Reviewer's report

**Title:** Estimation of Glomerular Filtration Rate from Serum Creatinine and Cystatin C in Octogenarians and Nonagenarians

**Version:** 1  **Date:** 1 August 2013

**Reviewer:** Jonas Bjork

**Reviewer's report:**

This is a well-written report on an important subject, estimation of GFR among elderly. I have the following comments and suggestions:

**Major Compulsory Revisions**

1. It is unclear whether the used cystatin C assay was calibrated to the recent IFCC standardization. The underestimation of the cystatin C-alone equation CKD-EPI Cystatin C, which was developed based on standardized cystatin C, in the present cohort could indicate that this was not the case. Using cystatin C has less relevance and results low generalizability unless a standardized assay is used.

2. Given the uncertainty about the cystatin C standardization, it is hard to assess the benefit of combining creatinine with cystatin C from this study. The analysis least affected by differences in standardization is probably the area under the ROC curve, something which is worth stressing. However, the author put too much emphasis on the improved classification (which does not reach statistical significance even focus is shifted to AUC) in the conclusion, given the statistical uncertainty that is present in a small study like this.

3. The authors conclude in the abstract that both CKD-EPI creatinine and BIS creatinine are satisfactory alternatives if cystatin C is not available. However, CKD-EPI creatinine has P30-accuracy (64%) that is below 75% when mGFR<60. By contrast, BIS creatinine has a more stable performance with respect to P30 in the two investigated GFR-groups (mGFR<60 and mGFR>=60). Thus, the study rather provides some evidence that BIS creatinine is superior to CKD-EPI creatinine at decreased mGFR-levels, mainly due to increased precision.

4. On the other hand, it should also be noted that BIS creatinine yields substantial underestimation in the present study in patients with mGFR>=60. Possible reasons for this should be discussed in more detail. Are there residual differences in creatinine standardization (which would be more influential at high mGFR-levels, i.e. low creatinine levels)? Differences in ethnicity?

5. There is a recent validation study of BIS creatinine in comparison with MDRD and CKD-EPI from France that ought to be cited (J Nephrol 2013;26:716-723). There are also studies from Sweden suggesting that MDRD and, to a lesser extent, CKD-EPI overestimate GFR with decreased accuracy as a result.
By contrast, another French study recently reported no such overestimation for MDRD and CKD-EPI among elderly (Am J Kidney Dis. 2012;60(5):847-849).

Among cited work, I do not quite agree with the authors regarding the results of Murata et al. (cited on page 11). Among patients older than 70 years with CKD, the overestimation was only 5% for CKD-EPI and 9% for MDRD.

6. No data on the non-participants (i.e. persons enrolled in the study that did not undergo the renal function study) are presented. In what respects did the participants and non-participants of the renal function study differ?

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.