidisciplinary and adapted management of these vulnerable patients, associating a joint nephrological and psychiatric follow-up in order to preserve their quality of life and their mental health.

#4691

LAPAROSCOPIC Nephrectomy in patients with autosomal dominant polycystic kidney disease

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1Republican Specialized Scientific Practical Medical Center of Nephrology and Kidney transplantation, Adult and children nephrology, Tashkent, Uzbekistan; 2Tashkent Pediatric Medical Institute, Nephrology and hemodialysis, Tashkent, Uzbekistan and 3Republican Specialized Scientific Practical Medical Center of Nephrology and Kidney transplantation, Scientific department, Tashkent, Uzbekistan

Background and Aims: At the present, discussions continue on the indications and timing of performing kidney nephrectomy in patients with autosomal dominant polycystic kidney (ADPK) disease who are on the waiting list for kidney transplantation. Large sizes of kidneys, traumatic access, accompanying these operations cause a high incidence of postoperative complications, mortality and aggravate the severity of patients. The aim of the present study was to find the preferred algorithm for preparing patients for kidney transplantation.

Method: The results of the nephrectomy of polycystic kidneys were analyzed in 28 patients (mean age 49±1.5 years, 16 men, 12 women), which were conditionally divided into two groups. The first group included 13 patients (46.4%) with open surgery using median laparotomy and lumbotomy, in the second group - 15 (53.6%) - laparoscopic nephrectomy. Surgical interventions for patients in both groups receiving renal replacement therapy dialysis, performed according to emergency and planned indications.

Results: The average duration of laparoscopic and open surgical interventions was 149±14 and 132±15 min, respectively. The maximum size of deleted polycystic-altered kidneys in the first group was 21.3±4.21 cm, in the second group it was 20.5±3.3 cm. The incidence of postoperative complications in the 1st and 2nd groups was 6 cases (46.1%) and 2 cases (13.3%), respectively. There was one fatal outcome (7.69%) in the 1st group as a result of septic complications. the average postoperative bed-day in the first group was 12-13 (12.7 ± 1.1), in the second - 8-9 (8.6±0.5). Patients after laparoscopic interventions are activated on the 2nd-3rd day (2.8±0.14), after open operations - on the 4th-5th (4.43±0.32).

Conclusion: The incidence of postoperative complications after laparoscopic nephrectomy in patients with ADPK does not exceed 13.3%. The use of laparoscopic technologies makes it possible to expand the possibilities of using nephrectomy for the treatment and preparation of patients with polycystic kidney transplantation.

#3003

IMPACT OF FULL CORRECTION OF HEMOGLOBIN AMONG POST-TRANSPLANT ANEMIC KIDNEY TRANSPLANT RECIPIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Torki Aloтаib1, Oasma Ashhy Ahmed Gheith1,2, Ayman Maher Nagib1,2, Medhat Abdulhalim1, Hasaneen Hasaneen Ahmed Aboaty Aboaty1, Tarek S.H. Mahmoud3, Prasad Nair1, Hany Adel1, Ahmed Mossaad1, Ahmed Atta1 and Mohamed Abdullahm1

1Hamed Alesa Organ Transplant Center, Kuwait, Nephrology, Kuwait, Kuwait and 2Mansoura University, Nephrology, Mansoura, Egypt

Background and Aims: Several studies have shown that post-transplant anemia (PTA) might be associated with increased mortality and decreased graft survival and de-novo congestive heart failure. So we aimed from this prospective randomized controlled study to assess the impact of full correction of PTA on the cardiovascular system of renal transplant recipients receiving erythropoietin stimulating agents (ESA).

Method: We recruited 247 kidney recipients with stable graft function in this RCT with 2 groups according to their target hemoglobin (11-12 g/dl, group 1, n=183) and (13-15 g/dl, group 2, n=64). After correction of deficiencies, the target hemoglobin was achieved using ESA. All patients were followed up clinically and Laboratory and radiologically for 12 months.

Results: Diabetic nephropathy was the main cause of ESKD in group 1. The studied groups were comparable regarding pre-transplant co-morbidities. Most patients received thymoglobulin as induction then cyclosporine based maintenance immunosuppression. We did not find any significant difference between the two groups concerning post-transplant diabetes, BK viremia or malignancies and even cardiovascular events (TIA, stroke, ACS), (p>0.05).

Group 1 showed higher mean blood pressure (P = .003), lower LV internal
Conclusion: Full correction of PTA is associated with stabilized cardiac dimensions indices without any significant cardiovascular comorbidities.

#5364
LOW DOSE VALGANCICLOVIR AS A PRE-EMPTIVE THERAPY IS EFFECTIVE FOR CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

Jin Seok Jeon, Haekyung Lee, Hyoungnae Kim, Soon Hyo Kwon and Hyunjin Noh

Soonchunhyang University hospital, Department of Internal Medicine, Seoul, Rep. of South Korea

Background and Aims: Pre-emptive therapy, screen for and treat asymptomatic cytomegalovirus (CMV) viremia, is an important preventive strategy for CMV disease in kidney transplant (KT) recipients. Oral valganciclovir is the most commonly used as preventive strategy. However, the optimal dose and treatment duration of valganciclovir remains elusive.

Method: We retrospectively evaluated the efficacy and toxicity of low-dose of oral valganciclovir (250mg twice daily) as pre-emptive therapy in KT recipients who underwent KT between January 2015 and December 2021. CMV viral load was measured by polymerase chain reaction. Pre-emptive therapy with valganciclovir was applied for 2 weeks.

Results: of 33 kidney transplant recipients who received pre-emptive CMV therapy with valganciclovir (55 therapy cases), 32 (97.0%) were CMV seropositive except 1 patient who had no related information. Thirty-two (311.24 – 826.25), whereas 4420.00 (2535.00 – 137450.00) in patients who underwent KT between January 2015 and December 2021. CMV viral load was measured by polymerase chain reaction. Pre-emptive therapy with valganciclovir was applied for 2 weeks.

Conclusion: These results suggest that pre-emptive therapy with low dose oral valganciclovir for 2 weeks can be successfully used for preventing CMV disease among KT recipients with low-level CMV viremia. Further research is needed to replicate these findings in larger samples and assess long-term outcomes.

#6369
RESULTS OF KIDNEY TRANSPLANTATION IN PATIENTS WITH LOW MFI PREEMPTED DONOR SPECIFIC ANTIBODIES

Maria Paola Salerno1,2, Patrizia Silvestri2, Natalia Romina Zanoni2 and Franco Citterio3

1Italy and 2Roma, Italy

Background and Aims: Preempted DSA at transplantation, significantly increase risk of antibody-mediated rejection (ABMR). While pre-existing positive DSA with concomitant positive cross-match is a general contra-indication to kidney transplantation, DSA presence with negative cross-match is still a controversial topic. The presence of DSA with Mean Fluorescence Index (MFI) up to 3,000 and a negative cross-match is valued as a contraindication to transplantation and is widely accepted. In some transplant centers the chance of transplantation is also offered to DSA positive patients, with MFI up to 5,000. Aim of this study was to analyze graft and patient survival, acute cellular rejection, humoral rejection, renal function and side effects in kidney transplant recipients (KTR) with positive DSA (MFI up to 3,000) and negative cross-match.

Method: Nineteen pts (age 53+/−11) with chronic renal failure on chronic hemodialysis treatment (8+/−6 years) received a kidney transplant between May 2017 and December 2020. Median PRA was 66%; 100% pts had DSA with average MFI 2122 (min 1039, max 3779). As immunosuppressive therapies all pts received induction with Thymoglobuline plus Rituximab, followed by maintenance immunosuppression with Tacrolimus, MofetilMycoFenolate and Steroids. All pts were on periodic follow up in our Transplant Clinic. Median follow up was 26.5+/−14.4 months. Results were compared to a concomitant KTR group DSA and crossmatch negative.

Results: After 2y follow-up, 17/19 pts are alive (95.8%), one patient died (1/19, 5.2%) after treatment for ABMR. Three patients returned to dialysis treatment (15.8%) during the first year post-tx, because of: PNF 1pt; irreversible ABMR rejection 2 pts. One other patient had reversible ABMR. Cumulative one year graft survival was 79% and the cumulative incidence of ABMR was 15.8%. Average 2 years follow-up creatinine was 1.46+/−0.88 mg/dl, median 2 year GFR was 51+/−25 ml/min. Comparing the matched control group (19 pts DSA and crossmatch negative) 2 years patient survival, graft survival and GFR, acute rejection were not significantly different. Incidence of acute rejection was higher in the DSA positive group (16% vs 0%), as well as graft loss (21% vs 12%).

Conclusion: Our data suggest that low dose Thymoglobuline plus Rituximab induction allow kidney transplantation in recipient with high PRA (69%) and positive DSA with low MFI (< 3,000), with higher risk of acute rejection, and graft loss.

#6833
ARE KT RECIPIENTS TAKING THEIR IMMUNOSUPPRESSANT MEDICATION? PRELIMINARY EVIDENCE FROM A SUPER-SPECIALIZED TRANSPLANT CENTRE IN SUB-SAHARAN AFRICA

Olaelek Olatiise1, Michael Muoka2, Stephen Asaolu2, Adebowale Adekoya1, Adaku Olatiise1 and Adeboyega Faponle1

1Zenith Medical and Kidney Centre, Department of Medicine, Abuja, Nigeria, 2Zenith Medical and Kidney Centre, Department of Clinical Research, Abuja, Nigeria and 3Lagos State University Teaching Hospital (LASUTH), Ikeja, Nigeria

Background and Aims: Immunosuppressant non-adherence is a leading cause of preventable renal allograft dysfunction, rejection and graft loss. The barriers to immunosuppressant adherence as well as associated risk factors of non-adherence vary across studies in different locations. This study aimed to investigate the prevalence of immunosuppressant non-adherence among adult kidney transplant recipients and identify barriers to adherence in a renal transplant cohort.

Method: A cross sectional survey was conducted using the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS), the Immunosuppressant Therapy Barrier Scale and the Beliefs about Medicines Questionnaire. Adherence was defined according to the BAASIS, with barriers to adherence and beliefs about medicines compared between the two groups. Participants were recruited from the out-patient clinic at Zenith Medical and Kidney centre. An advert for the study was placed in consultation rooms and patients were approached to join the study when they attend appointments. IBM SPSS Statistics for Windows, Version 23 (Armonk, NY: IBM Corp) was used for data analysis.

Results: The rate of non-adherence was 50.7% out of 67 kidney transplant recipients attending outpatient clinic. There were statistically significant associations between non-adherence and occupation (P = 0.049). Participants who are on MMF were more adherent than those on sirolimus (97.0% vs 79.4% and 0.0% vs 8.8%) and this difference is statistically significant (P = 0.038). Also, participants who have had one or more post-transplant hospital admission are more non-adherent when compared with those that have never been admitted (P = 0.02). The only significant barrier to adherence was when patients travelled out of town (P < 0.005). Adherence was not associated with patients’ belief about their medicines.

Conclusion: Interventions aimed at ensuring constant access to immunosuppressant drugs and those based on habit forming may significantly improve adherence in this cohort.

E4 - COMPLICATIONS IN TRANSPLANTATION

#2649
INFECTIOUS COMPLICATIONS AFTER KIDNEY TRANSPLANTATION IN RELATION TO INDUCTION IMMUNOSUPPRESSIVE THERAPY

Matej Vnucák, Karol Grafiáčok, Monika Beliančinová, Patricia Kleinová and Ivana Dedinská

University Hospital Martin, Transplantation Center, Martin, Slovakia

Background and Aims: Infections are the most common non-cardiac cause of death after kidney transplantation (KT). The main goal of immunosuppressive therapy is to find a balance between the low incidence of acute rejection and infectious complications.

Method: We conducted a retrospective, monocentric analysis of transplant patients at the Transplant Center University Hospital Martin from 2011 to 2020 with various induction immunosuppressive therapies. We monitored the incidence of infections in terms of etiology, localization and severity at different intervals after KT.
Results: Our study included 39 patients on induction therapy with basiliximab to whom we paired 39 patients with induction therapy with thymoglobulin based on gender and age, in total our population consisted of 78 patients (56 men, 22 women), the mean age was 45 years. In the group of patients with induction therapy with thymoglobulin, we noted a higher proportion of fungal (P = 0.0409), urogenital infections (P = 0.0384), sepsis (P = 0.0497) and leukopenia (0.0384) from 1st to 6th month after KT, higher incidence of skin infections (P = 0.0218) and serious infections requiring hospitalization (P = 0.0269) from 6th-12th months to TO. On the other hand, in the basiliximab patient group, we identified a higher incidence of acute humoral and cellular rejection (P = 0.0218) after 6 months of TO. From the perspective of recurrent infections, in the Thymoglobulin induction group, we noted a higher incidence of infections by localization, etiology and severity. Risk factors for recurrent bacterial infections from 1st to 6th month after KT are: history of respiratory infections, in the Thymoglobulin induction group, we noted a higher incidence of rejection (P = 0.0218) from 6th-12th months to TO. On the other hand, in the basiliximab induction therapy with basiliximab have a higher risk of developing acute rejection. Therefore, it is essential to identify risk groups of patients benefiting from milder or more intensive inductive immunosuppressive therapy without a concomitant increased risk of infectious complications or acute graft rejection.

Conclusion: Patients on inductive immunosuppressive therapy with thymoglobulin are at a higher risk of recurrent, multidrug-resistant and severe infections after KT compared to induction with basiliximab with identical maintenance immunosuppressive therapy. On the other hand, patients on induction therapy with basiliximab have a higher risk of developing acute rejection. Therefore, it is essential to identify risk groups of patients benefiting from proatherosclerotic infectious complications or severe graft rejection.

Predictors of Kidney Function decline in Living Kidney Transplantation Donors

Predictors of Kidney Function decline in Living Kidney Transplantation Donors

**Lada Trajcheska 1, Irena Rambabova- Bushljetik 2,3, Igor Nikolov 2, Galina Severova- Andrevska 1, Stefan Filipovski 1, Zhaklina Shterjova- Markovska 1, Aleksandra Canevska Taneska 1, Mimoza Milenkova 1, Adriana Spasovska Vasilova 1 and Goce Spasovski 2**

1University Clinic of Nephrology, Transplantation, Skopje, Republic of North Macedonia, 2Skopje, University Clinic of Nephrology, Skopje, Skopje, Republic of North Macedonia, 3University Clinic of Nephrology Skopje, Transplantation, Skopje, Republic of North Macedonia and 4University Clinic of Nephrology Skopje, Transplantation, Skopje, Republic of North Macedonia

**Background and Aims:** After nephrectomy kidney transplant donors lose 50% of their renal mass. Shortage of donors and long waiting list for deceased donor transplantation expanded the living donor criteria. The aim of this study is to identify pretransplant donor related factors associated with renal function decline.

**Method:** We retrospectively studied LDKT donors from one transplant center in the period 2013 -2022. Data was retrieved from medical history charts and national electronic database system. Demographic characteristics as age, gender and relation to the recipient, patients preference to donate the kidney with higher measured split GFR, the presence of diabetes, hypertension, hyperlipidemia and BMI >30 kg/m² were analysed. Estimated GFR by CKD EPI was notified prior donation, one and two years afterwards. In a multivariate regression analysis the reduction ratio of CKD EPI was explored as dependent variable.

**Results:** We studied 121 donors. The average age at time of transplant was 59.18 ± 10.99 years. Donors' average eGFR was 91.53 ± 18.62 ml/min. Donor's age and eGFR were significantly correlated (r = -0.529). Male donors were 73 (60%), 11 (9%) were unrelated to recipients, 9 (7%) had BMI > 30, 17 (14%) diabetes, 53 (44%) hypertension 5 (4%) hyperlipidemia, and 65 (52%) had more than one comorbidity combined. Eight of donors (7%) decided to donate the better kidney. CKD EPI declined to 67.18±18.62 ml/min at first and 66.01±21.29 ml/min at the second year. The RR of 24.53 ± 20.60 % and 27.62±18.76% raised on yearly bases, respectively. In the univariate analysis of the GFR declination at the first year BMI > 30 kg/m² was associated with higher reduction of GFR (β=0.318, P = .003). At the second year the presence of diabetes emerged as worsening factor of GFR (β=0.227, P = .034) and BMI> 30 kg/m² kept its significance (β=0.426, P = .000). All the other parameters showed no significant associations to the GFR decline. In the multivariate analysis BMI> 30 kg/m² remained as most powerful predictor at 12 months reduction of eGFR.

**Conclusion:** Patients with diabetes and especially with obesity are at higher risk of rapid decline in kidney function after kidney donation. Careful assessment prior kidney donation should weight the risks.
Method: This is a retrospective, monocentric and observational cohort study. The study population consists of patients that underwent kidney transplantation in a single Kidney Transplant Unit from 1978 to 2012 and still in follow-up within the same Unit with a functioning graft. Data were extracted from the Hospital digital medical records after informed consent has been obtained. We analysed renal function at 5-year intervals from discharge to the last evaluation using eGFR calculated with the CKD-EPI formula. Data on demographic characteristics, comorbidities, immunosuppressive therapies and complication (divided as infectious, immunological and malignancy) has also been evaluated.

Results: We enrolled 332 patients with a mean follow-up of 17.9 ± 6.5 years, of whom 101 (30.4%) with a follow-up > 20 years. Figure 1 shows the trend of renal function during the follow-up years. In Table 1 are reported the comorbidities and immunological, infectious and neoplastic complications. 46 (14.5 %) patients underwent a “for cause” kidney biopsy. The main finding, with 62% was transplant glomerulopathy/interstitial fibrosis and tubular atrophy (TG/IFTA) with a mean post-transplant onset of 12.8 years (± 6.1), 9% of rejection findings with a mean time to onset of chronic rejection of 18 years (±8) and 1.3% of biopsied patients received a diagnosis of recurrence with a mean onset of 10.8 years (±4.4). 36.1% of the patients experienced at least one neoplasm with an average post-transplant onset time of 13.4 (±7.7). Infectious complications occurred in 36.1% of the transplanted patients.

Conclusion: This study provides an exhaustive overview of the characteristics and clinical complications in a “real life” experience with long survivor kidney transplants with the aim to better understand the needs and problems of this peculiar population in order to guide clinicians in a more targeted management.

Table 1: Comorbidities and immunological, infectious and neoplastic complications in the study population.

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>n° (%)</th>
<th>a. Time of onset, years (media, DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dislipidemia</td>
<td>208 (62,7)</td>
<td>11.7 (5,6)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>285 (85,8)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>69 (21)</td>
<td></td>
</tr>
<tr>
<td>Pre-transplant</td>
<td>10 (3)</td>
<td></td>
</tr>
<tr>
<td>Post-transplant</td>
<td>59 (18)</td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>46 (13,8)</td>
<td>11.4 (7,5)</td>
</tr>
<tr>
<td>Post-transplant</td>
<td>39 (11,7)</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>72 (21,7)</td>
<td></td>
</tr>
<tr>
<td>Pre-transplant</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Post-transplant</td>
<td>72 (21,7)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Continued.

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>n° (%)</th>
<th>a. Time of onset, years (media, DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant malignancy</td>
<td>120 (36,1)</td>
<td>13,4 (7,7)</td>
</tr>
<tr>
<td>Type</td>
<td>n° (%)</td>
<td></td>
</tr>
<tr>
<td>Cutaneous</td>
<td>119 (35,8)</td>
<td></td>
</tr>
<tr>
<td>Solid</td>
<td>50 (15)</td>
<td></td>
</tr>
<tr>
<td>Hematological</td>
<td>8 (2,4)</td>
<td></td>
</tr>
<tr>
<td>MGUS</td>
<td>35 (10,5)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infectious</th>
<th>n° (%)</th>
<th>a. Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant infections</td>
<td>120 (36,1)</td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>n° (%)</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>48 (14,5)</td>
<td></td>
</tr>
<tr>
<td>VZV</td>
<td>24 (7,2)</td>
<td></td>
</tr>
<tr>
<td>BSI</td>
<td>23 (6,9)</td>
<td></td>
</tr>
<tr>
<td>EBV</td>
<td>23 (6,9)</td>
<td></td>
</tr>
<tr>
<td>CMV</td>
<td>12 (3,6)</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>8 (2,4)</td>
<td></td>
</tr>
<tr>
<td>BKV</td>
<td>3 (0,9)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>17 (5,1)</td>
<td></td>
</tr>
</tbody>
</table>

Immunological

<table>
<thead>
<tr>
<th>Graft biopsy</th>
<th>n° (%)</th>
<th>a. Time of onset, years (media, DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transplant</td>
<td>48 (14,5)</td>
<td>12,8 (6,1)</td>
</tr>
<tr>
<td>TG/IFTA</td>
<td>18 (37,5)</td>
<td></td>
</tr>
<tr>
<td>Rejection</td>
<td>n° (%)</td>
<td>30 (62,5)</td>
</tr>
<tr>
<td>Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR</td>
<td>17 (5,3)</td>
<td></td>
</tr>
<tr>
<td>aAMR</td>
<td>1 (0,3)</td>
<td></td>
</tr>
<tr>
<td>cAMR</td>
<td>12 (3,8)</td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>n° (%)</td>
<td>4 (8,3)</td>
</tr>
<tr>
<td>Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time of onset</td>
<td>n° (%)</td>
<td>10,8 (4,4)</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>4 (100)</td>
<td></td>
</tr>
</tbody>
</table>


#4487
AN UNEXPECTED CASE OF 2,8-DIHYDROXYADENINE NEPHROPATHY AFTER KIDNEY TRANSPLANTATION RELATED TO

Figure 1: Evolution of renal function (eGFR).
NEW VARIANTS OF ADENINE PHOSPHORIBOSILTRANSFERASE GENE

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Background and Aims: Adenine phosphoribosyltransferase (APRT) deficiency is a rare autosomal recessive disorder of the purine metabolism which results in the conversion of adenine into 2,8 dihydroxyadenine (DHA) due to the activity of the xanthine oxidoreductase (XOR). Patients affected by APRT deficiency who do not receive inhibitors of XOR may develop 2,8-DHA nephropathy that might progress to end-stage kidney disease (ESKD) with the need of kidney transplant. The high rate of misdiagnosis of 2,8-DHA nephropathy in native kidneys could lead to the failure of kidney graft in transplanted patients affected by APRT deficiency.

Method: Here, we report the case of a female, 63-years old patient with ESKD of unknown cause on regular hemodialysis treatment from 2018 after a period of three years on peritoneal dialysis, who underwent kidney transplantation in our Center in 2022. Her medical history showed a metabolic syndrome. She did not experience episodes of renal colic whereas family history reported a brother affected by frequent renal colic of unknown cause. In March 2022, she underwent kidney transplantation from a deceased death brain donor. Induction therapy includes basiliximab, tacrolimus, mycophenolic acid and steroids. Due to the persistence of delay graft function, ten days after kidney transplantation an allograft biopsy has been performed. The histological examination revealed tubular damage surrounded by inflammation cells and intratubular crystals in the renal cortex. The crystals were reddish brown tinged in hematoxylin and eosin stain and were birefringent under polarized light. Fig. 1 A, B, so they were strongly related to the hypothesis of DHA crystals. Consistently, the urinalysis showed yellow-brown crystals of DHA. Thus, a genetic analysis of APRT gene has been performed showing two novel heterozygous variants c.388_397p.(Leu130ValfsTer4) and exon 3 deletion, expected pathogenic. The patient was treated with bolus of methylprednisolone (4mg/kg alternate to 50 mg) and a therapy with febuxostat 80 mg/die was started to reduce the amount of plasma DHA. In addition, based on our previous experience of recurrence DHA nephropathy after transplantation, we treated the patient with six consecutive hemodiafiltration (HDF) sessions without ultrafiltration, to promptly remove the serum DHA avoiding their precipitation in the graft while waiting for the lowering effect of febuxostat.

At discharge the patient showed an increase of the urine output not associated with a complete recovery of kidney function (sCr 3.88 mg/dl, uric acid 1.6 mg/dl), so two other hemodialysis treatments were performed in the next two weeks.

Results: At present, almost one year after kidney transplant, the patient is doing well and the graft function is stable with a sCr of 1.6 mg/dl without significant presence of DHA crystals in the urine.

Conclusion: In conclusion, we find out an unexpected recurrence of 2,8-DHA nephropathy due to novel expected pathogenetic variants of APRT gene in patient without medical history of kidney stones successfully treated with steroid, febuxostat and hemodiafiltration.

#4676

RETROSPECTIVE EVALUATION OF THE PREVALENCE OF DIABETES MELLITUS IN A SINGLE CENTER RENAL TRANSPLANT COHORT

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Background and Aims: Post-transplant diabetes mellitus (PTDM) might impact significantly in renal transplant (RTx) and RTx patients (RTxps) outcome. In this study we evaluated: 1) the prevalence of diabetic patients who access the RTx 2) the incidence of PTDM and 3) the most related factors for the development of diabetes after RTx.

Method: We retrospectively studied 522 RTxps transplanted in our Unit between January 2004 and December 2014. Each patient underwent: 1) to a collection of remote and pathological anamnesis and complete physical examination and to routine and specific clinical and biochemical determinations at 1 (T1), 6 (T6) and 12 (T12) months after RTx. At six months of RTx, the Oral Glucose Tolerance Test (OGTT) was performed.

Results: The age of RTxps was 48±12 years. Patients with glucose metabolism abnormalities were significantly older, without differences in gender. Inpatients with PTDM (12.6%), cyclosporine was used more than tacrolimus, and higher doses of steroids at T1 and T6 were prescribed. They had a worse general metabolic and glucose (HOMA index, glycaemia and HbA1c) status than normoglycemic. of note, no differences in 25-(OH)-D and in the other mineral metabolism parameters were found. In multivariate analysis, we found that age at transplant (OR 1.28 for 5 years older) (p = 0.006), BMI at T1 (OR 1.22 for 2 kg / m2 more) (p = 0.01) and the dose of steroid prescribed during the

Abstract

## Figure 1: Allograft kidney biopsy showed reddish brown tinged crystals in hematoxylin and eosin stain (A) birefringent under polarized light (B).
first post-RTx month (OR 2.7 per 100 mg additional drug) (p = 0.03) were independently correlated with PTDM.

Conclusion: In this study, we demonstrated that the prevalence of PTDM was relatively high in our cohort reflecting data present in the literature. Interestingly, age at RTx, BMI and cumulative dose of steroids resulted the variables that significantly and strongly influence its development. On the other hand, no relationship was observed between blood values of 25 (OH) D, PTH and the onset of PTDM. Future research, possibly involving a higher number of RTx pts could also evaluate the effects of PTDM on graft and patients on long-term outcome.

#4343
COMPARISONS OF CLINICAL OUTCOMES BETWEEN HYPERTENSIVE AND NORMOTENSIVE LIVING KIDNEY DONORS: A NATIONWIDE PROSPECTIVE COHORT STUDY

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Background and Aims: Living kidney donors with hypertension is potential candidates to solve the imbalance between supply and demand for renal transplantation. However, the safety of hypertensive donor is not sufficiently ensured after donor nephrectomy and there are limited studies, which compare the clinical outcomes between hypertensive and normotensive donors.

Method: All data from this study were obtained from the Korean Organ Transplantation Registry (KOTRY). A total 672 hypertensive donors and 5,134 normotensive living kidney donors were included from May 2014 to December 2020. Primary outcome was the occurrence of proteinuria and the development of lower renal function, defined as an estimated glomerular filtration rate (eGFR) less than 60 or 45 ml/min/1.73 m².

Results: Compared to normotensive donors, hypertensive donors had lower eGFR before nephrectomy and remained lower after kidney transplantation. However, the risk of eGFR below 60 ml/min/1.73 m² (adjusted HR, 0.87; 95% CI 0.70-1.09; P = 0.226) or below 45 ml/min/1.73 m² (adjusted HR, 1.49; 95% CI 0.77-2.86; P = 0.234) was not significantly increased in hypertensive donors after multiple adjustment. When comparing the rate of eGFR decline between the hypertensive and normotensive donors, there was no significant difference (adjusted unstandardized β = −0.19; −1.15 – 0.76, P = 0.691). The incidence of proteinuria occurrence in hypertensive donor was increased, and it tended to increase even after 4-5 years. Hypertensive donors were found to have significantly more proteinuria than normotensive donors (adjusted HR, 1.83; 95% CI 1.13-2.96; P = 0.014).

Conclusion: Our study indicated that the risk of proteinuria after donation was increased in hypertensive donor, while it was not translated into significant decline in renal function. The continuous and careful monitoring for proteinuria should be required in hypertensive donor after nephrectomy.

#2970
CYTOMEGALOVIRUS INFECTION AND RISK OF NEW-ONSET DIABETES AFTER TRANSPLANTATION: A RETROSPECTIVE STUDY

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Background and Aims: New-onset diabetes after transplantation (NODAT) is one of the common complications reported in patients with kidney transplantation and is associated with risk of infection, poor allograft and patient survival. There is conflicting research literature regarding the role of cytomegalovirus (CMV) infection in increasing the risk of NODAT development.

Method: A total of 59 kidney transplant patients were studied from March 2017 to February 2019. NODAT was defined as two readings of fasting plasma glucose of ≥126 mg/dl at three months post-transplant. CMV viral load was also documented. The 12 months post-transplant allograft and patient survival outcomes were also measured.

Results: Mean age was 43.4 ± 6.2 years. Nearly one-fourth, 14 (23.7%), of the patients had NODAT. CMV viral load and viremia were high in NODAT group; however, the result did not reach statistical significance. CMV DNA replication was statistically high during 1-6 months post-transplant for NODAT group (P<0.001). Only 7 (11.9%) recipients advanced to symptomatic CMV infection. Also, we found that high CMV viremia load was associated with poor kidney allograft function at 12 months.

Conclusion: In summary, this study showed that infection with CMV may not be a risk factor to develop NODAT in patients transplanted with kidney. An elevated CMV viral load may decrease the post-transplant allograft function at 12 months. The prompt diagnosis and timely management of CMV infection could substantially lessen the risk to develop NODAT subsequent worsening of allograft and patient survival.

#2502
THE FREQUENCY AND RISK FACTORS OF NODAT AND ELECTROLYTE DISORDERS IN KIDNEY TRANSPLANT PATIENTS

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Background and Aims: The purpose of the study is to investigate at the incidence and risk factors for post-transplant diabetes mellitus (PTDM) in non-diabetic kidney transplant patients (KTRs).

Method: The study included 120 KTRs who did not have diabetes in the pretransplant period. The diagnosis of PTDM was made according to the 2003 ADA DM diagnostic criteria. The relationship between PTDM and clinical and laboratory data on the 0th, 1st, 3rd, 6th, 12th and 24th months was investigated.

Results: The mean age of the patients was 33.3±11.5 years, 65% (78) of them were male. PTDM was developed in 29.1% (35) and 80% of PTDM at first 3 months. The risk factors for PTDM were found to be older (4.4%), family history of diabetes mellitus (5.24 times), beta-blocker use (2.55 times), KTRs with and without PTDM, Pretransplant dialysis type (Hemodialysis (P=0.822) and Peritoneal dialysis (P = 0.583), living donor (101/84.2%)/cadaveric donor (19/15.8%), donor age and gender were similar. Serum magnesium and potassium were different only in the first month between the groups with and without PTDM (P = .019 and 0.008 respectively). The negative effect of PTDM on GFR was not observed in the 2-year follow-up.

Conclusion: It can be predicted that diabetes mellitus may develop with a family history of diabetes, advanced age and the use of beta-blockers. The risk of developing PTDM is higher in the first 3 months and hypomagnesemia in the first month may contribute to diabetes development.
AN OBSERVATIONAL STUDY OF MICRO-VASCULAR COMPLICATIONS OF POST-TRANSPLANT DIABETES MELLITUS IN RENAL TRANSPLANT RECIPIENTS

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Background and Aims: The worldwide incidence of PTDM ranges between 2.5% and 20%. Although there is a good knowledge of PTDM pathogenesis, there is still uncertainty about its proper long-term management. DR, DKD and DSPN are microvascular complications frequently seen in type 1 and 2 DM. Few data are available regarding these complications in patients with PTDM. It remains unclear if the progression of chronic diabetic complications in transplant recipients is similar to that of patients with other types of diabetes. The study was conducted to assess micro-vascular complications in renal transplant recipients with ≥ 5 years duration of PTDM.

Method: This is a retrospective and prospective observational study of PTDM patients conducted between November 2018 to December 2020, at a tertiary care hospital. All renal transplant recipients on follow up at the institute with ≥ 5 years duration of PTDM were included in the study. Patient characteristics and laboratory values were noted from patient files and electronic records. Fundus evaluation was done by direct ophthalmoscopy. If graft kidney biopsy was done for clinical indications, it was included in evaluation. DSPN was assessed through MNSI and 10-g Semmes-Weinstein monofilament examination.

Results: 115 patients with PTDM duration ≥ 5 years were included in the study. Mean PTDM duration was 8.7 ± 3.0 years. None presented findings of diabetic retinopathy at fundus examination by direct ophthalmoscopy. 37.4% patients had DSPN which was associated with PTDM duration (p value < 0.03, 95% CI, 0.93 to 0.99). The mean eGFR was 59.2 ± 21.8 ml/min/1.73 m², 53.9% patients had eGFR ≥ 60 ml/min/1.73 m². 35.7% patients had proteinuria ≤ 300 mg/day. 23 (20%) patients with PTDM duration ≥ 5 years underwent graft kidney biopsy, 4 biopsies were reported as de-novo DKD, 6 biopsies were reported as suggestive of DKD. The patients with DKD had mean PTDM duration of 143.3 ± 52.4 months, mean eGFR 44.8 ± 21.8 of and a median proteinuria of 2653 mg (IQR 2758). In secondary analysis of the 23 biopsied patients PTDM duration was associated with DKD development (p value = 0.196; 4.2 ± 4.9 vs. 5.1 ± 2.9 months, p = 0.231 respectively). In multivariate logistic analysis, there was no significant difference regarding the total exposure to CNI and follow-up duration (sensitization group: multivariate odds ratio [OR] 1.188, 95% confidence interval [CI] 0.55–2.52, p = 0.655, OR 1.03, 95% CI 0.97–1.10, p = 0.282, respectively). In some patients, even prolonged immunosuppression

Conclusion: The initiation of microvascular complications does not seem to be as accelerated as previously supposed. DR may not be as strongly associated with de-novo DKD in PTDM patients as seen in type 1 and type 2 diabetes mellitus. PTDM seems to be a unique type of diabetes, and its consequences may be milder than expected in type 1 and type 2 diabetes.

IMMUNOSUPPRESSION FOR FAILED ALLOGRAFT: HOW PROlongED AND MUCH IS ADEQUATE?

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Background and Aims: The development of human leukocyte antigen (HLA) antibodies towards a failed allograft is a critical factor for the feasibility and outcomes of future transplantation. Therefore, we investigated the factors contributing to sensitization in patients with failed allografts.

Method: A single-center retrospective study of patients with failed allografts between 2010 and 2020 was performed. Samples for HLA antibodies were tested at the time of graft failure and after immunosuppression withdrawal. Sensitization was defined as more than 80% of calculated Korean panel reactive antibody (PRA) I or PRA II. In addition, variables for affecting sensitization were collected.

Results: Twenty-three patients were included in the study. The mean flow-up duration after failed allograft was 43 ± 33.3 months. The sensitized patients tended to have a longer flow-up period and were exposed to less total calcineurin inhibitor (CNI) than non-sensitized patients. (non-sensitized vs sensitized patients: 27.1 ± 12.9 vs 51.7 ± 37.8 months, p = 0.196; 4.2 ± 4.9 vs. 5.1 ± 2.9 months, p = 0.231 respectively). In multivariate logistic analysis, there was no significant difference regarding the total exposure to CNI and follow-up duration (sensitization group: multivariate odds ratio [OR] 1.188, 95% confidence interval [CI] 0.55–2.52, p = 0.655, OR 1.03, 95% CI 0.97–1.10, p = 0.282, respectively). In some patients, even prolonged immunosuppression
after returning dialysis therapy did not prevent sensitization toward failed allografts.

**Conclusion:** In this study, there was no significant difference regarding the contributing factors for sensitization in the multivariate logistic analysis. However, in sensitized patients, trends were showing longer follow-up duration and less CNI exposure. Sensitization towards a failed graft might be affected by the dose and duration of immunosuppressant. Finally, the small sample size is one of the limitations of this study, and additional prospective research analysis for patients with failed allografts is needed in the future.

## #5095

**THE CURIOUS CASE OF GAS IN THE GRAFT KIDNEY**

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**Background and Aims:** Emphysematous pyelonephritis (EPN) denotes a severe infection of renal parenchyma resulting in necrosis and gas accumulation in the renal and perirenal tissue. Risk factors for urinary tract infections in renal transplant recipients include advanced age, female gender, reflux nephropathy prior to transplantation, diabetes mellitus, deceased donor kidney, kidney–pancreas transplant, retransplantation, antibody induction for immunosuppression, urinary bladder catheterisation, history of allograft rejection with subsequent escalation of immunosuppressive therapy, and use of ureteral stents. There are no definite guidelines for management of EPN in renal allografts. If unstable and deteriorating, graft nephrectomy should be undertaken as soon as possible. Any delay in surgical intervention, be it percutaneous drainage or nephrectomy may result in death.

**Method:** A 25-year old male, diagnosed with IgA Nephropathy (IgAN) received a living donor renal transplant from his mother in 2013 after a diuresis vintage of 3 years. He received Basiliximab induction followed by maintenance immunosuppression with Tacrolimus, Mycophenolate mofetil and Prednisolone. He had no history of UTI in the immediate post-transplant period. His blood glucose levels were within normal limits and he had not had any urological intervention. In 2019, patient was diagnosed with IgAN recurrence as a cause of chronic renal allograft injury. His Creatinine at last follow up in July 2022 was 4.1 mg/dl. He presented in September 2022 with fever, chills, vomiting, pain in the right iliac fossa and inability to extend his right leg. At presentation, his BP was 86/60mmHg, with pyrexia and tachycardia. Ultrasonography revealed an ill-defined collection superomedial to the graft kidney with doubtful posterior extension and air foci. Non-contrast CT study revealed a large subcapsular collection, extending posteriorly into the right iliac fossa involving the right psoas major and inferiorly into the pelvis, with air foci and no evidence of any urinary tract obstruction suggestive of Acute Emphysematous pyelonephritis with ruptured abscess. He was started on broad-spectrum iv antibiotics- Meropenem and Levofloxacin. Immunosuppression was reduced. Laboratory investigations revealed total leucocyte count of 37,000 cells/mm³, Creatinine of 11 mg/dl, urine routine microscopy revealed field full of pus cells. Blood and urine cultures grew ESB1 Escherichia coli. He was taken up for urgent urological intervention in the form of percutaneous drain insertion. Frank pus was aspirated and 200ml drained instantaneously, cultures of which demonstrated the same organism. Within 24 hours of pus drainage, patient became afebrile and had pain relief. He was given 3 weeks of culture-propriate iv antibiotics, to continue another 3 weeks of oral Carbapenem. However, his graft dysfunction persisted, with no recovery and he became dialysis-dependent.

**Discussion:** EPN of the renal allograft is a rare occurrence. A study of EPN in renal transplant recipients by Alexander et al from 2012 revealed 18 out of 22 patients were diabetics, 9 necessitated graft nephrectomy and 7 required percutaneous drainage in addition to antibiotics. Till date, up to 30 cases of graft EPN have been reported in English literature. The striking feature is that more than 90% of these cases were diabetic.

**Conclusion:** The complete pathogenesis of renal allograft EPN, especially in patients with no apparent traditionally described risk factors remains yet to be understood. A high degree of suspicion and early intervention may help to save the allograft.

## #5691

**BK POLYOMAVIRUS VIREMIA AND VIRURIA ARE ASSOCIATED WITH SEVERE INFLAMMATION AND FIBROSIS IN RENAL ALLOGRAFTS, BUT NOT WITH GRAFT SURVIVAL**

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**Background and Aims:** Infection of the renal allograft by Polyomavirus BK (BKV) can cause acute tubular cell injury and interstitial inflammation, which leads to subsequent interstitial fibrosis and tubular atrophy (iIFTA). The presence and degree of inflammation within these areas (i-IFTA) is associated with worse outcomes in kidney transplant (KT) patients. The aim of this study was to investigate the association between BKV viremia and viruria and the presence of iIFTA and i-IFTA, decline of renal function, and graft loss.

**Method:** We conducted a single-center retrospective case-control study, which included all patients who underwent an allograft biopsy between January 2018 and December 2022. All biopsies were made for cause (allograft dysfunction with increased serum creatinine). Real-time polymerase chain reaction was used to detect and quantify BK viral load in serum and urine samples. Patients were included if they had at least 6 months since KT and if they had serial evaluation of BKV viremia and viruria previously to the biopsy. We calculated, in the graft biopsy, the percentage of iIFTA, and also i-IFTA. Estimated glomerular filtration rate (eGFR) was obtained at baseline and 1 year after the biopsy. Graft loss was evaluated at 6 months and 1 year after the biopsy. **Results:** Mean age of the population was 53.5 years and 67% were males. A total of 116 biopsies were performed during the studied period and 72 met the inclusion criteria. Ten percent of patients developed persistent (≥ 3 months) BKV viremia, 24% developed persistent BKV viruria, and 18% developed persistent JCV viruria. Five cases of polyomaviruses-associated nephropathy were diagnosed. The other most common diagnoses were T cell-mediated rejection (24%), antibody-mediated rejection (15%), and focal segmental glomerulosclerosis (15%). In patients with persistent BKV viremia, a higher viral load had a strong positive association with the degree of i-IFTA (r=0.954; \( P = 0.001 \)). Patients with BKV viremia and/or viruria were more likely to present more severe iIFTA (≥ 40%) and i-IFTA (grade ≥ 2) in allograft biopsy (\( P = 0.03 \)). Patients with higher degrees of iIFTA and i-IFTA were more likely to experience graft loss 1 year after the biopsy (\( P = 0.01 \)). There was no significant association between the presence of BKV viremia and/or viruria and the decline of eGFR, nor with the incidence of graft loss 1 year after the biopsy. In multivariable analysis adjusted for age, eGFR at the time of biopsy; the presence of donor-specific antibodies and the main diagnosis of allograft biopsy, the presence of BK viremia and/or viruria was a significant predictor of more severe iIFTA and i-IFTA (\( P = 0.04 \)).

**Conclusion:** In our population, higher BK viremia loads were associated with more extensive inflammation within areas of iIFTA. Patients with BK viremia and/or viruria, independently of the main diagnosis of the biopsy, were more likely to exhibit more severe iIFTA and i-IFTA in allograft biopsies, but no association with the incidence of dialysis at 1 year was shown. Longer prospective studies are needed to investigate whether BKV infection treatment/ reduction of immunosuppression can slow down fibrosis progression and minimizes i-IFTA.
for regular monitoring were collected from patients before RT, every 2 weeks first 3 months, then at 6, 9, 12 months after RT. In the case of complication development samples from patients were collected later then 1-year monitoring period. PyV DNA was detected by real-time PCR. Viral DNAs from 17 BKV-positive and 11 JCV-positive patients were molecular typed by partial sequencing of VP1 genome region. Confidence intervals for the proportions were calculated using Wald’s method.

Results: Results showed that PyV detection total frequency in the group 1 was 14.47% [11.32%; 18.3%], almost all patients developed viruria, only 2.54% [1.32%; 4.67%] had viremia. In the group 2 PyV DNA was detected in 46.07% [40.96%; 51.26%] of recipients: 19.10% [15.34%; 23.52%] had BKV infection, 19.94% [16.11%; 24.42%] – JCV, 7.02% [4.76%; 10.2%] – BKV+JCV mixed infection. Frequency of viremia was 6.74% [4.53%; 9.87%] in this group. Maximal BKV viral load levels reached 1.2 × 10^{12} copies/ml in urine and 5.9 × 10^7 copies/ml in serum. JCV loads were up to 3 × 10^9 copies/ml in urine and 1.2 × 10^8 copies/ml in serum. Then we analyzed frequency of PyV detection before RT and during the first year after RT among the 102 recipients. Results displayed on the fig.1 showed that the peak of PyV infection registration was 30 days after RT. Quantitative monitoring of viral load in posttransplant period was the basis for the correction of the applied immunosuppressive therapy regimens in relation to the recipients with a high viral load (higher than 1 × 10^10 copies/ml in urine or 1 × 10^8 copies/ml in serum). The results of molecular typing showed that 17 BKV isolates belonged to subgroups Ib-2 and IcV-2 (12 and 5 isolates, respectively). Within subgroups Ib-2 isolates formed 3 clusters corresponding 3 separate genovariants. JCV isolates belonged to subtype 1A, 1B and 2A (7, 17 BKV isolates belonged to subgroups Ib-2 and IcV-2, 12 and 5 isolates, respectively). The last one had 99% nucleotide sequence similarity with Greece and South Korea isolates.

Conclusion: Our data demonstrated an importance of PyV DNA monitoring of kidney recipients in the posttransplant period starting from the first days after RT to predict development of PyV complications as PyVAN, HC or others by correcting the immunosuppressive therapy.

