Reviewer's report

Title: Uromodulin Concentrations are not Associated with Incident CKD Among Persons with Coronary Artery Disease

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Reviewer: Karl Lhotta

Reviewer's report:

The manuscript deals with an important question, namely if uromodulin genotypes and urine levels are associated with incident and progressive CKD. The authors confirm previous results of genotype distribution and association with uromodulin excretion. In contrast to a previous study they did not find an association of high urinary uromodulin excretion with incidence and progression of CKD. Substudies 1 and 2 of the manuscript are well performed and described. I do, however, have some concerns about study 3, especially selection of cases.

Major Compulsory revisions

1. One major point of concern is the selection of incident CKD cases based on CrCl measurements. According to Table 3 cases lost on average 40 ml/min of CrCl within 5 years. This is quite unusual for individuals starting with a normal CrCl and without albuminuria. The cases seemed to have a rather aggressive form of renal disease. What were the clinical diagnoses in these cases? In addition, a reduction of CrCl of almost 50% would cause a doubling of serum creatinine. Was this really observed in the cases? I would feel much more confident if the case selection had been based on eGFR calculated from serum creatinine (for example with the CKD-EPI formula) or from cystatin C levels. Although the efforts of the authors to get accurate 24 hour urine collections are acknowledged, this method seems much more vulnerable to collection errors.

2. There are many factors causing CKD progression. Some of these factors such as BMI or diabetes were included in the calculations. Some other important factors should be available in the study. I suggest to include the following in study 3: blood pressure at baseline; smoking status; blockers of the renin angiotensin aldosterone system; statins. A difference in these factors between cases and controls could also explain disease progression

Discretionary revision

One interesting question that could be answered by the data of the study is whether the proportion of progressors differed between the G/G, G/T and T/T groups. I acknowledge that the statistical power may be limited by the small number of T/T patients.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests