Gender Differences in the Impact of Uric Acid on Features of Metabolic Syndrome and Subclinical Atherosclerosis

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Background and Purpose: The association between serum uric acid (SUA) and atherosclerotic cardiovascular disease has been widely reported, but its role as mechanistic factor or simple bystander has not been established. Furthermore, whether gender modulates this correlation is unclear. We thus aimed to investigate gender differences in the impact of SUA on components of the metabolic syndrome and markers of subclinical atherosclerosis.

Methods: We conducted a prospective cross-sectional study enrolling subjects with one or more traditional risk factor for atherosclerosis but no history of cardiovascular events, attending a dedicated Cardiometabolic Center of the Cardiology Unit at Modena University Hospital, for cardiovascular risk assessment. Patients were divided into 2 gender-specific groups (above versus below gender-specific median of SUA, 5.65 mg/dl in men and 4.55 mg/dl women). The Homeostatic Model Assessment formula (HOMA-IR) was used for the assessment of insulin resistance. Intima-media thickness (IMT) of the common carotid artery and brachial flow-mediated vasodilation (FMD) were measured by means of high-resolution vascular ultrasound. C-reactive protein (CRP) was measured as a marker of systemic inflammation.

Results: A total of 532 subjects were included (age 53.8±10.9 years), 51% women. Patients in the elevated SUA group had higher body mass index (BMI, p<0.001), waist circumference (p<0.001) and higher insulin resistance, irrespectively of gender (p=0.048). The number of metabolic syndrome features increased progressively with SUA levels, and this trend was stronger in females (p<0.001) than in males (p=0.004). SUA concentrations were also correlated with increased IMT in both men (p=0.023) and women (p=0.022). Impaired endothelium function was significantly associated with SUA in females (r=-0.18, p=0.011), but not in males (p>0.05). In addition, only in women SUA was correlated with increased levels of CRP (p=0.031).

Conclusions: Uric acid is associated with features of the metabolic syndrome, particularly with central obesity. However, this cardiovascular biomarker appears to have a significant gender-specific impact on atherosclerosis, with a more detrimental impact in women than in men.

Disclosures: No conflicts of interest or relationships with pharmaceutical companies, biomedical device manufacturers, or other corporations were involved in the work.