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# S262
# ISCHEMIC WHITE MATTER LESIONS ARE ASSOCIATED WITH COGNITIVE DYSFUNCTION IN ADULTS WITH SICKLE CELL DISEASE

Topic: 26. Sickle cell disease

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**Background:** At least 33% of adults with sickle cell disease (SCD) have neurocognitive deficits and up to 50% show radiological signs of ischemia on cerebral imaging. In adults, evidence about the possible association between ischemic white matter lesions (IWML) and cognitive function remains controversial.

**Aims:** 1) Describe the prevalence of neuroradiological abnormalities on routine screening magnetic resonance imaging and angiography (MRI/A) in a contemporary Canadian cohort of adults with SCD. 2) Test for associations between the presence and severity of brain lesions on MRI/MRA, and performance on cognitive screening using the Rowland Universal Dementia Assessment Scale (RUDAS). We hypothesized that the presence and severity of IWML on screening MRI/A is associated with lower RUDAS performance in SCD adults.

**Methods:** Design: cross-sectional study, two Canadian comprehensive SCD centers (CHUM, Montréal and UHN, Toronto). Inclusion criteria: adult out-patients, all SCD phenotypes, tested with RUDAS. Patient characteristics/outcomes: Patient information was extracted from electronic patient records. Brain MRI/A reports <1 year from date of cognitive screening were reviewed. Findings were categorized: white matter hyperintensities (WMH), lacunae, cortical infarct (CI), atrophy, Moya-Moya, arterial stenosis or aneurysm. IWML was defined as a WMH and/or lacunae and its burden was graded with an adapted Fazekas score. Previous literature defined a RUDAS score of <23 as suggestive of dementia. Statistics: T-test and Fisher exact were used to test for association between RUDAS performance and brain MRI/A findings. The effect of genotype subgroup on the association was assessed using Mantel-Haenszel test. Statistical significance was established at $p<0.05$.

**Results:**

Between July 2018 and September 2019, 252 patients were screened (CHUM 92, UHN 160) with the RUDAS. Contemporary screening MRI/A was available for 166 (65.9%) patients. Mean age was 31.0 [range 18-75] and 83 (50.0%) were female. Phenotype distribution was 108 (65.1%) with SS or $Sb^0$ and 58 (34.9%) with SC or $Sb^+$. A history of stroke was recorded in 17 (10.2%). WMH were reported in 71 (42.8%) patients, lacunae in 31 (18.7%), aneurysms in 20 (12.0%), stenosis in 12 (7.2%), atrophy in 8 (4.8%), CI in 4 (2.4%) and Moya Moya in 4 (2.4%). An IWML was described in 92 (55.4%). A RUDAS score <23 was found in 13 (7.8%) patients with recent MRI/MRA, compared to 29 (11.5%) in the overall cohort. Patients with IWML had significantly lower RUDAS scores ($t= -2.66$, $p= 0.009$). The odds of having RUDAS <23 was 4.9 times higher in patients with IWML than those without. A significant interaction between genotype subgroup and the association was found. In the presence of IWML, the SC and $Sb^+$ subgroup had 5.2 times higher odds of low RUDAS score than SS and $Sb^0$ subgroup (Table).

**Image:**

**Table:** Distribution of suspected dementia in adults with sickle cell disease, according to the presence or absence of ischemic white matter lesions on routine screening MRI/A. Results are also presented according to phenotype strata.

| | N (%) | RUDAS | | Odds ratio [95% confidence interval], p-value |
|---|---|---|---|---|
| | | < 23 | 23 - 30 | |
| **All phenotypes** | **166** | | | |
| Presence of IWML | 92 (55.4) | 11 (12.0) | 81 (88.0) | OR=4.9 [1.0-22.8], p=0.04* |
| Absence of IWML | 74 (44.6) | 2 (2.7) | 72 (97.3) | |
| **SS and Sβ⁰** | **108** | | | OR=5.2 [1.1-24.6], p=0.04** |
| Presence of IWML | 64 (59.3) | 6 (9.4) | 58 (90.6) | |
| Absence of IWML | 44 (40.7) | 1 (0.9) | 43 (99.1) | |
| **SC and Sβ⁺** | **58** | | | |
| Presence of IWML | 28 (48.3) | 5 (17.9) | 23 (82.1) | |
| Absence of IWML | 30 (51.7) | 1 (3.3) | 29 (96.7) | |

*Fisher exact test
** Mantel-Haenszel test
Abbreviations: IWML= ischemic white matter lesion, MRI/A= magnetic resonance imaging and angiography, OR= odds ratio, RUDAS= Rowland Universal Dementia Assessment Scale

**Summary/Conclusion:** This is the largest study reporting on results from concurrent systematic cognitive screening and MRI/A surveillance in adults with SCD, with all major phenotypes represented. These data confirm the high prevalence of neurologic lesions in a contemporary cohort. The presence of IWML on screening MRI/A is associated with neurocognitive deficits. Independent radiological assessment is under way to grade the severity of the radiological lesions and correlate these findings with dementia. Multivariable analysis will be presented at the meeting. These findings highlight an area of unmet need in the management of neurocognitive morbidity in SCD.



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