HYPERTENSION & DIABETES

F1 - BASIC SCIENCE & EXPERIMENTAL

#3293
ESTRADIOL REPLACEMENT MITIGATED BLOOD PRESSURE ELEVATION VIA SUPPRESSION OF NCC IN ANGIOTENSIN II-INFUSED OVARIECTOMIZED FEMALE RATS

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Background and Aims: Female rats excrete more urine sodium than male rats with similar blood pressure (BP). However, it is not clear whether the sex difference in pressure natriuresis is conserved in menopausal rats. We assessed whether the natriuretic response and renal sodium transporter activity in ovariectomized female rats infused with angiotensin II (ANGII) could be affected by estrogen supplementation.

Method: Six-week-old female Sprague-Dawley rats (n = 30) were ovariectomized (OVX, n = 20) or sham-operated (n = 10) (−4 weeks, −4W). After 2 weeks, subcutaneous estradiol was administered to half of the OVX rats (n = 10) for 4 weeks (−2W~−2W).

Results: ANGII-infused VP1 genome region. Confidence intervals for the proportions were calculated using Wald’s method.

Results: ANGII-induced BP elevation was highest in the OA group, followed by the FA and OEA groups. Urine sodium tended to increase after ANGII infusion in OA and OEA but decreased in OA. Western blot results showed that cortical phosphorylated sodium chloride cotransporter (pNCC) tended to be augmented by ANGII treatment in FA and OA, but mitigated in OEA. Cortical ANGII type 2 receptor (AT2R) expression was significantly higher in estradiol-treated OVX rats than in OVX rats, irrespective of ANGII infusion. Similarly, the enhanced pNCC in ANGII-treated distal convoluted tubular cells was reversed by estradiol treatment. In KoGES data, urine sodium was significantly lower in postmenopausal women than in premenopausal women, despite the higher BP.

Conclusion: Estradiol reversed BP elevation and augmented the natriuretic response in ANGII-infused OVX rats and distal tubular cells via suppression of pNCC and increase of AT2R.

#4313
AN ANTI-FIBROTIC GENE ATTENUATES DIABETIC KIDNEY INJURY IN DB/DB MICE BY INHIBITING FIBROSIS VIA EPITHELIAL-MESENCHYMAL TRANSITION PATHWAY

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Background and Aims: Diabetic nephropathy (DN) is a major cause of mortality in patients with diabetes and chronic kidney disease, but there is a lack of effective therapeutic drugs for this disease. The development and progression of DN is influenced by fibrosis. Transforming growth factor (TGF)-β1 is a key cytokine involved in fibrosis in many different organ systems. Anti-fibrotic gene (Anti-F) is a TGF-β/Smad signaling. Here we examined the therapeutic effect of Anti-F in a model of DN using db/db mice with streptozotocin (STZ) treatment.

Method: The db/db mice were divided into five groups; db/db + (wild type), db/db + saline, db/db + STZ, db/db + STZ + CMV-Anti-F, and db/db + STZ + TGF-β - Anti-F. STZ was peritoneally injected for five consecutive days (50mg/kg) and Anti-F (40μg/head) was peritoneally administered once every two weeks. Mice were sacrificed four months after STZ injection.

Results: The Anti-F with CMV and TGF-β promoter administration markedly alleviated metabolic syndrome assessed by obesity and hyperglycemia, and renal dysfunction assessed by renal overweight and albuminuria in db/db + STZ mice. The administration obviously mitigated glomerular damage in diabetic mice, as reflected by the reduced increase mesangial expansion and the expression of nephrin and podocin in db/db + STZ mice. Additionally, renal interstitial fibrosis was also significantly inhibited by Anti-F through suppressing epithelial-mesenchymal transition (EMT) signaling including α-
SMA, Twist, and Snail, as well as inflammation reflected by IL-1β, MMP-2, and MMP-9 in diabetic rats.

**Conclusion:** Anti-F attenuated the development of DN in db/db mice with type 2 diabetes. The protective effect was associated with decreased inflammation and subsequent attenuation of EMT-mediated renal fibrosis. Thus, this study suggests that targeting the Anti-F could be considered as a novel therapeutic approach for preventing the progression of DN.

#4419

**THE IMPACT OF TRANSGlutaminase 2 INHIBITION ON HYPERTENSION-INDUCED FIBROSIS IN HYPERTENSIVE NEPHROPATHY**

Jiwon Lee, Sang-Woong Han, Seung Hee Yang and Mi-Yeon Yu

Rep. of South Korea

**Background and Aims:** Hypertensive nephropathy is a chronic disease that requires the novel treatment. Transglutaminase 2 (TG2), linked to various diseases including cardiovascular and kidney diseases, has been suggested to play a role in the development of hypertensive nephropathy through its contribution to fibrous tissue formation, oxidative stress regulation, and inflammation. This study aimed to explore the role of TG2 in the development of hypertensive nephropathy and evaluate its potential as a therapeutic target.

**Method:** An in vitro hypertensive model was established using a device that mimics hypertension by applying rotational force. An in vivo hypertensive model was established in rats through subtotal 5/6 nephrectomy to induce fibrosis. The relationship between TG2 expression and the progression of hypertension-induced fibrosis was analyzed, and the impact of TG2 inhibition on fibrosis was evaluated using the TG2 inhibitor, cysteamine.

**Results:** In the in vitro study, rotational force was applied to induce hypertension using a hypertensive mimic device, which resulted in fibrosis in primary human glomerular endothelial cells and tubular epithelial cells and increased expression of TG2. The administration of cysteamine at concentrations of 0.5 mM, 1 mM, and 2 mM decreased fibrosis and phosphorylated P65 in a dose-dependent manner. The in vivo hypertensive model demonstrated a significant increase in blood pressure (P < 0.001) and kidney fibrosis (P < 0.001) over time at 4 and 8 weeks after surgery. A significant increase in TG2 expression was observed as hypertension and fibrosis progressed (P < 0.001).

**Conclusion:** The progression of hypertension-induced fibrosis was accompanied by an increase in TG2 expression. Inhibition of TG2 showed improvement in fibrosis, suggesting further study of its mechanism may provide new therapeutic options for hypertensive nephropathy.

#4945

**NEPHROPROTECTIVE EFFECTS OF Dipeptidyl peptidase–IV INHIBITORS FROM PHENOLIC RICH FRACTION OF TRIGONELLA FOENUM IN DIABETIC NEPHROPATHY RATS**

Anand Krishna Singh and Purnima Tripathi

Shri Vaishnav Vidyapeeth Vishwavidyalaya, Life science, Indore, India

**Background and Aims:** The most common effect of renal disease in the world is diabetic nephropathy (DN). Dipeptidyl peptidase-IV (DPP-IV) enzyme is most abundant present in kidney, which is increased in diabetic nephropathy. A novel approach to treat type 2 diabetes mellitus (T2DM) along with DN, based on incretin hormones: glucagon-like peptide-1 (GLP-1) which regulated by DPP-IV. We hypothesized that DPP-IV inhibitors isolated from phenolic rich fraction of Trigonella foenum (TF) will regulate DPP-IV activity as well as DN: *in vivo; in-silico* and kidney histology.

**Method:** DPP-IV inhibitors from phenolic rich fraction of TF in high sucrose diet along with dexamethasone induced T2DM was explored *in-vivo* in rat. Apart from serum glucose, DPP-IV, and inhibition activity, HbA1c, Insulin was estimated. We also examined GLP-1, albuminuria, and antioxidant properties in kidney tissue along with histology. Molecular docking of phenolic rich fraction (Gallic acid) of TF with DPP-IV.

**Results:** High sucrose diet with Dexamethasone administration (1 mg /kg BW 45 days) increased concentration of serum glucose, DPP-IV and albuminuria, cholesterol and renal LPO with increase in tissue antioxidant to scavenging free radicals generated by oxidative stress, but after some time antioxidants such as SOD, CAT, GSH was decreased. However, after administration of phenolic rich fraction of TF, DPP-IV inhibition activity increase in TF (71.1%), as compared to Sitagliptin (89.5%) with significant reduction in levels of glucose, albuminuria, TC, TG and with increased Insulin and GLP-1. Kidney histology showed some significant change as compared to diabetes control. Isolated Gallic acid depicts the conformer and affinity energy was – 5.3 and distance from RMSD 1b was 38.669. Sitagliptin depicted the conformer and affinity energy was – 8.9 and distance from RMSD 1b was 3.826.

**Conclusion:** DPP-IV inhibitors isolated from TF are nephroprotective, with novel antioxidant properties. DPP-IV inhibition lower blood glucose by decreasing DPP-IV activity, albuminuria and increasing levels of GLP-1.

#5018

**EFFECTS OF CANDESARTAN COMPARED TO LOSARTAN ON INHIBITING MESANGIAL EXPANSION IN DIABETIC MODEL RATS RECEIVING ROSMARINIC ACID**

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**Background and Aims:** Oxidative stress and activation of the renin-angiotensin system (RAS) due to chronic hyperglycemia are the pathogenesis of diabetic nephropathy (DN). Until now, therapy for DN has not shown satisfactory results. Rosmarinic acid (RA) which has antioxidant, anti-inflammatory, anti-fibrosis effects, and ARB which can inhibit RAS activation may have a synergistic effect to prevent DN progression. This study aims to determine the effect of inhibiting mesangial expansion in diabetic rat models after being given a combination of RA and ARB (candesartan or losartan).

**Method:** True experimental laboratory trial with randomized post-test only control group method on Rattus norvegicus strain Wistar rats. Diabetic rats were prepared by giving a high-fat diet (60% fat calories) and a single injection of 40 mg/kg streptozotocin. Mice were divided into 4 groups, each consisting of 4 rats: negative control (healthy rats); positive control (placebo diabetic rats); diabetic rats that received RA and candesartan; diabetic rats that received RA and losartan. The rat glomerulus was evaluated to assess mesangial expansion using ImageJ 1.48 software after 8 weeks of treatment by a pathologist blindly. Data analysis with One-way ANOVA and Tukey’s post hoc tests.

**Results:** The results of the percentage of the mesangial matrix in the positive control group (81.49% ± 1.45) were higher than the negative control group (58.82% ± 0.99). The results of the percentage of the mesangial matrix in the RA + candesartan treatment group (61.56% ± 0.35) and the RA + losartan treatment group (62.28% ± 0.77) showed lower results than the positive control group, with the One-way ANOVA test results showing significant differences (p < 0.000). Tukey’s post hoc tests showed the positive control group that received a high-fat diet and induced diabetes with STZ significantly increased mesangial expansion compared to negative control (MD: [22.66]; 95% CI: [20.62], [24.72]; p: 0.000). The RA + candesartan treatment group significantly inhibited mesangial expansion compared to the positive control (MD: [19.92]; 95% CI: [-21.97], [-17.87]; p: 0.000), as well as the RA + losartan treatment group (MD: [19.21]; 95% CI: [-21.26], [-17.16]; p: 0.000). The RA + candesartan treatment group showed a better effect in inhibiting mesangial expansion compared to the RA + losartan treatment group, but not significantly (p: 0.735).

**Conclusion:** The combination of rosmarinic acid with candesartan or losartan has the effect of inhibiting mesangial expansion in diabetic rats.
INVESTIGATING TREM2 MACROPHAGES IN CHRONIC KIDNEY DISEASE

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¹Cambridge University Hospitals, Nephrology, Cambridge, United Kingdom, ²University of Cambridge, Medicine, Cambridge, United Kingdom, ³Broad Institute of MIT and Harvard, Cambridge, United States of America and ⁴Sun Yat-sen University, P.R. China

Background and Aims: Kidney macrophages have been implicated in interstitial fibrosis and inflammation in various forms of chronic kidney disease (CKD), but subsets with different markers and putative functions have been identified through the application of single cell technologies. A recent study from the Greka Lab revealed distinct macrophage populations in the human kidney bearing lymphatic endothelium hyaluronic receptor-1 (LYVE1) and triggering receptor expressed on myeloid cells-2 (TREM2). Notably, TREM2⁺ macrophages, which have been implicated in limiting metabolic toxicity in chronic diseases, were enriched in diabetic mouse kidneys and human kidneys from obese individuals (Subramanian et al. BioRxiv 2021). To support these findings, we aimed at characterizing LYVE1⁺ and TREM2⁺ macrophages in kidney samples taken from subjects with CKD-associated co-morbidities, including hypertension, diabetes mellitus and obesity.

Method: We performed immunofluorescence microscopy of samples collected from the cortex of kidneys donated for transplantation but deemed unsuitable for implantation. Each sample was stained with anti-CD163, -LYVE1, and -
TREM2 antibodies, plus Hoechst to stain nuclei. Two identically sized fields of view were imaged in each sample. Macrophages were identified based on CD163 expression and the expression of the LYVE1 and TREM2 in macrophages delineated. Macrophage subsets were compared according to age, BMI, eGFR and the presence of hypertension, obesity and diabetes.

**Results:** of 49 donors assessed, 19 (39%) were “healthy”, six (12%) “hypertensive” without obesity or diabetes, 16 (33%) “obese” with no evidence of diabetes, and 8 (16%) “diabetic” (all had type 2 diabetes and 6/8 were also obese) The median eGFR at donation was 95 mL/min/1.73 m² and none of the donors had a history of CKD. Gender, median age and cause of death were not significantly different as well (Table 1). “Healthy”, “hypertensive” and “obese” donors had similar numbers of total macrophages, LYVE1+ and TREM2+ macrophages per region of interest. In contrast, “diabetic” subjects had a tendency towards a higher macrophage count ($P = .10$) and significantly higher numbers of LYVE1+ ($P = .02$) and TREM2+ macrophages ($P = .002$), compared to “healthy” ones (see Figure 1). The median LYVE1+/CD163+ ratio was 0.69 and did not differ substantially between the groups ($P = .18$), while the TREM2+/CD163+ ratio was higher among “diabetic” compared to “healthy” donors ($0.43$ vs $0.34$, $P = .06$).

**Conclusion:** Diabetes is associated with an increase in kidney macrophages, particularly in those expressing TREM2. Further investigation is required to determine the role these cells may play in CKD progression.

### Table 1: Main donors’ demographic and clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>All N = 49</th>
<th>Healthy (A) N = 19</th>
<th>HTN (B) N = 6</th>
<th>P value A vs B</th>
<th>Obese (C) N = 16</th>
<th>P value A vs C</th>
<th>Diabetic (D) N = 8</th>
<th>P value A vs D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>32 (65)</td>
<td>11 (58)</td>
<td>3 (50)</td>
<td>1</td>
<td>12 (75)</td>
<td>0.47</td>
<td>6 (75)</td>
<td>0.66</td>
</tr>
<tr>
<td>Age, median (IQR) – years</td>
<td>61 (49-70)</td>
<td>49 (28-64)</td>
<td>64 (58-74)</td>
<td>0.08</td>
<td>62 (58-70)</td>
<td>0.76</td>
<td>69 (58-72)</td>
<td>0.15</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral event, n (%)</td>
<td>34 (69)</td>
<td>10 (53)</td>
<td>5 (83)</td>
<td>0.34</td>
<td>12 (75)</td>
<td>0.29</td>
<td>7 (87)</td>
<td>0.18</td>
</tr>
<tr>
<td>Cardiorespiratory, n (%)</td>
<td>10 (20)</td>
<td>5 (26)</td>
<td>1 (17)</td>
<td>1</td>
<td>3 (19)</td>
<td>0.70</td>
<td>1 (13)</td>
<td>0.63</td>
</tr>
<tr>
<td>Trauma, n (%)</td>
<td>4 (8)</td>
<td>3 (16)</td>
<td>0</td>
<td>0.55</td>
<td>1 (6)</td>
<td>0.60</td>
<td>0</td>
<td>0.53</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>1 (2)</td>
<td>1 (5)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>eGFR at admission, median (IQR) – mL/min/1.73 m²</td>
<td>95 (85-111)</td>
<td>93 (81-111)</td>
<td>110 (103-114)</td>
<td>0.30</td>
<td>94 (88-104)</td>
<td>0.96</td>
<td>96 (90-101)</td>
<td>0.89</td>
</tr>
<tr>
<td>Arterial hypertension, n (%)</td>
<td>25 (51)</td>
<td>0</td>
<td>6 (100)</td>
<td>$&lt;$0.001</td>
<td>13 (81)</td>
<td>$&lt;$0.001</td>
<td>6 (75)</td>
<td>$&lt;$0.001</td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>27 (24-32)</td>
<td>25 (21-27)</td>
<td>24 (22-28)</td>
<td>0.95</td>
<td>33 (32-35)</td>
<td>$&lt;$0.001</td>
<td>32 (28-34)</td>
<td>0.012</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>8 (16)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>16 (100)</td>
<td>$&lt;$0.001</td>
<td>6 (75)</td>
<td>$&lt;$0.001</td>
</tr>
</tbody>
</table>

**BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; HTN, hypertensive**

Figure 1:
**Background and Aims:** Diabetic mellitus (DM) is the most common cause of chronic kidney disease (CKD) [1]. The prevalence of CKD is therefore increasing worldwide with increasing prevalence of DM [1]. Among those with DM, CKD prevalence varies widely between countries. The actual prevalence of CKD in patients with DM in Turkey is unknown. This study aimed to determine frequency of CKD among diabetic patients of Cappadocia cohort and patients’ awareness about the disease.

**Method:** A total of 1591 diabetic patients from the Cappadocia cohort were invited to this cross-sectional study. A trained study team administered a questionnaire for patients’ medical history, knowledge, attitudes, and awareness of the disease and measured patients’ blood pressures (BPs) at least three times using an automated device. Serum creatinine was measured and spot urine albumin/creatinine ratio (ACR) measurements were performed for three consecutive days. A diagnosis of CKD was established if glomerular filtration rate (GFR) is < 60 mL/min or ACR is > 30 mg/g.

**Results:** The mean age of the patients was 63±10 years. Overall, 60.9% patients were obese (body mass index ≥ 30 kg/m²), and 70% patients were hypertensive. HbA1c was analyzed in 98.2% of the patients; HbA1c was <7% in 27.4%, ≥7%–<8% in 20.8%, >8%–<9% in 17.7%, and >9% in 34.1% of the patients. 1535 patients with blood and urine analyses, 231 of 1008 (22.9%) females and 154 of 527 (29.2%) males had CKD (P = .007). Among patients with GFR values, 11.4% had a GFR of <60 mL/min and 88.6% had a GFR of ≥60 mL/min. Among 1544 patients with ACR measurements, 18.2% had values ≥30 mg/g and 4.4% had values ≥300 mg/g. CKD was detected in 385 (25.1%) of 1535 patients with both GFR and ACR values (Figure 1). Of these patients, 28.1% had Stage 1, 25.7% had Stage 2, 32.5% had Stage 3A, 11.2% had Stage 3B and 2.6% had Stage 4 or 5 CKD. Excluding two patients with missing data, 36 of 383 CKD patients (9.4%) knew that they had CKD. In the logistic regression analysis, old age (OR = 1.05, 95% CI 1.03-1.07; P < 0.001), male sex (OR = 2.11, 95% CI 1.43-3.12; p < 0.001), duration of DM (OR = 1.03, 95% CI 1.00-1.05; P = .022), morbid obesity (OR = 3.58, 95% CI 1.28-10.03, P = .015), a CRP level of >5 mg/L (OR = 1.60, 95% CI 1.12-2.27; P = .009), a triglyceride level of ≥150 mg/L (OR = 1.74, 95% CI 1.24-2.45; P = .002), and grade 3 hypertension (OR = 2.13, 95% CI 1.02-4.44; P = .043) were found to be significantly associated with an increased risk of CKD in patients with DM.

**Conclusion:** In the present study, CKD prevalence among diabetic patients in Turkey was 25.1%. Overall, 53.8% of the patients with CKD had a GFR of ≥60 mL/min although they had an ACR of ≥30 mg/dL; that is, if albuminuria was not studied, this subgroup of patients would have been considered to have normal kidney function according to GFR. The awareness of CKD was found to be quite low in the patients. Therefore, periodic screening of diabetic patients should always include urinalysis, particularly ACR, as well as serum creatinine, fasting blood glucose and HbA1c.

**Reference**
A common clinical finding in patients with type 2 diabetes mellitus is hypertension. A recent study conducted at the Nephrology department of a tertiary healthcare center in Italy aimed to determine the prevalence and etiology of biopsy-proven non-diabetic renal disease (NDRD) and to explore the clinical differences encountered in the diabetic patient with NDRD.

**Background and Aims:** The study was conducted at a university hospital, which served as a tertiary healthcare center. One hundred and three diabetic patients underwent a renal biopsy due to suspicion of NDRD from January 2012 to December 2022 at Nephrology department. Collected data comprised demographic information, indication and result of renal biopsy, lab results (serum creatinine, HbA1c, proteinuria, albuminemia, hematuria, presence of active urinary sediment and presence of auto antibodies) and disease's characteristics (duration of diabetes, presence of diabetic retinopathy).

**Method:** A retrospective study of the medical records of all diabetic patients who underwent a renal biopsy due to suspicion of NDRD from January 2012 to December 2022 at Nephrology department. Collected data comprised demographic information, indication and result of renal biopsy, lab results (serum creatinine, HbA1c, proteinuria, albuminemia, hematuria, presence of active urinary sediment and presence of auto antibodies) and disease's characteristics (duration of diabetes, presence of diabetic retinopathy).

**Categorical variables are presented as frequencies and percentages, continuous variables as means and standard deviations, or medians and interquartile ranges (IQR) for variables with skewed distributions. A p-value < 0.05 was considered statistically significant.** Statistical analysis was performed using SPSS version 28.1 for MacOS X. The most frequent indication for renal biopsy was chronic kidney disease (CKD) (26.3%), followed by rapidly progressive renal failure and nephrotic syndrome (26.3%). In our population, 22.9% had DN and 77.1% had NDRD. Pauciimmune Glomerulonephritis (14%) and Membranous Nephropathy (10.5%) were the most common causes of NDRD. A chi-square test was performed to examine the relation between the two groups (ND vs NDRD) and the presence of diabetic retinopathy. There was a statistically significant association between the two variables (χ²=7.778, p=0.01). Mann-Whitney test was performed to compare the median of the duration of the diabetes and HbA1c in two groups. That showed a statistically significant difference (U = 357, P = 0.018 and U=335.5, P = 0.013 respectively).

**Conclusion:** Since renal biopsy is critical to establish the correct diagnosis and provide an appropriate treatment, it should be performed in patients with high suspicion of NDRD, especially in patients with a recent diagnosis of diabetes, good metabolic control and the absence of diabetic retinopathy.

