DISPARITIES OF THE SEXES IN THE PREVALENCE AND CLINICAL CHARACTERISTICS OF MGUS; RESULTS FROM THE SCREENED POPULATION-BASED iSTOPMM STUDY

Topic: 13. Myeloma and other monoclonal gammopathies - Biology & translational research

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Background:

Multiple myeloma (MM) and its precursor monoclonal gammopathy of undetermined significance (MGUS) are consistently found to be more common in men than women. MM incidence is 1.5 times higher in men than women, and the male/female ratio in the prevalence of MGUS has been reported to range from 1.3 to 1.8. Though widely accepted as fact, the reasons for this are still unknown. The association of MGUS and exposure to sex hormones has not been investigated previously.

Aims:

The study aimed to describe differences in MGUS prevalence of the sexes in the Iceland Screens, Treats or Prevents Multiple Myeloma (iStopMM) study and to explore the effect of exogenous sex hormones on the risk of developing MGUS.

Methods:

All residents of Iceland over 40 years old were offered screening with serum protein electrophoresis (SPEP) and free light chain (FLC) assay in the iStopMM study. All individuals with abnormal screening results were included as cases (MGUS) and those with a negative screening as controls. Clinical characteristics in MGUS, M-protein isotype and concentration, immunoparesis and abnormal FLC ratio, were compared for the sexes. Information on previous treatment with oestrogen in women was acquired (ACT codes) from the Icelandic Prescription Medicines Registry. Logistic regression analysis was used to calculate the age-adjusted odds ratio (aOR) with corresponding 95% confidence intervals (95% CI). All analyses were adjusted for age and BMI in a sensitivity analysis.

Results:

The study included 3,554 individuals with MGUS and 71,049 controls. Males comprised 54% of all individuals with MGUS and 45% of controls. The median age at screening was 69 years (interquartile range (IQR) = 62-77) in the MGUS group and 61 years (IQR = 52-69) in the controls.

Males were 1.35 times more likely to be diagnosed with MGUS than females (aOR = 1.35, 95% CI: [1.26, 1.44]). OR was similar in all age groups. Males were statistically significantly less likely to have IgG MGUS (aOR = 0.85, 95% CI: [0.74, 0.97]) and more likely to have an abnormal FLC ratio (aOR = 1.35, 95% CI: [1.18, 1.56]) and had 11% higher M-protein concentration (g/L, exp(β) = 1.11, 95% CI: [1.03, 1.21] (Figure). Adjusting for BMI did not change the results, and there was no statistically significant interaction between sex and BMI in the risk of having MGUS (p=0.28). Lastly, 845 women (51.5%) in the MGUS group were prescribed oestrogen at some point before screening, and 17,464 women (44.5%) in the control group. Any exogenous oestrogen exposure was not associated with the risk of MGUS in women (aOR 0.93 95% CI: 0.82-1.05).
Exogenous oestrogen exposure for five years or longer before screening was borderline significantly protective for MGUS in women (aOR = 0.89, 95% CI: [0.78, 1.00]).

Summary/Conclusion:

In our unique study on the largest cohort screened for MGUS, we found that males were at a higher risk of having MGUS. Males were more likely to have clinical characteristics associated with more aggressive disease, such as higher m-protein concentration, an abnormal FLC ratio and non-IgG isotype. When investigating possible reasons for this disparity, we found that exogenous oestrogen exposure for five years or longer was possibly protective against MGUS among women. These findings provide clues on the biological underpinnings of observed sex-related disparities in plasma cell disorders. Future functional studies are needed to validate our findings; if confirmed, our observations may play a role in efforts geared toward prevention.

Figure: Forest plot with age-adjusted odds ratios (aOR) comparing males with MGUS to females with MGUS estimated from logistic regression models adjusting for age. *exp(β) coefficient estimated from a linear regression model.