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Use of Proteomics To Investigate Kidney Function Decline over 5 Years

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Abstract

Background and objectives Using a discovery/replication approach, we investigated associations between a multiplex panel of 80 circulating proteins associated with cardiovascular pathology or inflammation, and eGFR decline per year and CKD incidence.

Design, setting, participants, & measurements We used two cohorts, the Prospective Investigation of the Vasculature in Uppsala Seniors Study (PIVUS; *n*=687, mean age of 70 years, 51% women) and the Uppsala Longitudinal Study of Adult Men (ULSAM; *n*=360 men, mean age of 78 years), with 5-year follow-up data on eGFR. There were 231 and 206 incident cases of CKD during follow-up in the PIVUS and ULSAM studies, respectively. Proteomic profiling of 80 proteins was assessed by a multiplex assay (proximity extension assay). The assay uses two antibodies for each protein and a PCR step to achieve a high-specific binding and the possibility to measure multiple proteins in parallel, but gives no absolute concentrations.

Results In the discovery cohort from the PIVUS Study, 28 plasma proteins were significantly associated with eGFR decline per year, taking into account the multiple testing. Twenty of these proteins were significantly associated with eGFR decline per year in the replication cohort from the ULSAM Study after adjustment for age, sex, cardiovascular risk factors, medications, and urinary albumin-to-creatinine ratio (in order of significance: TNF-related apoptosis-inducing ligand receptor 2*, CD40L receptor, TNF receptor 1*, placenta growth factor*, thrombomodulin*, urokinase plasminogen activator surface receptor*, growth/differentiation factor 15*, macrophage colony-stimulating factor 1, fatty acid-binding protein*, cathepsin D, resistin, kallikrein 11*, C-C motif chemokine 3, proteinase-activated receptor 1*, cathepsin L, chitinase 3-like protein 1, TNF receptor 2*, fibroblast growth factor 23*, monocyte chemotactic protein 1, and kallikrein 6). Moreover, 11 of the proteins predicted CKD incidence (marked with * above). No protein consistently predicted eGFR decline per year independently of baseline eGFR in both cohorts.

Conclusions Several circulating proteins involved in phosphate homeostasis, inflammation, apoptosis, extracellular matrix remodeling, angiogenesis, and endothelial dysfunction were associated with worsening kidney function. Multiplex proteomics appears to be a promising way of discovering novel aspects of kidney disease pathology.

Adult | Aged | Albumins | apoptosis | Cardiovascular Diseases | creatinine | extracellular matrix | Fatty Acid-Binding Proteins | Fibroblast Growth Factors | Follow-Up Studies | glomerular filtration rate | Homeostasis | Longitudinal Studies | Phosphates | Plasminogen | Prospective Studies | Proteomics | risk factors | Urokinase-Type Plasminogen Activator

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