**Method:** The study was conducted at a university hospital, which served as a tertiary healthcare center. One hundred and three diabetic patients who underwent a renal biopsy due to suspicion of NDRD were involved in the study. Demographic characteristics, physical examination findings, laboratory tests and kidney biopsy findings were retrospectively evaluated.

**Results:** According to kidney biopsy findings 30 patients (29.1%) had isolated diabetic nephropathy. NDKDs were present in 73 (70.9%) of the patients. 78.1% of the patients with NDKDs had non-diabetic glomerular diseases. Among glomerular diseases, focal segmental glomerulosclerosis (36.9%), IgA nephropathy (17.8%) and membranous nephropathy (13.7%) were the leading three diseases. The duration of diabetes (p=0.00), HBA1C level (p=0.00) and the amount of proteinuria (p=0.02) were higher in patients who had isolated diabetic nephropathy. Presence of diabetic retinopathy (p=0.00), concomitant vascular diseases (p=0.02) and the use of insulin treatment were also more often in patients with isolated diabetic nephropathy. Multivariate analysis revealed that patients with higher HBA1C levels and longer diabetes duration had more tendencies to have isolated diabetic nephropathy. Immunosuppressive treatments for glomerular diseases were administered in around 50% of the patients. However, renal and overall survivals were not different between patients who received immunosuppressive treatments and those who didn’t.

**Conclusion:** A renal biopsy in diabetic patients might be preserved for those with shorter diabetes duration and lower HBA1C levels. As poor glycomic control and susceptibility to infections pose additional risks, immunosuppressive treatments might not always be beneficial.

**Method:** A retrospective, cross-sectional study at the Department of Nephrology at Mongi SL Hospital, and we studied the relation between blood pressure levels and CKD stages. The stage of chronic kidney disease (CKD) was defined according to the KDIGO 2012 classification.

**Results:** A total of 99 patients were enrolled in this study. The mean age was 69.19 years (range 30-96) with a gender ratio M/F of 1.225. The patients who had hypertension were 41 (46.06%). We noted the presence of chronic kidney disease stage 3 or more in 64 patients (71.91%) among whom 32 patients had hypertension. Thirty-seven patients had a stage 3 CKD, 14 had a stage 4, and 13 had a stage 5. As for blood pressure levels, the mean systolic blood pressure was 137.94 mmHg, and the diastolic 79.52 mmHg. Twenty-three patients had stage 1 hypertension and 13 presented a stage 2 hypertension. Stage 3 hypertension was noted in 5 patients, who all had a stage 3 or 4 chronic kidney disease. Higher blood pressure levels were noted in patients with CKD stage 3 or more: Among the 13 patients who had a stage 5 chronic kidney disease, 7 had hypertension.

**Conclusion:** Hypertension is ubiquitous in the chronic kidney disease, and it can be a cause or consequence of CKD. Both hypertension and CKD contribute to each other and it has been noted that patients with CKD are at higher risk for hypertension-related adverse outcomes, including cardiovascular disease, and therefore, the management of hypertension is particularly important in patients with CKD.
evaluate the genetic aspects of pathways related to hypertension and renal failure, and to Na-k-pump activity such as endogenous ouabain and RAAS system, in order to partly dissect the wide clinical spectrum of the disease in hospitalized patients infected by SARS-CoV-2, with various degrees of symptoms.

**Method:** We investigated the relationship between three outcomes and genetic determinants in the COVID-BioB study (ClinicalTrials.gov NCT04318366), a characterization of an Italian cohort of about 500 patients, a SARS-CoV-2 positive population recruited during the first wave of pandemic at San Raffaele Scientific Institute with biological samples and clinical assessment data available in an internal biobank. Targeted DNA genotyping was performed by custom arrays on TaqMan OpenArray system (ThermoFisher) for single nucleotide polymorphisms (SNPs). The genetic variants were selected as candidates for salt-sensitive hypertension and renal failure. Associations with genetic markers and outcomes were carried out with logistic regression analysis for outcome absence/presence comparison.

**Results:** COVID-19 patients were all hospitalized, with mean age 67.4±13.5 (30.2% female), pneumonia 96.9%, hypertension 51.8%, coronary arterial disease 26.8%, emergency department AKI stage 1-11.1%, AKI stage 2-0.4%, CKD stage>311.5%, Chronic Obstructive Pulmonary Disease 8.2%, creatinine 1.19±0.70, all at emergency department admission, in-hospital AKI 37.8%, Intensive Care unit admission 18.3%, and in-hospital death 20.6%. The main outcomes for the analysis of SNPs were in-hospital death, AKI and onset of proteinuria. The main findings for the SNP analysis concerned different genetic markers, each specific for different outcomes. A SNP in renin gene (REN), rs10900555, was associated with the in-hospital death (OR 3.84 [95%CI 1.58;9.25], P = .044), with the same risk alleles previously linked to salt-sensitive hypertension. TT genotype (at risk for salt-sensitivity) in uromodulin gene (UMOD, SNP rs4293393) increases the risk of proteinuria development (OR 1.86 [95%CI 1.02;3.40], P = .044). The genetic variants were selected as candidates for salt-sensitive hypertension and renal failure. Associations with genetic markers and outcomes were carried out with logistic regression analysis for outcome absence/presence comparison.

**Conclusion:** This genetic analysis, firstly reported on the COVID-BioB cohort, showed an intriguing relation between some polymorphisms previously associated with salt-sensitive hypertension and worst outcome or renal damage, during COVID-19. This genetic stratification may help to identify patients at risk AKI, and (directly or not) for death and renal damage (proteinuria) during COVID-19. Moreover, it may explain, at least in part, the debated relationship between hypertension and severity of COVID-19.

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### #5555

**TAKAYASU ARTERITIS IN THE TIME OF SARS-COV-2**

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**Background and Aims:** SARS CoV 2 infection is characterized by pulmonary, cardiovascular, neurological and other complications. New onset hypertension after SARS CoV 2 infection was observed in various studies with an unclear mechanism. Vessel inflammation is a common finding in these patients.

**Case:** A young woman (24 years old) referred to our Unit for high blood pressure levels appeared few days after SARS COVID 2 infection. She had a positive familiar history of hypertension. A 24 hours blood pressure monitoring confirmed hypertension and the patient was treated with a beta-blocker and referred to the nephrologist. Physical examination was negative and peripheral pulses were palpable. Blood pressure was 150/90 mmHg without significant discrepancy (<10 mmHg) between right and left arm and between upper and lower limbs. Carotid-femoral and carotid-radial pulse wave velocity was in the upper limit of the normal range (9.8 and 8.0 m/sec respectively), renal function was preserved (serum creatinine 0.6 mg/dl, eGFR 154 ml/min) and proteinuria was 450 mg/die. C-reactive protein was 13 mg/L. Complement components C3 and C4 as well as IgG and anti-neutrophil cytoplasmatic antibody (ANCA) levels were in the normal range. IgA and IgM were slightly elevated and anti-nuclear antibody (ANA) levels were 1:160. TSH was in the normal range. Patient was switched to calcium channel blockers and a screening to exclude secondary hypertension was performed. Hormonal profile showed hypersecretion of cortex and medullary adrenal gland (high renin and aldosterone, plasma and urinary cortisol, and epinephrine levels). Patient was treated with ACE inhibitor and showed an optimal blood pressure profile. Abdominal-Chest CT angiography detected no increase in adrenal gland dimension. Conversely, a left renal artery stenosis and a mild enlargement of the para-aortic tissue, suggestive of a retroperitoneal fibrosis, was described (Figure 1). A Doppler ultrasound examination confirmed a high systolic peak velocity in left renal artery and a low resistive index in the left kidney. According to the diagnosis of renal fibrosis, patient was treated with oral prednisone at a dosage of 1 mg/Kg/BW. Three months later, Doppler ultrasound and CT were materially unchanged. After a case revision and a negative evidence of inflammation at PET-FDG examination, the Takayasu Arteritis diagnosis was formulated and the patient underwent left renal artery angioplasty. Oral prednisone was tapered and methotrexate was started. One month later blood pressure and Doppler ultrasound velocimetric parameters were normalized.

**Conclusion:** This case report suggests that Takayasu arteritis may occur after SARS COVID 2 infection.

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### #2665

**EFFECT OF RENAL DENERVATION ON THE PLASMA LEPTIN CONCENTRATION IN PATIENTS WITH RESISTANT HYPERTENSION**

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1 Medical University of Silesia, Department of Nephrology, Transplantation and Internal Medicine, Katowice, Poland and 2 Medical University of Silesia, 1st Department of Cardiology, Katowice, Poland

**Background and Aims:** Leptin is mainly produced by adipose tissue and has hypotensive properties. In patients with arterial hypertension, plasma concentration of leptin is higher than in healthy subjects. Percutaneous ablation of the sympathetic nervous system fibers located in the wall of the renal arteries by radio frequency waves (renal denervation - RDN), was introduced as a method of invasive treatment of resistant arterial hypertension. The aim of this single center, interventional, clinical study was to assess the effect of RDN on the plasma leptin concentration in patients with resistant arterial hypertension.

**Method:** Eighteen patients (9 women, 9 men) aged 53.2±6.5 years with resistant hypertension who underwent RDN using Simplicity catheters (Medtronic, Inc., Northridge, CA) before RDN denervation and 6 months after RDN. Additionally, patients were divided into two subgroups: responders (systolic and diastolic blood pressure - BP reduction 6 months after RDN >25

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**F3 - PREVENTION, TREATMENT & CLINICAL TRIALS**

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**Abstract**

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**Figure 1:**
mmHg and > 12 mmHg, respectively; n=9) and low responders (systolic and diastolic BP reduction 6 months after RDN ≤25 mmHg and ≤12 mmHg, respectively; n=9).

**Results:** Systolic and diastolic BP was significantly reduced after RDN (196.6±28.2 and 162.9±15.6; p<0.001 and 117.9±26.4 and 90.7±8.6 mmHg; p<0.001, respectively). Body mass index (BMI) before RDN and 6 months after RDN did not change significantly in the entire studied group (27.2±14.3 and 24.6±13.1 [ng/mL], NS), as well as both in responders (29.5±14.4 and 28.2±12.9 [ng/mL], NS) and low-responders subgroups (24.4±14.7 and 21.0±12.9 [ng/mL], NS), respectively.

**Conclusion:** Renal denervation is effective in the treatment of patients with resistant hypertension, however this effect is not mediated by the influence on plasma leptin concentration.

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**#3250**

**RENA MENAEMODYNAMIC PARAMETERS IN DIABETIC NEPHROPATHY**

Pavlos Malidretos¹, Nikolaos Anagnostou¹, Dimitrios Palaiologos¹, Kalliopi Tanou² and Georgios Koutroumpas¹

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**Background and Aims:** Diabetic nephropathy is the leading cause of chronic kidney disease in modern world. Timely diagnosis is of paramount importance, especially after the recent introduction of novel therapies. The presence of an already altered renal haemodynamic profile was investigated in all patients referred with suspected diabetic nephropathy, upon their initial presentation to our renal department.

**Method:** During the past seven years, from January 2015 to December 2022, 578 patients were referred to the Renal Department for ultrasound assessment. Additionally to their standard assessment, they underwent renal ultrasound and triplex examination. Diabetic nephropathy (DN) was diagnosed in 149 patients. A group of patients with an estimated GFR> 60 ml/min, without diabetic nephropathy, was randomly selected from the same pull of patients for comparison reasons (control group). Renal haemodynamics assessment, including renal arteries, aorta and intrarenal resistive indexes (RI) of both kidneys, estimated glomerular filtration rate (CKDEPI) and 24h albuminuria, were evaluated in all patients.

**Results:** The mean age of the patients was 72.5 ±10.4 vs 65.8 ±6.9 years, for the DN and control group respectively. Renal length was comparable in both groups, renal diameter of left kidney was 10.61 ±1.28 vs. 10.59 ±1.44 cm and renal diameter of right kidney was 10.53 ±1.38 vs. 9.86 ±2.89 cm for DN group and control respectively. The estimated GFR was significantly lower in the DN group, 42.1±23.6 vs. 82.7 ±11.3 ml/min (p<0.05). Both renal arteries presented higher velocity values in the DN group, 53.4 ±22.2 vs. 21.7 ±28.9 cm/sec (p<0.0001) and 52.4 ±23.9 vs. 24.8 ±32.3 (p<0.0001), for the left and right renal artery. DN patients showed RI values above upper normal limit of 0.70, being at the same time significantly higher compared to control group, 0.73 ±0.06 vs. 0.61 ±0.17 (p<0.0001) and 0.72 ±0.06 vs. 0.59 ±0.20 (p<0.0001), for the left and right kidney respectively.

**Conclusion:** The presence of significantly increased renal artery velocity in diabetic nephropathy patients compared to control patients has not been described earlier to the best of our knowledge. It represents a new finding that is mainly attributed to the presence of arteriopathy. Evaluation of renal haemodynamics using triplex ultrasound, represents a non – invasive, readily available, inexpensive examination. When performed at initial patient presentation, constitutes an invaluable tool, timely assisting to diagnosis and treatment of diabetic patients.

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**#4391**

**SALT SENSITIVITY AND HYPERTENSIVE NEPHROPATHY: A LINK TO BE DISCOVERED**

Chiara Livia Lanzi¹, Marco Simonini¹,²,³, Lorena Citterio², Laura Zagato², Luz Maria Gonzalez⁴, Francesca Tunesi³, Marianna Contursi¹, Paolo Maiuccchi¹, Paolo Manunta¹,²,³

¹IRCCS San Raffaele Scientific Institute, Division of Nephrology and Dialysis, Milan, Italy, ²IRCCS San Raffaele Scientific Institute, Genomics of Renal Diseases and Hypertension Unit, Milan, Italy, ³Università Vita Salute San Raffaele, Chair and School of Nephrology, Milan, Italy and ⁴Universidad de Extremadura, Dept. Medical Surgery Therapeutics, Badajoz, Spain

**Background and Aims:** Sodium sensitivity is defined as a change in blood pressure depending on sodium intake, which is present in about 30% of the adult population. According to blood pressure variation in salt load test we can classify the population in 3 categories: sodium sensitive (SS), sodium resistant (SR), inverse sodium sensitivity (ISS), based on, respectively, an increase, a non-significant variation or a decrease in the blood pressure values following the administration of sodium. It is reported that SS subjects have, independently from other risk factors, an increased risk of cardiovascular diseases. Moreover, SNPs located in genes related with Na+ metabolism, aldosterone synthesis and tubular sodium reabsorption in the kidney are related to salt sensitivity phenotype. The aim of this study is to analyze the relationship between sodium sensitivity and the development of hypertensive kidney damage in patients with primary hypertension.

**Method:** A cohort of 712 naïve hypertensive patients were classified for salt-sensitivity using acute saline test (NaCl 308 mEq/2h/iv).127 patients (follow-up > 5 years- median 11) were selected for the present analysis (SS, n= 40; 0 SR, n= 46; RSS, n= 41). We analyzed annual decline of the eGFR (CDK-EPI) (Delta-eGFR) and development of microalbuminuria (MicrAlb) as renal outcome. Moreover, genetic polymorphism involved in salt sensitive hypertension has been investigated.

**Results:** No differences in Delta-eGFR was observed among the groups. However, SR subjects develop earlier microalbuminuria (P = 0.002) even with an adequate pressure control. Genotypes analysis revealed: polymorphism in CYP11B2 and NEDD4L to be protective against decline in eGFR. For
Conclusion: Unexpectedly these finding suggests that SR patients are more at risk of developing hypertensive nephropathy than other groups of patients. Moreover genotypes associated with salt sensitivity play different and complex role in kidney damage in hypertension. Improvement in salt sensitivity testing and standardization will be needed to allow all this pathophysiological knowledge to be translated in a clinical setting.

#4646
CT-DERIVED RADIOMICS ANALYSIS OF DIABETIC NEPHROPATHY BY MACHINE LEARNING MODELS
Eui Seok Chung1, Eun Ji Lee1, Jongsin Yoon3, Haeyung Lee5, Hyongnae Kim5, Hyunjin Noh1, Soon Hyo Kwon1 and Jin Seok Jeon1
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Background and Aims: Kidney radiomics has been used to develop more accurate diagnostic tools of renal tumor and predict outcomes. However, radiomics studies for diabetic kidney disease (DKD) remain few in this light. We hypothesized that computed tomography (CT) radiomics features could differentiate DKD from normal kidneys and assess the severity of DKD.

Method: This retrospective study included 343 subjects with type 2 diabetes mellitus (T2DM) (male 65.5%, mean age 63.6±14.8) and 90 healthy controls (HC) (male 34.4%, mean age 41.9±8.5) who underwent abdominal CT. Whole volumetric CT data of both kidneys were automatically extracted using a deep-learning based model and radiomics features were extracted. T2DM were categorized into three groups according to eGFR (mL/min/1.73 m²) (group 1, eGFR > 60; group 2, 15 < eGFR < 60; and group 3, eGFR < 15). The capability of CT radiomics features to distinguish not only DKD from HC but also various DKD groups based on eGFR, was evaluated using machine learning models.

Results: A total of 1,723 radiomics features were extracted from the volumetric CT data of both kidneys. A combination of LASSO filter and random forest showed the best performance in differentiating between HC and DKD with an area under curve (AUC) of 0.98 and accuracy of 95.7%. It also showed an excellent performance in differentiating between HC and DKD group 1 with AUC of 0.97 and accuracy of 91.7%, and also it was able to differentiate between DKD groups (AUCs > 0.78). CT radiomics features and eGFR had a moderate degree of correlation (R=−0.50 to R=0.63, all P<.001). This study suggests that radiomics features can be used to differentiate DKD from normal kidneys as well as assessing the severity of DKD.

#5423
THE FUNCTIONAL STATE OF THE KIDNEYS IN PATIENTS WITH CHRONIC ISCHEMIA OF THE RENAL AND PERIPHERAL ARTERIES
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Background and Aims: to study the functional state of the kidneys in patients with chronic ischemia of the renal and peripheral arteries.

Methods: We examined 120 patients with chronic lower limb ischemia (CLLI) on the background of coronary heart disease and type 2 diabetes mellitus. All examined patients were hospitalized in the department of Interventional Cardiology of the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation. Inclusion criteria for the study was the presence of intermittent claudication in the patient of II A-II B degree of CLLI, while the walking distance without pain in these patients was 50-1000 meters. Assessment of the functional state of the kidneys was carried out on the basis of determining the level of serum creatinine (Cr), glomerular filtration rate (GFR), calculated according to the EPI GFR formula, which takes into account race, gender, age, and serum creatinine level. To calculate GFR using the CKD-EPI formula, can be used special applications for mobile devices (QxMD Calculator) (based on the criteria of the clinical guidelines for the diagnosis, classification and treatment of CKD KDIGO - 2013).

Results: Analysis of the functional state of the kidneys depending on the severity of CKD and the level of GFR in accordance with the KDIGO classification (2013) showed that all 100% of patients with CLLI belonged to CKD categories: CKD C2 - 62 (51.7%), CKD with 3a-b - 51 (42.5%) and CKD with 4 - 7 (5.83%). In other words, there was not a single patient with CLLI with normal GFR values. We have revealed a significant increase in the concentration of blood creatinine by 2.1 times, blood urea by 77.9%, and a decrease in GFR by 64.3% (p<0.001). The concentration of urea in the blood serum was 12.1±2.47 mmol/l in the CLLI group versus 6.8±0.33 mmol/l in the control group. The parameters of the functional state of the kidneys depending on the severity of CLLI showed that in the group of patients with stage IIB an increase in serum creatinine clearance by 47.2%, amounting to 179.2 ± 15.5 μmol/l versus the data of IIA 121,2±13.3 μmol/l (p<0.01). There was also a decrease in the level of GFR in patients with stage IIB by 29.1% (p<0.01) in relation to the data of stage IIA.

Conclusion: In all patients with CLLI, there was deterioration in the functional state of the kidneys, which was manifested by an increase in the concentration of blood creatinine, a decrease in GFR and the severity of albuminuria.

#6442
HOW CAN IT BE NEPHROANGIOSCLEROSIS? HE’ S BEING TREATED ONLY WITH ONE ANTHYHYPERTENSIVE DRUG
Carolina González García1, Eva Marquez2, Júlia Farrera-Núñez1, Clara Barrios-Barrera1, Andres Ribas3, Laia Sans1, Javier Gimeno2, Marta Crespo1 and Eva Rodríguez García1
1 Parc de Salut Mar, Nephrology, Barcelona, Spain and 2 Parc de Salut Mar, Pathology, Barcelona, Spain

Background and Aims: Nephroangiosclerosis is a frequent renal disease due to chronic arterial hypertension and it is one of the main causes leading to renal replacement therapy. A minority of these patients have nephroangiosclerosis although they apparently have hypertension under control with minimal treatment.

Objectives: To describe the characteristics of this group of patients when compared to the rest of patients with histological diagnosis of nephroangiosclerosis.

Method: Observational, retrospective and descriptive study. Review of 67 patients with nephroangiosclerosis as the sole diagnosis in the renal biopsy (consecutive biopsies from 2010 to 2020). We divided the population in two different groups according to the number of prescribed antihypertensive drugs: Group 1 (0-1 antihypertensive drugs) vs Group 2 (≥2 antihypertensive drugs).

Results: Both groups had similar demographics and renal function/proteinuria. Both groups had the same adequate/inadequate blood pressure control, but group 1 had significantly less time of hypertension evolution. The histological differences (although not statistically significant) are noteworthy: Group 1 had a higher percentage of global glomerulosclerosis, interstitial fibrosis and tubular atrophy than Group 2. In addition, after 3-years of follow-up, in Group 1 there were more patients requiring renal replacement therapy. We hypothesize that a factor that could explain these results could be the lower use of RASIs (33.3% vs 73.9%, P = .003) and a higher percentage of history of dyslipidemia in Group 1 (62.5% vs 22.2%, p=0.017*).

Conclusion: Patients with hypertension requiring a maximum of one drug for its control, presented histological results of more marked nephroangiosclerosis, than the group of patients with more than one drug, despite similar time of evolution and degree of blood pressure control. These findings could be related to a lower rate of RASi use. Our study reinforces the indication for RASi as a first-line hypertension treatment in this population.

