Reviewer's report

**Title:** Association of Cystatin C and Creatinine with Inflammatory and Procoagulant Markers in a Diverse Cohort: A Cross-Sectional Analysis from the Multi-Ethnic Study of Atherosclerosis (MESA)

**Version:** 1  **Date:** 25 March 2008

**Reviewer:** Anders Larsson

**Reviewer's report:**

Regarding the manuscript by Keller et al. Association of cystatin C and creatinine with inflammatory and procoagulant markers in a diverse cohort: a cross-sectional analysis from the multi-ethnic study of atherosclerosis (MESA).

A well-written and clear manuscript on an important issue. I only have minor comments to the manuscript.

The questions posed by the authors are well defined.
The methods are appropriate and well described.
The data are sound.
The discussion and conclusions are well balanced and adequately supported by the data.
Limitations of the work are clearly stated.
The citations are appropriate
Title and abstract are appropriate
The writing is acceptable.

I only have some minor revisions that the author can be trusted to correct:

In the Methods section
Page 6: CVs are provided for cystatin C. CV should also be provided for creatinine or even more appropriate for MDRD estimated GFR. The CV for estimated GFR is higher than for creatinine concentration due to the non-linear relationship between creatinine and eGFR.

Friedewalds equation can only be used if the TG values are below a certain level. If there was a substantial number of high TG values that made it impossible to calculate LDL this should be commented.

Chronic kidney disease was defined as eGFR < 60…. The authors should add that this was MDRD eGFR as there are also cystatin C eGFR.

The authors should provide the detection levels for CRP IL-6 and TNFR1 as high sensitivity assays were used.
Page 7, end of second paragraph: divided by height (m2). This could be misinterpreted (?) as m2 usually describes an area. height (m)2. ?

One interesting aspect of this study is that it includes several ethnic groups. There was a difference in cystatin C levels in the different ethnic populations but this could be due to differences in age or sex (?). If the authors adjust for age and sex, is there still an ethnic difference for cystatin c and creatinine.

General comment to the authors that they do not have to respond to:
I have a personal impression that the results obtained with the Dade Cystatin C assay may have changed slightly over time (possibly 10-15% variation over the last 3 or 4 years even if I can not verify it). The samples in this study have been frozen at –70 and probably been analyzed over a short period of time, possibly with a single reagent lot (?) so this should not be a problem in this study. A shift over time may hide interesting associations. We thus normally run ten patient sample pools before and after each batch shift to verify that there is no drift in our cystatin C assay. It could be worth considering if you use more than one reagent lot in future studies.

I find the strong association between TNFR1 and cystatin C very interesting. The impact of kidney function on TNFR1 in the discussion seems very plausible. This could also fit with observations that TNFR1 is more strongly associated with CVD mortality than e.g. CRP or IL6.

**What next?:** Accept after minor essential revisions

**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.