Postprint

Abstract - Urinary osteopontin predicts incident chronic kidney disease, while plasma osteopontin predicts cardiovascular death in elderly men

Background and objectives The matricellular protein osteopontin is involved in the pathogenesis of both kidney and cardiovascular disease. However, whether circulating and urinary osteopontin levels are associated with the risk of these diseases is less studied.

Design, setting, participants and measurements A community-based cohort of elderly (Uppsala Longitudinal Study of Adult Men [ULSAM; n=741; mean age: 77 years]) was used to study the associations between plasma and urinary osteopontin, incident chronic kidney disease, and the risk of cardiovascular death during a median of 8 years of follow-up.

Results There was no significant cross-sectional correlation between plasma and urinary osteopontin (Spearman rho=0.07, p=0.13). Higher urinary, but not plasma osteopontin, was associated with incident chronic kidney disease in multivariable models adjusted for age, cardiovascular risk factors, baseline glomerular filtration rate (GFR), urinary albumin/creatinine ratio, and inflammatory markers interleukin 6 and high sensitivity C-reactive protein (Odds ratio for 1-standard deviation (SD) of urinary osteopontin, 1.42, 95% CI (1.00-2.02), p=0.048). Conversely, plasma osteopontin, but not urinary osteopontin, was independently associated with cardiovascular death (multivariable hazard ratio per SD increase, 1.35, 95% CI (1.14-1.58), p<0.001, and 1.00, 95% CI (0.79-1.26), p=0.99, respectively). The addition of plasma osteopontin to a model with established cardiovascular risk factors significantly increased the C-statistics for the prediction of cardiovascular death (p<0.002).

Conclusions Higher urinary osteopontin specifically predicts incident chronic kidney disease while plasma osteopontin specifically predicts cardiovascular death. Our data put forward osteopontin as an important factor in the detrimental interplay between the kidney and the cardiovascular system. The clinical implications, and why plasma and urinary osteopontin mirror different pathologies, remains to be established.