Abstract
i1251
**Table 1:**

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>Group 1 (n=21)</th>
<th>Group 2 (n=46)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.7±12.4</td>
<td>62.4±11.1</td>
<td>0.410</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>61.9</td>
<td>73.9</td>
<td>0.319</td>
</tr>
<tr>
<td>Body mass index (Kg/m²)</td>
<td>27±4</td>
<td>28±6</td>
<td>0.630</td>
</tr>
<tr>
<td>Family history of hypertension (%)</td>
<td>12.5</td>
<td>30.4</td>
<td>0.063</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>28.6</td>
<td>46.5</td>
<td>0.245</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>28.6</td>
<td>45.7</td>
<td>0.186</td>
</tr>
<tr>
<td>Dyslipemia (%)</td>
<td>62.5</td>
<td>22.2</td>
<td>0.017*</td>
</tr>
<tr>
<td>Age at diagnosis of hypertension (years)</td>
<td>53±11</td>
<td>50±12</td>
<td>0.650</td>
</tr>
<tr>
<td>Time of evolution of hypertension (months)</td>
<td>92.9±1</td>
<td>140±80</td>
<td>0.035*</td>
</tr>
<tr>
<td>Target blood pressure (%)</td>
<td>42.9</td>
<td>43.5</td>
<td>0.962</td>
</tr>
<tr>
<td>Antihypertensive treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renin-Angiotensin system inhibitors (RASI) (%)</td>
<td>33.3</td>
<td>73.9</td>
<td>0.003*</td>
</tr>
<tr>
<td>Calcium antagonists (%)</td>
<td>42.9</td>
<td>56.5</td>
<td>0.416</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>9.5</td>
<td>63</td>
<td>0.000</td>
</tr>
<tr>
<td>Beta-blockers (%)</td>
<td>9.5</td>
<td>41.3</td>
<td>0.009</td>
</tr>
<tr>
<td>No pharmacological treatment (%)</td>
<td>19</td>
<td>0</td>
<td>0.000</td>
</tr>
<tr>
<td>Analytical data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dl (mean±SD)</td>
<td>2.3±1.7</td>
<td>2.1±1.3</td>
<td>0.482</td>
</tr>
<tr>
<td>eGFR by CKD-EPI, ml/min/1.73m² (mean±SD)</td>
<td>40±25</td>
<td>45±25</td>
<td>0.517</td>
</tr>
<tr>
<td>Protein/creatinine ratio, mg/g (median±IQR)</td>
<td>1293±1748</td>
<td>1370±1450</td>
<td>0.390</td>
</tr>
<tr>
<td>Histological data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global glomerulosclerosis (% glomeruli)</td>
<td>46±23</td>
<td>24±22</td>
<td>0.062</td>
</tr>
<tr>
<td>Partial glomerulosclerosis (% glomeruli)</td>
<td>9±10</td>
<td>7±11</td>
<td>0.550</td>
</tr>
<tr>
<td>Moderate-severe interstitial fibrosis (% patients)</td>
<td>66.7</td>
<td>47.8</td>
<td>0.151</td>
</tr>
<tr>
<td>Moderate-severe tubular atrophy (% patients)</td>
<td>71.4</td>
<td>47.8</td>
<td>0.072</td>
</tr>
<tr>
<td>Moderate-severe atherosclerosis (% patients)</td>
<td>71.4</td>
<td>67.4</td>
<td>0.741</td>
</tr>
<tr>
<td>Moderate-severe arteriolar sclerosis (% patients)</td>
<td>76.2</td>
<td>67.4</td>
<td>0.465</td>
</tr>
<tr>
<td>3 years follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>2.3±41.6</td>
<td>2.5±1.6</td>
<td>0.829</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate (CKD-EPI, ml/min/1.73m²)</td>
<td>29±19</td>
<td>31±17</td>
<td>0.700</td>
</tr>
<tr>
<td>Urinary protein/creatinine ratio, mg/g (median±IQR)</td>
<td>353±1113</td>
<td>1372±1709</td>
<td>0.122</td>
</tr>
<tr>
<td>Initiation of renal replacement therapy (%)</td>
<td>26.3</td>
<td>14.3</td>
<td>0.304</td>
</tr>
</tbody>
</table>

*a* Target blood pressure according to medical criteria. b* Renal replacement therapy: Hemodialysis, peritoneal dialysis, renal transplantation.

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**F4 - HYPERTENSIVE & KIDNEY DISEASES IN PREGNANCY**

**3885**

**KIDNEY TRANSPLANTATION IN EARLY PREGNANCY-ASSOCIATED ATYPICAL HEMOLYTIC UREMIC SYNDROME**

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**Background and Aims:** Clinical differentiation of pregnancy-associated thrombotic microangiopathies is challenging and can occur in conjunction with or mimic conditions including hemolysis, elevated liver enzymes, low platelet count (HELLP syndrome), pre-eclampsia (PET), thrombotic thrombocytopenia purpura (TTP) and atypical HUS (aHUS). aHUS that occurs during pregnancy classically presents in the third trimester. When kidney transplantation is performed in aHUS patients, disease recurrence is high and can be associated with transplant failure. Here, we report a unique case of aHUS that presented early during pregnancy where the patient subsequently underwent kidney transplantation.

**Method:** We present a case report. Ethics approval was obtained by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

**Results:** A 30 year old G2P0A1 diabetic African American woman presents at 9 weeks gestation with new hypertension. At 18 weeks, she developed acute kidney injury and proteinuria. Further investigations revealed hemoglobin 68 g/L, platelets 120 x 10⁹/L, increased LDH 588 U/L, undetectable haptoglobin and schistocytes on blood smear. Creatinine was 88 umol/L, increased from a baseline of 50 umol/L, and proteinuria greater than 1 g/day. Pre-eclampsia was ruled out as her presentation began at 9 weeks gestation, prior to placentation implantation. Placental growth factor levels at 24 and 28 weeks remained >100 pg/mL. HELLP syndrome was excluded given the timing in pregnancy and normal liver enzymes. TTP was excluded with a normal ADAMTS13. Complement Factor H autoantibody was negative. Complement studies revealed grossly elevated soluble C5b-9 level (sC5b-9) of 1.05 (normal <0.3 mg/L). aHUS was diagnosed and she began treatment with eculizumab (ECU). Ex-vivo serum C5b-9 deposition on human microvascular endothelial cells was assessed and was severely abnormal pre-treatment with ECU (activated 223%, normal <150%), and normalized with ECU therapy (activated 123%, normal <150%). Genetic testing eventually revealed a Complement Factor I mutation, NM_000204.3:c.550G/A, p.Vall84Met reported as likely pathogenic.

**Conclusion:** aHUS, although described to occur late in pregnancy or post-partum, remained on ECU and had excellent graft function without proteinuria (urine ACR 2.2 mg/mmol) or evidence of aHUS recurrence.
is not always PET or HELLP. aHUS is a treatable condition in pregnancy, and should be considered as a possibility particularly for presentations occurring prior to 20 weeks gestation. Complement function studies may aid in aHUS diagnosis. Despite extra ECU dosing and therapeutic ECU levels for this patient and kidney transplantation, she had evidence of massive C5 release (grossly elevated sC5b-9 level). sC5b-9 measurement posttransplantation may be useful to guide ECU dosing.

#5576
SYSTEMATIC REVIEW AND META-ANALYSIS OF THE SAFETY AND EFFICACY OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS FOR THE MANAGEMENT OF POSTPARTUM PAIN
Arunima Jain1, Lauren Heath1, David Tian2,3, Sai Sirittharan1, Florencia Natali1, Mudith Jayasekara1, Lauren Thurgate1, Sean Seeho1, Anthony Delaney1,2 and Amanda Mather1
1Royal North Shore Hospital, Department of Renal Medicine, Sydney, Australia, 2Westmead Hospital, Department of Anaesthesia and Perioperative Medicine, Sydney, Australia, 3University of Melbourne, Melbourne, Australia, 4University of Sydney, Medical School, Sydney, Australia, 5Royal North Shore Hospital, Department of Intensive Care Medicine, Sydney, Australia, 6Women and Babies Research, Kolling Institute, Faculty of Medicine and Health, Sydney, Australia and 7George Institute for Global Health, Division of Critical Care, Sydney, Australia

Background and Aims: Effective pain management is critical for postpartum recovery. While commonly prescribed, systematically reviewed data regarding efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) are limited. Moreover, guidelines suggest avoiding NSAIDs in women with hypertensive disorders of pregnancy (HDP) due to risks of hypertension and adverse events (AE). However, these AE have not been consistently observed in cohort studies following postpartum NSAID use. This systematic review aims to provide further insight into the postpartum safety and efficacy of NSAIDs.

Method: A systematic review of eight databases and four clinical trial registries was conducted in July 2020 (PROSPERO Protocol CRD42020196054). RCTs which assessed the safety and/or efficacy of NSAIDs in postpartum women after the year 2000 were included. The primary outcome was incidence of hypertension, with secondary outcomes categorised into three groups: hypertension, secondary safety and efficacy. Data were tabulated and analysed using R (version 4.0.2). Due to heterogeneity in study design, NSAIDs were grouped based on mechanism to facilitate meta-analysis. Risk of bias was assessed using the RoB 2 tool with a plan to assess quality of evidence for the primary outcome.

Results: 12,172 records were identified with the inclusion of 92 RCTs. Eight studies, with four that included women with HDP, reported hypertension-related data (Table 1). The primary outcome was included in one RCT. Secondary safety outcomes such as acute kidney injury or eclampsia were not reported. The odds of nausea, vomiting and sedation were similar between groups. NSAIDs were effective when compared with placebo, as assessed by mean differences (MD) in visual assessment scores (VAS) at 12 hours (MD -1.57, 95% confidence intervals (CI) -2.47 to -0.66), 24 hours (MD -0.82, 95% CI -1.42 to -0.22) and need for additional analgesia (odds ratio 0.17, 95% CI 0.05 to 0.61). There were no significant differences in VAS between NSAIDs and other comparators at 12 and 24 hours. Further interpretation of results is limited due to heterogeneity in intervention and comparator groups, inclusion criteria and reported outcomes.

Conclusion: Our study confirms the efficacy of NSAIDs for postpartum pain, but current data are inconclusive regarding the risk of developing hypertension. Available data do not demonstrate trends toward AE although further research is required to determine long term, clinically-relevant outcomes to guide decision making.

#4946
PREVALENCE OF CHRONIC KIDNEY DISEASE IN WOMEN OF REPRODUCTIVE AGE AND OBSERVED BIRTH RATES
Willemin Vrijlandt1,2, Margriet De Jong3,2, Jelmer Prins3,2, Kate Bramham4, Patrick Vrijlandt2,3, Roemer J. Janse5,7, Faizan Mazhar7 and Juan Jesus Carrero1
1University Medical Center Groningen, Internal Medicine, Nephrology, Groningen, Netherlands, 2University of Groningen, Groningen, Netherlands, 3University Medical Center Groningen, Obstetrics and Gynaecology, Netherlands, 4King’s College London, Women and Children’s Health, London, United Kingdom, 5University Medical Center Groningen, Clinical Pharmacy and Pharmacology, Netherlands, 6Leiden University Medical Center, Clinical Epidemiology, Leiden, Netherlands and 7Karolinska Institutet, Medical Epidemiology and Biostatistics, Solna, Sweden

Background and Aims: Women of reproductive age with chronic kidney disease (CKD) are recognised to have decreased fertility and a higher risk of adverse pregnancy outcomes, such as hypertensive diseases, preterm birth and longer hospital stays. How often CKD affects women of reproductive age and

<p>| Table 1: Characteristics and outcomes of studies with reported hypertension data. |
|----------------------------------------|----------------|----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>First Author / Year</th>
<th>Study population (n)</th>
<th>NSAID / frequency</th>
<th>Comparator</th>
<th>Mode of birth</th>
<th>Inclusion criteria (HTN-related)</th>
<th>HTN outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue (2018)</td>
<td>100</td>
<td>Ibuprofen q6h</td>
<td>Paracetamol</td>
<td>CS, V</td>
<td>Severe PET, CHTN with severe PET or HELLP</td>
<td>ND in: duration and presence of severe HTN, postpartum MAP, max sBP/dBP, need/time to need for short-acting antiHTN, length of stay, antiHTN use on discharge</td>
</tr>
<tr>
<td>Carvalho (2006)</td>
<td>48</td>
<td>Valdecoxib q12h</td>
<td>Placebo</td>
<td>CS</td>
<td>–</td>
<td>ND in postpartum HTN</td>
</tr>
<tr>
<td>Pour (2020)</td>
<td>86</td>
<td>Diclofenac q8h</td>
<td>E lacinata</td>
<td>CS</td>
<td>–</td>
<td>ND in postpartum HTN</td>
</tr>
<tr>
<td>Matsota (2013)</td>
<td>64</td>
<td>Celecoxib, single dose</td>
<td>Fentanyl + ropivacaine</td>
<td>CS</td>
<td>–</td>
<td>MAP lower at 6h postpartum in celecoxib group; otherwise ND</td>
</tr>
<tr>
<td>Munishankar (2008)</td>
<td>78</td>
<td>Diclofenac q8h</td>
<td>Paracetamol</td>
<td>CS</td>
<td>–</td>
<td>ND in sBP/dBP</td>
</tr>
<tr>
<td>Penfield (2019)</td>
<td>61</td>
<td>Ibuprofen q6h</td>
<td>Paracetamol</td>
<td>CS, V</td>
<td>New HDP</td>
<td>ND in mean postpartum MAP</td>
</tr>
<tr>
<td>Triebwasser (2019)</td>
<td>37</td>
<td>Ibuprofen q6h</td>
<td>Paracetamol</td>
<td>V</td>
<td>gHTN and non-severe PET</td>
<td>ND in mean sBP/dBP, need for antiHTN, or incidence of severe HTN</td>
</tr>
<tr>
<td>Vigil-De Gracia (2017)</td>
<td>113</td>
<td>Ibuprofen q6h</td>
<td>Paracetamol</td>
<td>V</td>
<td>Severe PET as defined in study</td>
<td>Higher incidence of BP ≥150/100 in ibuprofen group, but ND in severe HTN (≥160/110)</td>
</tr>
</tbody>
</table>

*HTN = hypertension; CS = caesarean; V = vaginal; PET = preeclampsia; HELLP = haemolysis, elevated liver function tests, and low platelets; CHTN = chronic HTN; gHTN = gestational HTN; ND = no difference; BP = blood pressure; sBP = systolic BP; dBP = diastolic BP; HDP = hypertensive disorders of pregnancy; antiHTN = antihypertensive; MAP = mean arterial pressure
how many pregnancies are affected is not well known. This study aimed to evaluate the burden of CKD and associated birth rates in an entire region. **Method:** This was a retrospective cohort study including women of childbearing age in Stockholm during 2006–2015. We estimated the prevalence of CKD by the presence of an ICD-10 diagnosis of CKD, a single estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² or history of maintenance dialysis. By linkage with the Swedish Medical Birth Register we identified births during the subsequent three years from study inclusion and evaluated birth rates. For CKD prevalence, we reported overall counts and the age-averaged prevalence to adjust for the uneven age distribution in the cohort. A linear regression model was fitted to identify the increase in prevalence and 95% confidence interval (CI) per additional year in age. Birth rate was calculated per 1000 person years. All analyses were performed using R version 4.2.1. **Results:** We identified 817,730 women in our region, of whom 55% had at least one creatinine measurement. A total of 3938 women were identified as having CKD, providing an age-averaged CKD prevalence of 0.50%. Women with probable CKD showed a lower birth rate 3 years after the index date (35.7 children per 1000 person years) than the remaining women free from CKD (46.5 children per 1000 person years). **Conclusion:** As many as 0.50% of individuals in this cohort had CKD, defined on the basis of at least one eGFR<60 mL/min/1.73 m² test result, dialysis treatment (i.e. CKD stages 3–5) or an ICD-10 diagnosis of CKD. This prevalence is lower than previous estimates. Women with CKD had a lower birth rate than those without CKD, illustrating the challenges of this population to successfully conceive. Future research should be done to identify impeding factors.

**AKI & CRITICAL CARE NEPHROLOGY**

## #3419 LINARIN PROTECTS THE KIDNEY FROM ISCHEMIA-REPERFUSION INJURY AND SUPPRESSES ETS2 INDUCED ACUTE KIDNEY INJURY

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**Background and Aims:** Ischemia/reperfusion injury (IRI), a participant in acute kidney injury (AKI), can occur as a series of pathological processes such as inflammation. Linarin (LIN) has been widely used for different diseases. To confirm the anti-inflammatory value and relevant mechanism of LIN during IRI, in vivo and vitro model were established. **Method:** LIN or isovolumetric DMSO was given, and histologic analysis, quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR), serum creatinine (SCr) testing and blood urea nitrogen (BUN) were used to evaluate kidney injury. Microarray analysis, protein–protein interaction (PPI) analysis and molecular docking were used to identify target protein of LIN. **Results:** At first, we find that LIN could inhabbit the kidney injury in vivo IRI model and decrease the expression of IL-12 p40 in vitro IRI model. To explore the mechanism of LIN, we collected raw data from public microarray database and identified E26 oncogene homolog 2 (ETS2) as a target protein of LIN according to microarray analysis, PPI and molecular docking. The contact area is highly conserved and located on a protein–protein interaction domain of ETS2 which indicated that LIN may alter the interaction with synergistical protein in the regulation of IL-12 p40 expression. **Conclusion:** Our study demonstrated the anti-inflammatory effect of LIN during IRI-triggered AKI, broadening the medicinal value of LIN and the therapeutic options for IRI-triggered AKI.
Figure 1: LIN protect kidney from IRI in vivo.

Figure 2: Effects of LIN on HK2 cells.

Figure 3: Volcanic plot of microarray data.
Background and Aims: Acute kidney injury (AKI) is a major medical complication associated with a markedly increased risk of death, particularly in patients admitted to the ICU where in-hospital mortality exceeds 50%. This study aimed to determine the accuracy of MPV, platelet count, and PDW as predictors of adverse outcomes in patients with AKI who received initiation renal replacement therapy (RRT).

Method: A retrospective cohort single-center study was done in a local private tertiary hospital in Cebu. Four hundred ninety-one patients with AKI who underwent RRT between January 2018 and December 2021 were enrolled. A retrieval of data on demographic and clinical parameters during the initiation of RRT was done. The impact of mortality-related factors were identified using univariate and multivariate logistic regression analysis. Determination of optimal cut-off values of platelet indices for in-hospital mortality was done.

Results: This study showed that the in-hospital mortality of patients was 58.45%, with a mean age of 68.6 ± 16.28 years among non-survivors. Among the platelet indices, platelet count and PDW were good predictors of in-hospital mortality in patients who received initiation renal replacement therapy. The optimal cut-off value of platelet count was 173 x 103/uL (sensitivity 56.45%, specificity 62.25%, PPV 67.78%, NPV 50.40%, AUC 0.604). The optimal cut-off value of PDW was 16.45% (sensitivity 50.87%, specificity 71.57%, PPV 71.57%, NPV 50.87%, AUC 0.611).

Conclusion: Platelet indices are feasible parameters that can be used as prognostic markers for mortality in patients with AKI requiring RRT. The in-hospital mortality of patients with AKI requiring initiation RRT is high (58.45%). Low platelet counts, high MPV values, and high PDW values are associated with poorer outcomes and higher mortality risk as compared to patients with normal indices.
CHARACTERIZATION OF KIDNEY FUNCTIONAL DAMAGE ASSOCIATED TO CO-TREATMENT WITH IMMUNE CHECKPOINT INHIBITORS AND CISPLATIN

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Background and Aims: Advances in the knowledge of the immune response against tumors and the evasion mechanisms of these have led to develop new cancer therapies focused on improving the immune response and thus increasing patient survival. This is the case of immunotherapeutic treatment based on immune checkpoint inhibitors (ICI). However, treatment based on these antibodies is associated with autoimmune side effects, in most of the body organs, that limit their use. Although nephrotoxicity is rare, renal effects have been shown to worsen the prognosis of cancer patients. Recently, therapies based on the combination of immuno and chemotherapy have been approved. They have improved efficacy but have increased the risk of suffering nephrotoxic adverse effects. Our hypothesis is that kidney damage associated with ICIs could be subclinical and not evidenced by the parameters used in clinical practice (mainly plasma creatinine). The aim of this work was to characterize functional kidney damage associated with ICI (anti-CTLA-4) in combination with chemotherapy (cисплатин) in a murine model.

Method: C57BL/6 mice were treated with combined therapy of cisplatin (10 mg/kg, single dose) and anti-CTLA-4 (10 or 15 mg/kg/day, for 6 days) administrated by intraperitoneal injection. In addition, groups treated with drug monotherapies and a control group were included. Urine and blood samples were collected at baseline, on day 3 and on day 6 (sacrifice). Biomarkers of subclinical kidney damage were determined by ELISA in urine samples. There were albumin, neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule 1 (KIM-1). Blood samples were centrifuged to obtain plasma, in which creatinine and urea were measured using colorimetric techniques. Data were analyzed with the statistical software SPSS®.

Results: Plasma creatinine and urea were elevated in the combined therapy group with respect to monotherapies and control group. Multivariate logistic regression analysis showed that serum bicarbonate concentration on admission remained significant predictors of AKI in patient with glufosinate poisoning.

Conclusion: Serum bicarbonate is helpful to predict the development of patients with glufosinate poisoning.

G2 - EPIDEMIOLOGY & OUTCOME

2572

CLINICAL CHARACTERISTICS OF ACUTE KIDNEY INJURY IN PATIENTS WITH GLUFOSINATE POISONING

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Background and Aims: Glufosinate-containing herbicide is widely used in agriculture. According to previous reports, glufosinate poisoning causes various complications, but there are few reports of nephrotoxicity. In this study, we investigated the incidence and clinical characteristics of acute kidney injury (AKI) in patients with glufosinate poisoning.

Method: This study performed between 2008 and 2021 included 76 patients categorized into the AKI and the non-AKI groups. The incidence, clinical characteristics, and severity of AKI were compared between the AKI (n=54) and the non-AKI (n=22) groups, based on the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease classification.

Results: The incidence of AKI was 71.1%, of which 40.9%, 26.3%, and 3.9% patients were classified into the Risk, Injury, and Failure categories, respectively. Patients in the AKI group were older (62.6±14.2 years vs. 54.9±16.2 years, P=0.045) and poorer renal function (73.9±25.2 mL/min/1.73 m² vs. 94.5±35.5 mL/min/1.73 m², P=0.006) on admission. The length of hospitalization was longer (17.2±17.2 days vs. 7.6±7.6 days, P=0.014) in AKI group, and the mean amount of glufosinate ingested was higher in AKI group than that in non-AKI group (250±172 mL vs. 152±121 mL, P=0.032). In addition, the serum bicarbonate level was lower in AKI group than in non-AKI group (19.9±4.7 vs. 23.0±3.3, P=0.006). Notably, intensive care unit admissions (81.5% vs. 40.9%, P=0.001) and mechanical ventilator support (68.5% vs. 22.7%, P<0.001) were more frequently required in the AKI group. Multivariate logistic regression analysis showed that serum bicarbonate concentration on admission remained significant predictors of AKI in patient with glufosinate poisoning.

Conclusion: Serum bicarbonate is helpful to predict the development of patients with glufosinate poisoning.

5301

COVID-19 AND ACUTE KIDNEY INJURY IN ELDERLY PATIENTS: A COMPARATIVE COHORT STUDY BETWEEN THE FIRST AND SECOND WAVE OF THE PANDEMIC IN BRAZIL

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Faculty of Medicine of Botucatu, UNESP, Brazil

Background and Aims: In the different waves of the pandemic caused by the SARS-CoV-2 virus, the elderly continued to be affected with more severe cases
of the disease and possible progression to death. The objective of this study was to
evaluate the incidence of acute kidney injury (AKI) in the elderly during the first and second waves of the pandemic in Brazil, the risk factors associated with its development and death.

Method: Retrospective cohort study that evaluated patients over 60 years of age admitted to a Public, Tertiary, and Reference Hospital for COVID-19 with a diagnosis of SARS-CoV-2 infection, from March to December/2020 (first wave), and from January to May/2021 (second wave), from admission to hospital outcome (death, dialysis discharge or death).

Results: Throughout the entire period, 434 elderly patients diagnosed with COVID-19 were admitted, 173 in the first wave and 261 patients in the second wave. These two groups of patients were similar in terms of age (71±8.41 vs 70±8.32, p = 0.3329), need for intensive care unit admission (56.1% vs 58.2%, p = 0.655), vasoactive drug use (43.9% vs 52.9%, p = 0.686), need for mechanical ventilation (43.4% vs 52.5%, p = 0.062), higher APACHE values (19.7±5.3 vs 17 ±±5.64, p = 0.312), SOFA (9.4±7.07 vs 7±5.36, p = 0.332), CPK (95±570.75 vs 150±4830.47, p = 0.0886), the incidence of AKI (56.6% vs 58.6%, p = 0.684) and mortality (46.8% vs 55.2%, p = 0.088). However, they differed in terms of white race (77.3% vs 86.8%, p = 0.01), use of corticosteroids (56.6 vs 93.9%, p = 0.001), presence of proteinuria (44.8% vs 58.2%, p = 0.031), higher values of ATN-ISS (0.76±0.23 vs 0.86±0.21, p = 0.004) and D Dimer (5098.6±5995.04 vs 2436.5±8398.38, p = 0.0147). The two waves were similar regarding the following factors associated with the development of AKI: higher baseline creatinine, CPK, and D-Dimer values during hospitalization, higher APACHE values, need for mechanical ventilation, use of vasoactive drugs, presence of proteinuria and hematuria in the urine on hospital admission. There was a difference in terms of the waves regarding males (47.40% vs 46.08%, p = 0.037), a relevant factor in the development of AKI in the first wave; while the presence of SAH (63.9% vs 77.8%, p = 0.002), the use of ACEIARB (42.6% vs 56.2%, p = 0.0412) and the filtration rate basal glomerular (91±29.61 vs 80±5±26.79, p = 0.0021) were observed as factors associated with AKI only in the second wave. In the logistic regression of both waves, mechanical ventilation remained a risk factor for the development of AKI. In the first wave, the highest baseline creatinine value was also maintained as a risk factor (OR 10.5, CI 1.22-90.61, p = 0.032); while in the second, SAH (OR 1.646, CI 1.150-1.839, p = 0.018), hematuria (OR 1.681, CI 1.124-1.882, p = 0.018) and higher value of D Dimer (OR 1.977, CI 2.000-2.003, p = 0.023) remained as relevant factors for the development of AKI. As factors associated with mortality in the first wave, the highest value of CPK (OR 1.009, CI 1.001-1.017, p = 0.042) and the need for mechanical ventilation (OR 17.71, CI 1.13-277.62, p = 0.002) in the second wave, the factors associated with death were the presence of DM (OR 4.875 CI 2.602-7.094, p = 0.001), ARF (OR 1.858, CI 1.070-1.287, p < 0.001), need for dialysis (OR 1.813, CI 1.086-1.407, p = 0.001), proteinuria (OR 1.968, CI 1.142-1.913, p = 0.032) and higher ATN- ISS value (OR 5865.316, CI 1.325-25967740, p = 0.043).

Conclusion: The incidence of AKI was similar between the two waves of the pandemic; however, its severity was greater in the second wave, in which it was identified as a factor associated with death. Despite the greater severity of AKI, evidenced by the higher ATN-ISS, there was no higher patient mortality during the second wave of the pandemic.

#3235
ELECTROLYTE DISORDERS IN COMMUNITY-ACQUIRED ACUTE KIDNEY INJURY
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Background and Aims: The kidney plays a decisive role in regulating the homeostasis of the internal environment. Acute kidney injury (AKI) compromises the kidney’s ability to maintain this regulation intact, and the appearance of various electrolyte disorders in this situation is frequent. There are few data in the literature that describe these alterations in patients with community-acquired AKI (CA-AKI). The purpose of this study is to analyze the incidence of electrolyte disorders in a cohort of patients with CA-AKI admitted to the nephrology service of a tertiary level hospital.

Method: This is a single-center, observational, longitudinal, and retrospective study based on a cohort of patients with CA-AKI admitted to the Nephrology Service of a third level hospital from January 2010 to December 2018. We analyzed the incidence of changes in sodium, potassium, chloride, bicarbonate, calcium, and phosphorus in these patients and their clinical consequences during admission and follow-up after hospital discharge.

Results: A total of 693 patients were included in the final analyses. The mean age was 72±13.1 years. Charlson comorbidity index was 5.87 ±2.4 points. The length of stay was 11.6±10.14 days. In view of the Etiology of AKI, 72.1% had prerenal AKI and 27.9% non-prerenal. 436 patients had a history of previous chronic kidney disease (CKD) (68.23%), AKI KDIGO stages were: stage I, 105 cases (16.4%); stage II, 67 cases (10.5%); stage III 467 cases (63.1%). Hemodialysis (HD) was required in 114 patients (17.8%). 62 patients (9.7%) died during hospital stay. The percentage of patients with alterations in the different ions was: chloride 54%, potassium 60.1%, sodium 45.23%, bicarbonate 85.67%, calcium 52.68%, phosphorus 54.49%. The most frequent ionic alterations at a global level were low bicarbonate (78.3%), hyperkalemia (53.03%), hypocalcemia (49.6%) and hyponatremia (49.49%). These alterations were significant different when comparing patients with previous CKD with respect to carriers of normal baseline renal function (glomerular filtration rate > 60 ml/min). When analyzing whether electrolyte alterations occurred simultaneously: 2.2% of cases did not present any, 6.3% only one, 18.2% two, 26.4% three, 26.1% four, 14.9% five and 5.9% six simultaneous alterations. In the univariate analysis, patient age (OR 1.977, CI 22.7; p = 0.001), hyperkalemia (Chi square 9.7; p = 0.008) and hyperphosphatemia (Chi square 18.5; p < 0.001) had higher mortality during admission. In the multivariate analysis using logistic regression, the variables that were independently associated with mortality during hospitalization were phosphorus (OR 1.425; 95% CI 1.212 - 1.676) and chloride (OR 1.045; 95% CI 1.002 - 1.089). In the follow-up after hospital discharge, the Kaplan-Meier curves in the univariate analysis showed higher mortality in patients who presented hyperkalemia (log rank test: Chi square 15.5; p = 0.0001), hypernatremia (log rank test: Chi square 47.7; p < 0.0001), hypocalcemia (log rank test: Chi square 6.73; p < 0.034) and hyperphosphatemia (log rank test: Chi square 10.24; p < 0.006). In the multivariate analysis using Cox regression, the variables that were independently associated with mortality after hospital discharge were sodium (Exp(B) 1.001; 95% CI 1.002 - 1.048; p = 0.048), potassium (Exp(B) 1.140; 95% CI 1.055 - 1.233; p = 0.001) and phosphorus (Exp(B) 1.087; 95% CI 1.023 - 1.048; p = 0.154).

Conclusion: In our series of patients with CA-AKI, we detected a high prevalence of electrolyte disorders, without a history of previous CKD having any influence on it. The most frequent was the finding of three or four simultaneous alterations. Phosphorus and chloride independently influenced mortality during admission. In the follow-up after hospital discharge, sodium, potassium, and phosphorus were independent predictors of mortality. The clinician who treats cases of CA-AKI must expect the appearance of frequent electrolyte disorders and must be prepared for their correct management.
during their stay in ICU none during treatment with TPE, all of them were diagnosed to have severe sepsis as a cause of death.

Conclusion: According to our experience, membrane therapeutic plasma exchange is a successful and secure treatment for a variety of illnesses including thrombotic microangiopathies, systemic vasculitis, myasthenia gravis, proliferative lupus nephritis, and Guillain-Barré syndrome. The main reason for death was sepsis.

#3462

A STUDY OF ETIOLOGY OF ACUTE KIDNEY INJURY AND ACUTE ON CHRONIC KIDNEY DISEASE AMONGST IN-HOSPITAL PATIENTS IN A TERTIARY CARE CENTRE IN INDIA

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Background and Aims: Acute kidney injury (AKI) is the leading cause of nephrology consultation and is associated with high mortality rates. The primary causes of AKI include sepsis, ischemia, hypoxia or nephrotoxicity. An underlying feature is a rapid decline in GFR usually associated with a decrease in renal blood flow. Inflammation represents an important additional component of AKI leading to the extension phase of injury, which may be associated with insensitivity to vasodilator therapy. Recent data suggest that AKI represents a potential link to chronic kidney disease (CKD) in surviving patients. Patients with CKD may be at risk for the development of a transient decrease in renal function consistent with AKI. Such rapidly declining renal function causing an acute deterioration of CKD is termed acute-on-chronic kidney disease (ACKD). The mechanisms by which these occur include failure of auto-regulation, abnormal vasodilatation, susceptibility to antihypertensive agents & side effects of medication. The successful recovery from AKI depends on the degree to which these repair processes ensue & these may be compromised in elderly or CKD patients.

Aim: To determine the burden of AKI among the in-hospital patients & their progression to CKD if at all along with the number & cause of the cases of CKD who develop ACKD due to an acute insult.

Method: The first 100 consecutive patients admitted with Acute Kidney Injury and Acute on Chronic Kidney Disease in the Department of General Medicine, Nephrology, Intensive care unit in KPC Medical College & Hospital, Kolkata, were selected for the study.

Inclusion criteria:
- Patients admitted with AKI, ACKD or developing them during the course of stay.
- CKD stages I to V with acute exacerbation (reduced GFR, reduced urine output).

Exclusion criteria:
- Patients <14 years
- ESRD patients already on hemodialysis.
- Patients with acute Glomerulonephritis (due to the unavailability of biopsy in our institution)
- Patients not giving consent to participate in the study.

For statistical analysis, data were entered into an Microsoft excel spreadsheet and then analyzed by SPSS and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Unpaired proportions were compared by Chi-square test or Fischer’s exact test, as appropriate. p-value 0.05 was considered statistically significant.

Results:

Table 1: AKI.

<table>
<thead>
<tr>
<th>Clinically Dehydrated</th>
<th>Absent</th>
<th>Present</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>12</td>
<td>14</td>
<td>26</td>
</tr>
<tr>
<td>Row %</td>
<td>46.2</td>
<td>53.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>80.0</td>
<td>42.4</td>
<td>54.2</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>19</td>
<td>22</td>
</tr>
<tr>
<td>Row %</td>
<td>13.6</td>
<td>86.4</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>20.0</td>
<td>57.6</td>
<td>45.8</td>
</tr>
<tr>
<td>TOTAL</td>
<td>15</td>
<td>33</td>
<td>48</td>
</tr>
<tr>
<td>Row %</td>
<td>31.3</td>
<td>68.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Clinically significant (P = .0154).

Table 2: ACKD.

<table>
<thead>
<tr>
<th>SEPSIS</th>
<th>Absent</th>
<th>Present</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>16</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Row %</td>
<td>88.9</td>
<td>11.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>48.5</td>
<td>13.3</td>
<td>37.5</td>
</tr>
<tr>
<td>Present</td>
<td>17</td>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>Row %</td>
<td>56.7</td>
<td>43.3</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>51.5</td>
<td>86.7</td>
<td>62.5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>33</td>
<td>15</td>
<td>48</td>
</tr>
<tr>
<td>Row %</td>
<td>68.8</td>
<td>31.3</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Clinically significant (P = .0197).

- Out of the first 100 consecutive patients fulfilling the study criteria, 33 patients had AKI & 15 patients had ACKD.
- The male population was higher than the female population.
- T2DM and HTN were more common in ACKD patients than the AKI patients.
- Patients with AKI were clinically dehydrated compared to patients with ACKD.
- Most of the ACKD patients had sepsis than the AKI patients.
- Conclusion: The most common etiology of AKI amongst in-hospital patients is dehydration whereas that of ACKD is sepsis associated with more incidence of metabolic acidosis & comorbidities. Earlier diagnosis of AKI represents an important area in treating patients with AKI that has spawned increased awareness of the potential that biomarkers of AKI may play in the future.

#3740

AFTER ALL A TYPICAL HUS

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Background and Aims: Typical Hemolytic Uremic Syndrome (HUS) is a thrombotic microangiopathy (TMA) characterized by the triad of acute renal failure, hemolytic anemia and thrombocytopenia. TMA are classified into three types: Inherited or primary acquired (atypical HUS), secondary or infection associated. Infection with Shiga-toxin–producing Escherichia coli (E. coli), mainly of serotype O157:H7, is the most common cause of typical HUS, but other serotypes have been rarely associated such as Enteraggregative Escherichia coli (EAE) serotype O104:H4.

Method: Case Report

Results: We report a case of a 51-years-old male with past medical history of arterial hypertension (treated with Perindopril) and IgG Multiple Myeloma (MM) diagnosed 10 years prior submitted to two bone marrow autotransplants (9 and 4 years prior) and multiple chemotherapy agents including Carfilzomib–Pomalidomide-Dexamethasone (last cycle 4 days before the onset of symptoms). One week after returning from a trip to Brazil, he was admitted to the emergency department with a two-day history of non-bloody diarrhea (≥5 liquid stools per day) and asthenia, with similar positive familiar epidemiology. He denied abdominal pain, fever, nausea or vomiting. At physical examination, he was hypertensive (177/90 mmHg), anuric (12.5 ml/h), dehydrated and apyretic. Abdominal palpation was painless and there were no signs of peritoneal irritation. Laboratory tests showed hemoglobin 10.5 g/dl, new onset thrombocytopenia (261 000/uL » 21 000/uL), kidney dysfunction (serum creatinine (SCr) 0.74 mg/dL to 9 mg/dL and serum urea (SU) 41 mg/dL to 260 mg/dL), hyperkalemia (6 mEq/L) and metabolic acidosis (pH 7.39 and bicarbonate 18.4 mEq/L). LDH was 1949 U/L, C-reactive protein 30.6 mg/L, procalcitonin 3.77 mg/mL, haptoglobin <0.07 g/L and with normal complement levels (C3 and C4). Schistocytes were present in peripheral blood smear. The diagnosis of Acute Kidney Injury related with TMA was established and the patient was transferred to the Nephrology ward and urgent hemodialysis was started. Exhaustive study was performed showing normal renal ultrasound, non-nephrotic proteinuria (1.6 g/g), urinalysis showed leukocyturia and erythrocyturia. Autoimmune study including PR3-ANCA, MPO-ANCA, anti-GBM antibody, anti-dsDNA antibody, anti-beta 2-glycoprotein I antibodies, antiphospholipid antibodies, anti-ADAMTS13 antibodies and ADAMTS13 activity, as well as study of complement C3, C5, C4, factor B, H and I, anti-factor H ac. AH 50 and CH50b were unremarkable. Blood and urine culture and antistreptolysin O titers were negative. Specific stool cultures for E. coli O157, Shigella, Salmonella, Yersinia and Campylobacter were negative. Stool evaluation for parasites were
also negative. Viral serology for HIV, HBV, HCV and Plasmodium tests were negative. PCR stool was required due to high suspicion of E.coli infection. The suspicion of a Carfilzomib induced TMA was also raised, while molecular techniques results were awaited. MM was stable and treatment was held until recovery of kidney function. During hospitalization the patient recovered diuresis and creatinine decreased. On the 11th day of hospitalization, he was discharged but still depended on hemodialysis. Finally, stool PCR techniques identified aatA and aggR genes associated with EAEC O104:H4 allowing the diagnosis of acquired infectious HUS rather than drug-related TMA. One week after discharge, the dialysis was stopped due to sCr 3 mg/dL. Four months later, he resumed Carfilzomib and kidney function remained stable with sCr 0.9 mg/dL, despite sustained proteinuria of 1.2 g.

Conclusion: The authors emphasize the importance of considering other causes of TMA when E.coli O157 infection is excluded, namely drug-related causes (as Carfilzomib) or less frequent infectious agents such as EAEC O104:H4. This case reveals the importance of requesting PCR in the stool even when the E.coli test is negative. This is of particular relevance in immunosuppressed patients. This diagnosis allowed continuing MM treatment.

#5395
ASSOCIATION BETWEEN PARABEN EXPOSURE AND EARLY RENAL INJURY IN A MIDDLE-AGED ADULT IN TAIWAN
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Background and Aims: Parabens are a class of preservatives used in the cosmetics industry and are widely used in people's daily lives, including personal care products (PCPs), pharmaceuticals and food. Epidemiological studies concerning the relations of exposure to parabens with renal function were limited. We aimed to investigate the potential sources of paraben exposure, estimate the daily intake (DI) of four parabens based on their urinary levels and the association between urinary paraben and renal function in a middle-aged adult population in Taiwan.

Method: We recruited 591 subjects aged from ≥40 to <65 years old (yrs) who have participated in Taiwan Environmental Survey for Toxicants (TEST) study from 2013-2016. Urinary parabens including methylparaben (MeP), ethylparaben (EtP), propylparaben (PrP), and butylparaben (BuP) are measured by liquid chromatography/tandem mass spectrometry. The cross-sectional analysis of the association between urinary paraben and biomarkers of renal function have also been established.

Results: The urinary MeP, EtP, PrP and BuP (median) levels were measured at 442, 42.9, 107 and 5.92 μg/L, respectively, which were also 10 times higher than those in other countries. Subjects aged from ≥55 to <65 yrs had higher urinary MeP and EtP levels and DI than those aged from ≥40 to <55 yrs (Fig. 1 & Fig. 2). The median of DI was higher in lotion, perfume and nail
Tubulointerstitial nephritis (TIN) in pediatrics is not always performed due to the rapid and good evolution of some patients. The diagnosis is defined by histology, but renal biopsy is typically performed only when other causes are ruled out. The causes are multiple (pharmacological 70%) and can be associated with a variety of manifestations, even with oligosymptomatic pictures, with the classic triad (fever, eosinophilia and exanthema) being observed in only 10% of cases. The most common symptom was abdominal pain (94%) and the most frequent sign was fever (94%), with prolonged febrile syndrome in 4 children. The most common symptom was abdominal pain (94%) and the most frequent sign was fever (44.4%), with prolonged febrile syndrome in 4 children. The classic triad was detected in two cases (11.1%). On admission, all patients had normal BP, with only one patient oliguric on debut. The delay from clinical onset to diagnosis was a median of 8.5 days (IQR 20.5). Renal ultrasound showed renal hyperechogenicity (25%) and associated nephromegaly (12.5%). Median eGFR at one month was 79.72 mL/min/1.73 m², with only 1 case of recurrence and 2 of chronicity. Seven cases received treatment with corticosteroids and 2 of them with immunosuppressants.

Conclusion: In every child with ARD, acute tubulointerstitial nephritis is one of the causes that we must always keep in mind in our differential diagnosis. In the series we confirm the wide forms of presentation of the disease and its various etiologies. Likewise, the evolution of the disease and the prognosis will depend on the cause and the early diagnosis, conditioning the treatment.

#2537
EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE IN THE REPUBLIC OF UZBEKISTAN

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Background and Aims: Chronic kidney disease (CKD) is an emerging global health problem, currently affecting up to 15% of the global adult population, and is independently associated with an increased risk of cardiovascular disease (CVD) similar to that of diabetes mellitus or coronary artery disease. heart [Reddy K.S., Shah B., Varghese S., Ramados A. 2005; 366: 1744-1749]. To assess the epidemiological characteristics of the development of CKD in the Republic of Uzbekistan (RUz) for 2020.

Method: The object of the study is the database of the Republican Specialized Scientific and Practical Medical Center for Nephrology and Kidney Transplantation of the Republic of Uzbekistan.

Results: According to the Institute of Health and Medical Statistics of the Ministry of Health of the Republic of Uzbekistan, the number of patients with end-stage renal disease (ESRD) decreased between 2011 and 2015. However, according to the data for 2020, the number of patients with stage 5 CKD reached 23,773 thousand and its increase is expected. The proportion of patients with chronic renal failure older than 18 years was registered 21,003 thousand in 2011 and 19,149 thousand in 2015, in those years there was a decrease. However, according to the national registry for 2020, CKD cases in the Republic of Uzbekistan, identified in all regions, amounted to 118,026, there were 2,378 renal failure receiving hemodialysis - 449. The number of registered patients with CKD in the Autonomous Republic of Karakalpakstan was 9013, with CRF - 912, in need of hemodialysis - 115, receiving hemodialysis - 98, in need of transplantation - 21. In Andijan region, 416 persons were registered, with CRF - 201, in need of replacement therapy 137, receiving dialysis - 137, needing in transplantation - 11. In the Bukhara region, 4500 such patients were registered. CKD - 501, in need of substitution therapy - 172, receiving dialysis - 364 and in need of transplantation - 36.

Conclusion: With a general increase in the prevalence of CKD in the Republic of Uzbekistan in the dynamics of 2020, there is an improvement in the quality of diagnosing complications at earlier stages, at a later age and with a longer duration of CKD. Advances in the management of patients with CKD in recent years do not reduce the risk of end-stage chronic renal failure, but delay its development. Pronounced interregional differences in the frequency of registration of CKD in the database indicate problems in diagnosing CKD in a number of regions where the standard for examining patients with CKD with a mandatory assessment of glomerular filtration rate (GFR) and albuminuria at least once a year is not met.
CLINICAL FEATURES AND OUTCOMES OF COVID-19-ASSOCIATED ACUTE KIDNEY INJURY REQUIRING DIALYSIS: EXPERIENCE FROM THE FIRST COVID-19 HOSPITAL IN SERBIA

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Background and Aims: The new coronavirus disease (COVID-19) pandemic faced the healthcare sector worldwide with an unprecedented challenge. Although respiratory failure is the main feature of the disease, renal involvement is also common, particularly in critically ill patients, and often requires urgent dialysis treatment. This study aimed to analyse clinical features and risk factors for poor outcomes in patients with COVID-19-associated acute kidney injury (AKI) requiring dialysis. Methods: All 98 patients included in this retrospective observational study were treated in the first hospital in Serbia transformed to exclusively admit COVID-19 patients at the onset of the epidemic. Data were collected from clinical charts and patient histories for the period between March 19, 2020, and March 19, 2022, and analysed with SPSS software, version 22 (IBM Corporation, New York, USA).

Results: Out of 6,540 non-pregnant adult patients hospitalized for COVID-19 (1,955 in the intensive care unit) in the observed period, 98 (85.7% male, age range 25-89 years) developed dialysis-requiring AKI. A total of 312 hemodialyses (HD) treatments were performed (3.18±2.39, range 1-12, per patient), mostly intermittent HD (85.7% of patients) pertaining to technical resources. The majority of patients (90.8%) had at least one comorbidity – hypertension (38.8%), diabetes (28.6%), cardiovascular disease (11.2%), cerebrovascular disease (3.1%), chronic respiratory disease (7.1%), malignancy (6.1%), or autoimmune disease (1.0%). Most patients (90.8%) required mechanical ventilation. Only 8 (8.2%) were vaccinated. Nearly half (49.0%) of the patients had bilateral pneumonia and 2.0% had ARDS at presentation, with an average CT severity score of 14.65±6.72 (range 1-25) at presentation. Time to AKI presentation was 8.96±5.14 days (range 2-25). The overall mortality rate was 91.8%. Surviving patients had significantly more HD procedures performed (5.00±2.29 vs 3.02±2.23; P = .024) and significantly lower procalcitonin level (1.89±0.16 ng/mL vs 6.14±9.57 ng/mL; P = .015) at presentation. Fatal outcome was significantly more common in individuals requiring mechanical ventilation (p<0.001). Other demographic (age, sex, smoking habit), clinical (comorbidities, vaccination status, radiographic finding, CT severity score, time to AKI onset, type of dialysis) and laboratory parameters (WBC, neutrophil/lymphocyte ratio, CK, LDH, urea, creatinine, CRP, IL-6, D-dimer, ferritin) were not significantly associated with adverse outcome. Multiple logistic regression showed that fewer HD procedures were associated with patients with higher mortality rate. Higher procalcitonin, the need for mechanical ventilation and a lower number of HD procedures are significantly associated with fatal outcomes in this population.

ANCA ASSOCIATED VASCULITIS AFTER COVID-19

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Background and Aims: ANCA associated vasculitis (AAV) is a group of systemic autoimmune diseases characterized by inflammation of small and medium sized vessels. The three main types of AAV are granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Similar pathways are involved in the pathogenesis of COVID-19 and ANCA vasculitis. For instance, neutrophil extracellular traps (NETs) are induced in both entities.

Method: We describe 3 cases reports of patients with ANCA associated vasculitis after COVID19.

Results: Case 1: A 46-year-old female patient was hospitalized in intensive care unit for COVID19 pneumonia. She has fever, cough and dyspnea. A few days before, the SARS-CoV-2 polymerase chain reaction (PCR) was positive on nasopharyngeal swab. She received high flu nasal canula. She presented a pulmonary-renal syndrome with intra-alveolar hemorrhage and acute kidney injury. Chest scanner shows lesions on bilateral lung parenchyma, and an acute kidney injury (AKI) on admission. Urinalysis revealed an active sediment with dysmorphic erythrocytes and significant proteinuria. Renal function gradually deteriorated. So intermittent hemodialysis treatment was initiated. Serological evaluation showed negative antinuclear antibody, and anti-dsDNA, normal serum complements, and an elevated MPO. In kidney biopsy, pauci-immune necrotizing GN with cellular crescents was detected. The patient received pulse dose corticosteroids and subsequently, she was transitioned to oral prednisone. She underwent 2 sessions of plasmapheresis, which were stopped in the absence of confirmation of pulmonary involvement. She received cyclophosphamide during the hospitalization. While hematura and proteinuria was persistent in the most recent urinalysis, the sCr level decreased to 159 μmol/L. In addition, she developed adenral insufficiency after stopping corticosteroid therapy, requiring her to be put on Cortef.

Case 2: A 63-year-old female patient with past medical history of hypertension, was hospitalized in intensive care unit for dyspnea and hemoptysis. A few months before, the SARS-CoV-2 polymerase chain reaction (PCR) was positive on nasopharyngeal swab. She received high flu nasal canula (HFNC). At this moment, she had acute kidney injury with a sCr level of 165μmol/L that was not explored. Currently she presented a pneu-mo-renal syndrome with a rapidly progressive glomerulonephritis and intra-alveolar hemorrhage. Renal function gradually deteriorated and peak sCr level of 30μmol/L. Chest scanner shows ground glass lesions of bilateral lung parenchyma, and hemoglobin at 4.9 g/dL. Urinalysis revealed an active sediment with dysmorphic erythrocytes and significant proteinuria. Hemoptysis was not explored. Currently she presented a pneu-mo-renal syndrome with a rapidly progressive glomerulonephritis and intra-alveolar hemorrhage. Urinalysis revealed an active sediment with dysmorphic erythrocytes and significant proteinuria. Anti-neutrophil cytoplasmic antibodies (ANCA) were positive on serum from the previous patient. However, ANCA were negative on serum from the current patient. She underwent 6 sessions of plasmapheresis, for intra-alveolar hemorrhage. There was an improvement in respiratory and renal function.

Case 3: 57 years old, with a history of functional colopathy, covid infection 1 month before her hospitalization in nephrology department for kidney injury. Currently she presented a pneu-mo-renal syndrome with a rapidly progressive glomerulonephritis and intra-alveolar hemorrhage. Urinalysis revealed an active sediment with dysmorphic erythrocytes and significant proteinuria. Serological evaluation showed negative antineutrophil antibody, and anti-dsDNA, normal serum complements, and an elevated MPO. She underwent 6 sessions of plasmapheresis, for intra-alveolar hemorrhage. There was an improvement in respiratory and renal function.

Conclusion: SARS-CoV-2 infection can be a ‘trigger factor’ for vasculitis. ANCA associated vasculitis should be kept in mind in patients who develop acute kidney injury after COVID-19.
Background and Aims: Hemodialysis patients are at risk of infections due to various factors. Antibiotic resistance is an ever-changing issue. Initial empirical therapy depends on local epidemiology of infection, and antibiotic resistance pattern. Non-access related infections received lesser research attention worldwide. This study examines the spectrum of infections, and antibiotic resistance pattern.

Method: We retrospectively reviewed the records of 586 hemodialysis patients from May 2018 to April 2020 in a tertiary care hospital in North India.

Results: The study identified 99 episodes of confirmed infections. Urinary tract infections were the most common type of infections (55.5%), followed...
Uricase metabolizes uric acid into allantoin, a soluble compound that is easily excreted in the urine. Acute hyperuricemia is associated with endothelial injury and vasoconstriction, favoring acute renal failure. Preliminary studies show the protective role of lowering uric acid in cardiac patients.

Method: Pilot study conducted in patients with cardiorenal syndrome and hyperuricemia (>9 mg/dl). All received a single dose of rasburicase (0.20 mg/kg/day in the first 9 patients or a fixed dose of 6 mg in 14 patients) evaluating its effect on renal function and the need for renal replacement therapy.

Results: Twenty-three patients aged 68 ± 14 years were included, 14 men and 9 women, 87% hypertensive, 35% diabetic, 17% with liver disease, and 26% with cancer. Baseline: mean LVEF 40±14.1% (13-63), pro-BNP 19880±14000ng/L, basal Cr 1.55±0.58 mg/dl, uric acid 14±2.26, phosphorus 5 ±1.6 mg/dl and CRP 7±8 mg/L. The evolution of renal function after treatment is shown in Table 1. In all patients, uric acid after rasburicase decreased to 0.5 mg/dl. There were no differences in renal function, RRT, and hospitalization between patients who received a dose of 0.20 mg/kg/day or 6 mg iv. Only 3 patients required RRT for 21±23 hours, with recovery from acute renal failure. Comparing the patients who required RRT versus those who did not, these presented higher baseline uric acid levels: 16.5±2.5 vs 13.7±1.1 mg/dl, P = .049, and there were no differences in LVEF, pro-BNP and previous renal function. One patient died during the hospital stay due to terminal CHF and sepsis, but having recovered kidney function.

Conclusion: Rasburicase administration may prevent established renal failure in patients with cardiorenal syndrome and hyperuricemia. Early treatment, avoiding very high levels of hyperuricemia, could be more effective in reducing the need for renal replacement therapy.

ANCA ASSOCIATED VASCULITIS AND COVID

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Background and Aims: The coronavirus 2019 (COVID-19) pandemic has brought on challenges not only to acute care, but also chronic care of patients. Patients with ANCA-associated vasculitis (AAV) frequently require immunosuppression and may be at increased risk for developing COVID-19. The incidence and impact of COVID-19 in patients with AAV is currently not well known. We collected the data of patients with AAV infected with SARS-CoV-2, focused on the relationship with the employed immunosuppressants and the stage of chronic kidney disease.

Method: A retrospective study of AAV patients was conducted. Data regarding demographics, disease characteristics and therapy were confirmed by review of the electronic medical record. Information regarding current and previous therapies was collected.

Results: In our center there were 110 AAV patients who had data in the pandemic period. The majority was diagnosed with microscopic polyangiitis (MPA, n=61) or with granulomatosis with polyangiitis (GPA, n=44), there was 5 patients with eosiinophilic granulomatosis with polyangiitis (EGPA). Seventy pts (77%) were receiving immunosuppression treatment, sixteen (17.6%) of these patients employing rituximab during the pandemic period. Twelve patients on immunosuppression treatment for AAV was diagnosed with COVID infection. Eight pts had kidney transplantation, no one had positive PCR test. Thirty-two pts of the 110 pts with AAV was on chronic dialysis treatment, (29 pts on haemodialysis, 3 pts on peritoneal dialysis), eleven of them had positive PCR test for COVID-19. Among the 110 pts with AAV eighteen pts (19%) had positive PCR test for COVID-19. Seven pts had mild disease (with no or mild pneumonia), no specific therapy was applied. Five of them received immunosuppression (rituximab combined with azathioprine or micophenolate mofetil), two pts was on haemodialysis. Severe disease (dyspnea, hypoxia, or > 50 percent lung involvement on imaging within 48 hours) was reported in 7 pts. Five pts was on immunosuppression treatment (2 rituximab, 2 azathioprin, 1 leflunomide), 2 of them was on haemodialysis as well, 2 pts on HD without ISU. In the hospital four patients received favipiravir and prednisolone, no one of them died. Four pts was treated with critical disease (respiratory failure, shock, or multiorgan dysfunction). Two of them was on chronic haemodialysis, and received rituximab with azathioprine, one of them died. The other two pts was without immunosuppression, unfortunately both of them, one died. The incidence of COVID infection was higher among pts with AAV. The pts treated with immunosuppression has higher risk for COVID infection, but the mortality was not significantly higher than in other pts groups. The highest incidence of the COVID infection was in the pts on chronic dialysis treatment, mostly due to the infection during the transfer to the HD Unit.
A NEW SORBENT DEVICE FOR MULTIPLE CLINICAL PURPOSES: CURRENT EVIDENCE AT A PRIVATE HOSPITAL IN MEXICO
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Background and Aims: Adsorption is an extracorporeal technique utilized for blood purification, it also complements convection and diffusion for solute removal. Since 1991, we have used blood purification techniques, over the years, new adsorption cartridges had been developed, the new ones involving treatment for inflammatory conditions, chronic uremic symptoms and autoimmune diseases. HA130, HA230, and HA330 (Jafron, Zhuhai City, China) are among the widely used adsorption cartridges in China. We report highlights of the use of hemoperfusion using HA130 cartridges in the Mexican population cohorts in the context of multiple chronic inflammatory conditions in order to support evidence of effectiveness and safety.

Method: We retrospectively analyzed the medical records of 14 critically ill patients in the context of chronic inflammatory conditions such as acute kidney injury in chronic kidney disease, acute lung injury due to SARS-COV-2 infection and sepsis. Hemoperfusion in addition to standard therapy (fluid resuscitation, vasopressors, antimicrobial therapy and ventilatory support) resulted in the improvement of inflammatory substances levels when compared to standard therapy alone. Out of the 14 patients, 7 patients used HA130 cartridges and 7 patients with standard therapy alone.

Results: There were no significant side effects associated with HA130 cartridge use. HA 130 cartridges were found to be effective in reducing uremic symptoms in chronic hemodialysis patients, improvement of pruritus score and decreased parathyroid hormone and phosphate product (p<0.05) when compared to HD alone, creatinine (MARS: −24 μmol/L, −19.5 to −10.6, p < 0.001; SPAD: −2 μmol/L, −9.0 to +7.0/L, p = 0.314) and urea (MARS: −0.9 mmol/L, −318 to −0.189, p = 0.024; SPAD: −0.1 mmol/L, −1.0 to +0.68, p = 0.523). 66.6% of cost-effectiveness when compared to standard therapy.

Conclusion: In the group of patients that used HA130 cartridges we found statistically significant (p < 0.05) reduction of pruritus score, PTH, phosphate product, creatine and urea when compared to the group of patients with standard therapy alone. The development in new cartridges technology allows more wide applications for renal patients. As we expand to involve other indications for this therapy there is cost-effectiveness improvement for the patients. More studies in different clinical settings are needed in order to achieve adsorption therapy national recommendations. We also found that the HA130 cartridges are effective in reducing uremic symptoms and microinflammatory status in acute kidney injury in chronic kidney disease patients due to the elimination of middle and small molecule uremic toxins and inflammatory mediators and endotoxins. This may translate as an improvement of quality of life and survival rates in patients with chronic hemodialysis, even though more studies are needed in order to prove this assumption.

THE URINARY BIOMARKERS IGFBP7 AND IGFBP7 X TIMP2 PRE-EMPTIVELY IDENTIFY PATIENTS AT RISK OF CONTRAST NEPHROTOXICITY
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Background and Aims: Drug nephrotoxicity is a serious medical and economic concern. In fact, 25% of the 100 most used drugs in intensive care units are toxic to the kidney, which limits their use and, therefore, the correct therapy for the patient. The administration of contrast media (CM) during diagnostic tests or surgical interventions carries the risk of contrast-induced nephropathy (CIN), which is a clinical condition defined as an increase in plasma creatinine of 25% or 0.5 mg/dL above baseline within 3-5 days after administration. Because once instilled CM has no treatment, identification of new biomarkers predicting patients at risk of CIN before receiving CM may be crucial to prevent future kidney complications. Clinical studies conducted in other medical areas have identified new urinary biomarkers, such as insulin like growth factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases 2 (TIMP2), that anticipate the risk of developing kidney damage after the administration of different potentially nephrotoxic compounds. The objective of this work was to evaluate the usefulness of these biomarkers to predict CIN in cardiac patients.

Method: A clinical study was carried out with 154 patients from the University Hospital of Salamanca Cardiology Department who subsequently received a CM. Prior to contrast administration, urine samples were collected. In addition, their plasma creatinine level was registered for the following 5 days to evaluate the development of CIN. Patients were divided into Controls (who did not develop CIN) and Cases (who developed CIN). IGFBP7 and TIMP2 biomarkers were quantified in urine samples by ELISA. Subsequently, the differences between both groups were evaluated using the Mann-Whitney U test and the diagnostic capacity of each biomarker was analyzed through the generation of its receiver operating characteristic (ROC) curve.

Results: Of the total number of patients, 123 were assigned to the Controls group and 31 to the Cases group. In both groups the distribution of sex and risk factors was similar, except for the case of age and body mass index, which was slightly lower and higher, respectively, in the Controls group. IGFBP7 was significantly higher in Cases (p < 0.01) compared to the Controls, and the IGFBP7 x TIMP2 product further improved this significance (p < 0.001). Specifically, the area under the ROC curve for IGFBP7 was 0.67 (95% confidence interval of 0.56-0.78); while that for IGFBP7 x TIMP2 increased to 0.73 (with a 95% confidence interval of 0.63-0.84). In contrast, TIMP2 alone showed no differences between both groups of patients.

Conclusion: The biomarkers IGFBP7 and IGFBP7 x TIMP2 could therefore be used for the prophylactic identification and management of patients at risk of developing CIN.

ACUTE KIDNEY INJURY (AKI) AMONG COVID-19 POSITIVE PATIENTS INCREASES THE RISK OF MORTALITY: A SINGLE CENTER EXPERIENCE
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Background and Aims: Renal complications of COVID-19 are not yet well studied. We aimed to evaluate the prevalence of acute kidney injury (AKI) among positive COVID-19 hospitalized cases and explore its impact on patient outcomes.

Method: 586 hospitalized patients with COVID-19 were retrospectively evaluated. Of them, 267 (45.5%) developed AKI classified according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines- compared with 319 (54.5%) patients without AKI.

Results: Most cases were males (72.7% vs. 69.7%), and their ages ranged (60.8±14 vs. 51.7±16 years). Comorbid conditions significantly predominant among the AKI group were diabetes mellitus (64 vs. 42.9%), hypertension (72.6% vs. 43.5%), and ischemic heart disease (25% vs. 14.7%). Fever, cough, shortness of breath, and dehydration were the main presentations among the AKI group, and they had significant radiological findings concordant with COVID-19 (86.8% vs. 59.8%). Sepsis, volume depletion, shock, arrhythmias, and ARDS were significantly higher in the AKI group. Anticoagulation (85% vs. 59.2%), vasopressors, plasma infusions, antimicrobials, and steroids were more frequently used in the AKI group. Acute respiratory failure requiring mechanical ventilation and the overall mortality rate were significantly higher in the AKI group (62.3% vs. 32.9% and 63.2%. vs. 31.1%, respectively).

Conclusion: AKI associated with severe COVID-19 was more frequent than reports from Chinese, European, and North American cohorts. AKI risk factors included COVID-19 comorbidities like hypertension, diabetes, mechanical ventilation, male gender, and older age. Mortality was high in this population, especially elderly patients, and in those who develop KDIGO stage 3 AKI.

RISK FACTORS FOR RRT RESTART AFTER CESSATION OF CRRT: A MULTICENTER STUDY
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Background and Aims: Acute Kidney Injury occurs frequently in patients admitted to the Intensive Care Unit (ICU) and continuous renal replacement therapy (CRRT) is a commonly used treatment modality in these patients. Restart of renal replacement therapy (RRT) after initial discontinuation of

Abstract
CRRT is also frequently needed. The purpose of this study is to identify clinical characteristics and biomarkers influencing the restart of RRT after the cessation of CRRT, and to build a predictive model using these parameters.

**Method:** This multicenter retrospective study includes 891 patients who were treated using CRRT from July 2012 to December 2020 in the ICU of 3 academic hospitals. The primary end point observed was the restart of RRT during hospitalization. Baseline characteristics were compared between the no restart and restart RRT groups. Using univariate analysis and logistic regression, a prospective index was developed, and receiver operator characteristic (ROC) curve analysis was performed to confirm the predictivity of the prognostic index.

**Results:** Restart of RRT was needed in 632 (71.2%) patients. Compared to patients that did not restarting, patients in the restart RRT group demonstrated higher age, higher BMI, higher baseline serum creatinine (Cr), lower urine output, longer ICU admission, and more comorbid conditions (HTN, DM, HF, ischemic heart disease). In the multivariate analysis, five parameters demonstrated independent influence on restart of RRT: HTN, Cr, ICU admission duration, BMI, and mean blood pressure. The prognostic index, which was calculated from these variables, showed a satisfactory potential to predict the restart of RRT after discontinuation of CRRT. ROC analysis revealed an area under the curve of 0.738 (95% CI, 0.703-0.773, p < 0.001).

**Conclusion:** We found that 5 of the 40 parameters observed in our study were independent risk factors for the restart of RRT during admission and we successfully developed a prognostic index based on these variables to predict the restart of RRT after discontinuation of CRRT.

### #6376

**TREATMENT OF DABIGATRAN INTOXICATION IN CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY: THE ROLE OF SUSTAINED LOW-EFFICIENCY DIALYSIS**

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**Background and Aims:** Dabigatran, a direct thrombin inhibitor, is a commonly used direct oral anticoagulant (DOAC) prescribed for non-valvular atrial fibrillation. Despite its benefits in term of safety/effectiveness along with the possibility to treat patients who were ineligible for vitamin K inhibitors (VKAs), a great degree of attention is required in elderly patients with multiple comorbidities. Notably, dabigatran mainly undergoes renal elimination, and dose adjustment is recommended in patients with Chronic Kidney Disease (CKD). In this regard, the onset of an abrupt decrease of kidney function may further affect dabigatran pharmacokinetic profile, increasing the risk of acute intoxication. Idarucizumab is the approved antagonist in the case of dabigatran-associated major bleeding or concomitant need of urgent surgery, but its clinical use is limited by the lack of data in patients with Acute Kidney Injury (AKI). Given the dabigatran PK parameters (low MW, low Vd, negligible protein binding), the early start of Extracorporeal Kidney Replacement Therapy (EKRT) may represent the optimal reversal strategy. We present a case series of three critically ill patients with AKI and dabigatran overdose treated with Sustained Low-Efficiency Dialysis (SLED).

**Methods:** Three critically ill patients (Table 1) were admitted to the Renal Intensive Care Unit (ICU) for stage 3 AKI and intercurrent dabigatran intoxication. SLED sessions with Regional Citrate Anticoagulation (RCA) were prescribed with SURDIAL X machine, ELISIO-21M filter (Nipro Co., Osaka, Japan) [blood flow rate 200 mL/min, dialysis fluid rate 300 mL/min; citrate flow rate 350 mL/h (ACD Fresenius Kabi, Italia)]. Dabigatran plasma levels (dilute thrombin time, dTT) along with coagulation parameters were monitored before, during and after SLED session.

**Results:** A rapid and sustained decreased of plasma dabigatran level was observed in each patient in course of SLED sessions. No clinically relevant post-treatment rebound was reported (Figure 1).

**Conclusions:** SLED meets the requirements to be a viable reversal anticoagulation option in the context of dabigatran overdose. Indeed, it efficiently provides dabigatran removal, by reaching a safe plasma concentration within the first hours and avoiding significant rebound effect.

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**Figure 1:** Dabigatran plasma level (ng/mL) in course of SLED session.
Table 1: Demographic and clinical characteristics at ICU admission, and EKRT prescription.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pt. 1</th>
<th>Pt. 2</th>
<th>Pt. 3</th>
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<tbody>
<tr>
<td>Age, yr</td>
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<td>82</td>
<td>61</td>
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<tr>
<td>Male sex</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
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<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
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<tr>
<td>Arterial hypertension</td>
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<td>Y</td>
<td>Y</td>
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<tr>
<td>Diabetes mellitus</td>
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<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
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<tr>
<td>Liver failure</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Heart failure</td>
<td>N</td>
<td>N</td>
<td>Y</td>
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<tr>
<td>CKD, stage</td>
<td>2</td>
<td>3a</td>
<td>2</td>
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<tr>
<td>usual dabigatran dose, mg/day</td>
<td>300</td>
<td>220</td>
<td>300</td>
</tr>
<tr>
<td>CHA2 DS2 VASC</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>HAS BLED</td>
<td>17</td>
<td>32</td>
<td>19</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>17</td>
<td>32</td>
<td>19</td>
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<td>Vasopressors use for hemodynamic instability</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Oliguria</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
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<tr>
<td>Serum creatinine, mg/dl</td>
<td>9.8</td>
<td>6</td>
<td>14.1</td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>81</td>
<td>84</td>
<td>160</td>
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<tr>
<td>Sodium, mmol/L</td>
<td>133</td>
<td>137</td>
<td>119</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>3.1</td>
<td>4.2</td>
<td>4.5</td>
</tr>
<tr>
<td>Hb, g/dl</td>
<td>13.1</td>
<td>12.8</td>
<td>10.2</td>
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<td>Platelet count, x10^9/mL</td>
<td>246</td>
<td>52</td>
<td>419</td>
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<tr>
<td>INR</td>
<td>2.18</td>
<td>2.95</td>
<td>3.79</td>
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<td>aPTT ratio</td>
<td>2.39</td>
<td>2.77</td>
<td>3.9</td>
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<tr>
<td>Fibrinogen, U/l</td>
<td>366</td>
<td>543</td>
<td>493</td>
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<tr>
<td>GOT, U/l</td>
<td>24</td>
<td>100</td>
<td>10</td>
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<tr>
<td>GPT, U/l</td>
<td>31</td>
<td>157</td>
<td>11</td>
</tr>
<tr>
<td>Albumin, g/dl</td>
<td>2.9</td>
<td>3</td>
<td>5</td>
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<tr>
<td>s-Ca2+</td>
<td>1.22</td>
<td>0.98</td>
<td>0.95</td>
</tr>
<tr>
<td>Lactate, mmol/L</td>
<td>0.8</td>
<td>17</td>
<td>1.3</td>
</tr>
<tr>
<td>Bicarbonate, mmol/L</td>
<td>15</td>
<td>19</td>
<td>12</td>
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<tr>
<td>Blood transfusion needs, unit/day</td>
<td>955</td>
<td>449</td>
<td>1881</td>
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<td>Renal ICU stay, days</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<td>Death in the ICU</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Serum creatinine at hospital discharge, mg/dL</td>
<td>1.4</td>
<td>-</td>
<td>1.2</td>
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<tr>
<td>Prescribed EKRT sessions, n/patient</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Actual SLED duration, hours</td>
<td>8</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Causes of SLED interruption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Programmed end of treatment</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Circuit clotting</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>CVC malfunctioning</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Other clinical reasons</td>
<td>N</td>
<td>Y</td>
<td>N</td>
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</table>

Table 1: Laboratory parameters of the patient at admission, 1 week later and on discharge.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>On presentation</th>
<th>1 week later</th>
<th>On discharge</th>
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<tbody>
<tr>
<td>CBC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBCs</td>
<td>19 *10^9/l</td>
<td>22 *10^9/l</td>
<td>5.67 *10^9/l</td>
</tr>
<tr>
<td>HGB</td>
<td>8.1 g/dl</td>
<td>8.5 g/dl</td>
<td>9.1 g/dl</td>
</tr>
<tr>
<td>PLTs</td>
<td>55 *10^9/l</td>
<td>60 *10^9/l</td>
<td>199 *10^9/l</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>4.95 mg/dl</td>
<td>6.5 mg/dl</td>
<td>1.6 mg/dl</td>
</tr>
<tr>
<td>Blood urea</td>
<td>85 mg/dl</td>
<td>87 mg/dl</td>
<td>32 mg/dl</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>2.9 gm/dl</td>
<td>3.3 gm/dl</td>
<td>4.3 gm/dl</td>
</tr>
</tbody>
</table>

#6437

INTRABDOMINAL ABSCESS: AN UNEXPECTED CAUSE OF POSTPARTUM SEPSIS IN A VAGINALLY DELIVERED WOMAN WITH PREGNANCY RELATED ACUTE KIDNEY INJURY

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Pregnancy related-Acute kidney injury (PR-AKI) is a life-threatening complication with substantial fetal and maternal mortality and morbidity. AKI is associated with increased risk of infection and/or sepsis. Intra-abdominal infections account for 11.9% of infections that complicate AKI among critically ill patients. The pathophysiology is not fully understood, several theories have been proposed; of which, AKI associated hypervolemia leads to tissue edema and bacterial translocation. Moreover, AKI induces a hyper-inflammatory state and suppresses the immune system, this may present a greater predisposition for infection. Here we report a rare case of intra-abdominal abscess presented in a woman with recovering PR-AKI three months following normal vaginal delivery.

Case presentation: A 20-year-old, previously healthy female patient, was admitted due to severe postpartum hemorrhage (PPH) complicating a full-term vaginal delivery. On admission, blood pressure was 170/70, heart rate was 100 beats/min, and respiratory rate was 22 breaths/min. The patient developed oliguria, generalized edema, and fever (38.5°C). The blood tests are revealed in Table I. The patient had elevated liver enzymes (SGOT, SGPT, alkaline phosphatase). Plasminogen activator inhibitor-1 (PAI-1) was also noted to be elevated, indicating an ongoing inflammatory state. CT scan imaging revealed an intraperitoneal abscess which was subsequently treated with antibiotics and percutaneous drainage.

Abstract
97 IU/L, and SGPT 117 IU/L). The patient was started on supportive treatment with packed RBC, platelet transfusion, and fresh frozen plasma. Empiric antibiotic was administered. The patient subsequently had general improvement and was discharged 17 days after delivery with partial recovery of kidney function. Three months later, the patient presented with throbbing pain in the lower abdomen and fever. Abdominal examination revealed pelvi-abdominal fullness along with mild tenderness with no guarding or rigidity. No obvious palpable lumps were detected. No abnormalities were detected in per vaginal and per rectal examinations. CT scan was performed and revealed a large sized collection in the lower abdomen sized 6.5x5x9 cm. Ultrasound guided aspiration of 60 ml pus confirmed the diagnosis of intraabdominal abscess. Intravenous antibiotics were started with percutaneous drainage of the abscess.

Discussion: Intraabdominal abscess is a serious ailment, and it is associated with high mortality and morbidity if left untreated. An intra-abdominal abscess can cause symptoms such as prolonged ileus, anorexia, fever, and abdominal pain. Septic shock may eventually develop in case of delayed treatment. However rare, there should be a causative factor. Intraabdominal abscess following a normal vaginal delivery is very rare and not reported with PR-AKI. CT scan is still the most useful technique for diagnosis and treatment. Additionally, it can help guide percutaneous drainage by locating the abscess in relation to the viscera of the abdomen. The use of adequate antimicrobial drug therapy in combination is a fundamental approach. It is therefore of great importance to consider symptoms such as atypical abdominal distension or pain in women in the postpartum period and to provide thorough comprehensive evaluation. Early diagnostic consideration greatly lessens patients' morbidity and mortality.


#3616

NON-ANESTHETIC STENTING IS AN EQUIVALENTLY EFFECTIVE METHOD COMPARED WITH PERCUTANEOUS NEPHROSTOMY IN ACHIEVING EARLY RECOVERY IN STONE INFECTED PATIENTS

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Background and Aims: The prevalence of urinary tract stones is increasing. Although the importance of urgent decompression in managing this condition is well established, preferences for drainage methods (stenting vs. percutaneous nephrostomy [PCN]) differ depending on the treating institution. We therefore analyzed the effects of different drainage methods on early recovery.

Method: We retrospectively reviewed the medical records of patients hospitalized for infection with urinary obstruction due to urinary calculi at Gangneung Asan Hospital between January 2011 and December 2020. All patients underwent stenting or PCN. Early recovery was defined as subsided fever or discharge within 3 days after the procedure.

Results: A total of 178 patients, including 98 treated with double J stents and 80 treated with PCN were included. Univariate analysis revealed male sex, diabetes mellitus, coronary heart disease, mid ureter stone, upper ureter stone, stone size of 10-20 mm, and renal stone concomitance as significant prognostic factors for early recovery. In contrast, multivariate analysis revealed male sex, stonesize of 10-20 mm, and renal stone concomitance as significant prognostic factors for early recovery. (Table 2). When stenting was compared with PCN, the recovery period of fever and C-reactive protein and white blood cell levels showed similar trends.

Conclusion: Male patients and those without risk factors for stone-related complications tended to recover more easily after the procedure. The results demonstrate that non-anesthetic stenting is an effective method, compared with PCN, to achieve early recovery in infected patients due to stone obstruction.

#3813

EFFECT OF ORAL FLAVONOIDS ON ARTERIAL STIFFNESS IN CKD: A PILOT PROSPECTIVE STUDY

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Ptolemaida, Thesi Kouri 1, Ptolemaida, Greece

Background and Aims: Flavonoids, the main category of polyphenols possess antioxidant and antihypertensive properties mediated through endothelial protection, renin-angiotensin-aldosterone and sympathetic system suppression. The aim of the study was to evaluate the effect of oral flavonoids administration in arterial stiffness indices and of oxidative stress markers in patients with Chronic Kidney Disease (CKD).

Method: The enrolled patients received chocolate bars rich in polyphenols (200 mg) daily for a period of 3 months. The patients underwent clinical examination and laboratory test arterial stiffness measurements with SphygmoCor. Markers of oxidative stress (total phenols, total plasma antioxidant capacity, protein carbonyls) were also measured.

Results: Sixteen patients were enrolled in the study, [median age 62.5 years (± 8.2), 14 patients (87.5%) were male]. Clinical characteristics, blood pressure measurements, arterial stiffness indices and markers of oxidative stress are summarized in table 1, 2 and 3. Peripheral systolic Blood Pressure (PSBP) was decreased by 13.56 mmHg (± 2.57), (p<0.001). Pulse wave velocity (PWV) and central pulse pressure (CPP) were significantly decreased (8.2 m/sec (5.1-9.29), vs 8.85 m/sec (6.7-11.75), (p<0.001) and 47.63 (36.5-60) versus [59.13 mmHg (43.5-69 respectively) at the end of the study], (p=0.003). Markers of oxidative stress were also improved. A decreased in plasma proteinic carbonyls 52.54 nmol/ml ± 25.04 versus [73.50 nmol/ml ± 18.65, (p<0.001) was observed.

Table 1: Clinical characteristics of the study participants according to decompression procedures.

<table>
<thead>
<tr>
<th></th>
<th>PCN (N=80)</th>
<th>Stenting (N=98)</th>
<th>Total (N=178)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>54 (67.5)</td>
<td>71 (72.4%)</td>
<td>125 (70.2%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Male</td>
<td>26 (32.5%)</td>
<td>27 (27.6%)</td>
<td>53 (29.8%)</td>
<td></td>
</tr>
<tr>
<td>Median age (IQR)</td>
<td>73.0 [61.5;80.5]</td>
<td>66.0 [57.0;74.0]</td>
<td>68.5 [58.0;77.0]</td>
<td>0.001</td>
</tr>
<tr>
<td>Median BMI (IQR)</td>
<td>23.5 [20.3;25.9]</td>
<td>25.9 [22.9;29.0]</td>
<td>24.5 [21.7;27.7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DM</td>
<td>34 (42.5%)</td>
<td>33 (33.7)</td>
<td>67 (37.6)</td>
<td>0.292</td>
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<td>HTN</td>
<td>56 (70.0)</td>
<td>60 (61.2)</td>
<td>116 (65.2)</td>
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<td>Onset of fever</td>
<td></td>
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<td></td>
<td>0.158</td>
</tr>
<tr>
<td>1-3 d</td>
<td>72 (90.0)</td>
<td>74 (75.5)</td>
<td>146 (82.0)</td>
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</tr>
<tr>
<td>3 d-1 wk</td>
<td>4 (5.0)</td>
<td>12 (12.2)</td>
<td>16 (9.0)</td>
<td></td>
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<tr>
<td>1 wk</td>
<td>1 (1.2)</td>
<td>3 (3.0)</td>
<td>4 (2.3)</td>
<td></td>
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<tr>
<td>Unknown</td>
<td>3 (3.8)</td>
<td>9 (9.2)</td>
<td>12 (6.7)</td>
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<tr>
<td>Median hospital stay (IQR)</td>
<td>13.0 [8.5;16.0]</td>
<td>8.0 [6.0;12.0]</td>
<td>10.5 [7.0;15.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Location of stone</td>
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<td>0.268</td>
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<tr>
<td>Low</td>
<td>24 (30.0)</td>
<td>23 (23.5)</td>
<td>47 (26.4)</td>
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<tr>
<td>Mid</td>
<td>16 (20.0)</td>
<td>16 (16.3)</td>
<td>32 (18.0)</td>
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<tr>
<td>Upper</td>
<td>39 (48.8)</td>
<td>53 (54.1)</td>
<td>92 (51.7)</td>
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<tr>
<td>Kidney</td>
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<td>6 (6.1)</td>
<td>7 (3.9)</td>
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<td>Coexistence of renal stone</td>
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<td>0.491</td>
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<td>Free</td>
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<td>44 (44.9)</td>
<td>75 (42.1)</td>
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<tr>
<td>Both</td>
<td>19 (23.8)</td>
<td>21 (21.4)</td>
<td>40 (22.5)</td>
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<tr>
<td>Ipsilateral</td>
<td>22 (27.5)</td>
<td>19 (19.4)</td>
<td>41 (23.0)</td>
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<td>Contralateral</td>
<td>8 (10.0)</td>
<td>14 (14.3)</td>
<td>22 (12.4)</td>
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<td>Size of stone</td>
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<td></td>
<td>0.616</td>
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<tr>
<td>~5 mm</td>
<td>13 (16.2)</td>
<td>21 (21.4)</td>
<td>34 (19.1)</td>
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<td>5-9 mm</td>
<td>41 (51.2)</td>
<td>46 (46.9)</td>
<td>87 (48.9)</td>
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<tr>
<td>10-20 mm</td>
<td>18 (22.5)</td>
<td>25 (25.5)</td>
<td>43 (24.2)</td>
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<tr>
<td>20 mm</td>
<td>8 (10.0)</td>
<td>6 (6.1)</td>
<td>14 (7.9)</td>
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<tr>
<td>ESBL positivity</td>
<td>21 (26.2)</td>
<td>14 (14.3)</td>
<td>35 (19.7)</td>
<td>0.071</td>
</tr>
<tr>
<td>Procedure location</td>
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<td></td>
<td></td>
<td>0.342</td>
</tr>
<tr>
<td>Both</td>
<td>5 (6.2)</td>
<td>2 (2.0)</td>
<td>7 (3.9)</td>
<td></td>
</tr>
<tr>
<td>Rt</td>
<td>36 (45.0)</td>
<td>44 (44.9)</td>
<td>80 (44.9)</td>
<td></td>
</tr>
<tr>
<td>Lt</td>
<td>39 (48.8)</td>
<td>52 (53.1)</td>
<td>91 (51.1)</td>
<td></td>
</tr>
</tbody>
</table>

PCN, percutaneous nephrostomy; IQR, interquartile range; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; ESBL, extended-spectrum beta-lactamases
In this pilot study, oral flavonoid supplementation in the dose of 200 mg may improve arterial stiffness indices and systolic blood pressure observed while antioxidative capacity was increased 3.55% (1.15-6.38) versus 12.51% (6.26-17.66) (P = 0.013). Importantly no side effects were observed during the study period.

**Conclusion:** In this pilot study, oral flavonoid supplementation in the dose of 200 mg may improve arterial stiffness indices and systolic blood pressure measurements and contribute to the improvement of antioxidative capacity in CKD patients.

**Table 1: Patient’s characteristics.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Average ± standard deviation</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>62.5 ± 8.2</td>
</tr>
<tr>
<td>Gender (male,%)</td>
<td>14 (87.5%)</td>
</tr>
<tr>
<td>CKD stage (n%)</td>
<td></td>
</tr>
<tr>
<td>Stage I: 6 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Stage II-IIIA: 6 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Stage III-BIV: 4 (25%)</td>
<td></td>
</tr>
<tr>
<td>eGFR using CKD epi (ml/min/1,73m²)</td>
<td>84 (47.5-98.75)</td>
</tr>
<tr>
<td>HCT %</td>
<td>42.3% ± 5.2</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>14.3 ± 1.9</td>
</tr>
<tr>
<td>PLTs (10¹³/μL)</td>
<td>222 ± 51.27</td>
</tr>
<tr>
<td>Urea</td>
<td>51.02 (25.9-69.9)</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.3 (0.77-1.52)</td>
</tr>
<tr>
<td>24-hour urine protein</td>
<td>183 (91.2-94.9)</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>138.8 ± 1.57</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>4.85 (4.72-5)</td>
</tr>
<tr>
<td>LDH (IU/L)</td>
<td>183.2 ± 42.6</td>
</tr>
</tbody>
</table>

**Table 2: Parameters of pressure measurements in two visits.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>In the onset of the study</th>
<th>At the end of the study</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSAP (mmHg)</td>
<td>147.63 ± 15.86</td>
<td>134.06 ± 12.97</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PDAP (mmHg)</td>
<td>80.88 ± 8.19</td>
<td>75.56 ± 6.32</td>
<td>0.051</td>
</tr>
<tr>
<td>MPWV (m/sec)</td>
<td>8.85 (6.7 – 11.75)</td>
<td>8.2 m/sec (5.1 – 9.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CSAP (nmHg)</td>
<td>156 ± 23.09</td>
<td>137.19 ± 16.11</td>
<td>0.004</td>
</tr>
<tr>
<td>CDBP (mmHg)</td>
<td>90 ± 14.06</td>
<td>80.19 ± 10.30</td>
<td>0.002</td>
</tr>
<tr>
<td>CPP (mmHg)</td>
<td>59.13 (43.5-69)</td>
<td>47.63 (36.5 – 60)</td>
<td>0.003</td>
</tr>
<tr>
<td>Aix %</td>
<td>26.5 ± 10.01</td>
<td>32.5 ± 13.32</td>
<td>0.513</td>
</tr>
<tr>
<td>(Ap)</td>
<td>17.44 (9.5 – 21)</td>
<td>14.25 (9.5 – 18.75)</td>
<td>0.779</td>
</tr>
</tbody>
</table>

**Table 3: Oxidative stress parameters at the beginning and end of the study.**

<table>
<thead>
<tr>
<th>Oxidative stress parameters</th>
<th>1st visit</th>
<th>2nd visit</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteins carbonyls (nmol/ml)</td>
<td>73.50 ± 18.65</td>
<td>52.54 ± 25.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TPC (μg/ml)</td>
<td>25.11 (16.95 – 30.29)</td>
<td>31.91 (30.49 – 47.51)</td>
<td>0.004</td>
</tr>
<tr>
<td>TAC (%)</td>
<td>3.55 (1.15 – 6.38)</td>
<td>12.51 (6.26 – 67)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

TPC: Total phenolic contents, TAC: total antioxidant capacity, P value: probability value

**#5569 ASSOCIATION OF URINARY CCL14 WITH PLASMA PROTEIN BIOMARKERS IN CRITICALLY ILL SEPSIS PATIENTS WITH PERSISTENT ACUTE KIDNEY INJURY**

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4 Amsterdam UMC, location University of Amsterdam, Department of Intensive Care Medicine, and Laboratory of Experimental Intensive Care and Anesthesiology (L-E-I-C-A), Amsterdam, Netherlands and 5 Amsterdam UMC, location University of Amsterdam, Division of Infectious Diseases, Amsterdam, Netherlands

**Background and Aims:** The urinary concentration of CC chemokine ligand 14 (CCL14) – a chemoattractant for T-cells and monocytes – has recently been identified as a strong predictor of persistence of severe acute kidney injury (AKI). The mechanisms by which CCL14 mediates persistent severe AKI are not yet completely understood. With sepsis being the most frequent cause of AKI, we wanted to externally validate whether urinary CCL14 concentration can differentiate sepsis patients with and without persistence of AKI, and its association with plasma protein biomarkers reflective of three pathophysiologival pathways.

**Method:** Patients admitted with sepsis to the intensive care unit (ICU) were categorized according to the evolution of AKI (no-AKI, transient-AKI, and persistent-AKI, defined as lasting > 48h), and matched to a 1:1:1 ratio. AKI was assessed prospectively and daily, using the risk, injury, failure, loss, and end-stage kidney disease (RIFLE) classification. Transient- and persistent-AKI patients had at least injury or failure (severe) RIFLE stages. Urine samples collected at ICU admission were analyzed for CCL14 level; in the same patient cohort we measured 9 plasma biomarkers reflective of systemic inflammation and cytokine responses, endothelial cell activation, and loss of endothelial barrier function. We applied a recently proposed cutoff of 1.3 ng/mL for high CCL14 for the identification of patients at high risk for persistent severe AKI.

**Results:** Of 211 sepsis patients enrolled, 72 patients did not have AKI, 71 had transient AKI and 68 had persistent AKI. Majority of patients with high CCL14 had a persistent AKI (23 out of 31; 74.2%). CCL14 showed good discrimination between persistent-AKI and no-AKI (Area Under the ROC Curve [AUC], 0.82, 95%CI 0.75-0.89), and moderate discrimination between persistent-AKI and transient-AKI (AUC 0.71, 95%CI 0.55-0.87). High CCL14 was associated with lower severity scores, and source of infection being the urinary tract, and skin. The plasma protein analysis revealed that high urinary CCL14 was associated with more prominent systemic (anti-)inflammatory and cytokine responses, and signs of disrupted endothelial barrier function (shown by elevated interleukin [IL]-8 and IL-10, and decreased angiopoietin-1 [P = .005; P = .004; P = .009, respectively]). Within the persistent-AKI group, baseline characteristics (age, chronic comorbidities, and disease severity) did not differ between CCL14 groups, and high CCL14 was only associated with decreased angiopoietin-1 (P = .003).

**Conclusion:** External validation of urinary CCL14 showed good discrimination in critically ill sepsis patients between persistent AKI and no-AKI, and moderate discriminative ability to separate transient-AKI. High urinary CCL14 identifies persistent-AKI sepsis patients with more profound dysregulation of inflammatory pathways coupled with loss of endothelial barrier function. This could guide future therapeutic strategies targeting subgroups within the AKI population.