Reviewer's report

Title: Biomarker Enhanced Risk Prediction for Development of AKI after Cardiac Surgery

Version: 0 Date: 30 Dec 2017

Reviewer: Rakesh Malhotra

Reviewer's report:

1) It is unclear to me how the authors adjudicated incident AKI. It needs further explanation in the manuscript text. Was baseline sCR used and present in all subjects? Were baseline creatinine values imputed for missing values? If so how and what proportion had them? What reference sCr we use is critical to define AKI. Please consider what possible impact or sources of bias this could introduce.

2) The AKI outcome used in this analysis also raises some issues. Although the authors use the serum creatinine criteria (not standard KDIEGO/AKIN criteria), they failed to use the urine criteria. This is a commonplace in retrospective studies, but it should not be in a prospective study like this one. Please acknowledge this limitation in the discussion, and the impact of it on the performance of the Biomarkers is not considered.

3) I would like authors to provide some information about what to do with Biomarker information other than AKI prediction/detection? Does it change management? What is the next path forward? May be these studies will help inform to guide the development of future therapies. We need to ask these questions.

4) There is discrepancy in the number of reported AKI events. In method section Page 5 line 28 authors reported 15 AKI events and in Results number is 16. Please correct.

5) How was serum creatinine measured? Which assay was used? Please comment in the manuscript.

6) Please provide rationale for using 9 subjects for proteomic analysis instead of all 16 subjects who developed AKI. Why not 16 AKI and 16 control?

7) One of the limitations of database is small numbers (type 2 error?), no validation cohort and lack of racial diversity. Please acknowledged in limitation section.
8) I would also encourage authors to provide details of AKI staging for incident AKI in the results section/Table 1.

9) What was the median time to incident AKI in 16 patients? It will be interesting approach to look at the longitudinal changes in biomarkers prior to AKI event and not rely on one-time measurement. Could the authors show the prospective temporality of the biomarkers and its variation over time prior to AKI?

10) One can remove column of P-value as it does not add much to the table 1 content. It is only a suggestion.

11) As in all studies, issue of residual confounding (unmeasured or unknown confounders) play a role and thus may influence relationship between biomarkers and AKI.

12) Please do comment on limitations of using NRI and IDI in the manuscript.

13) Please comment on biomarker assay precision? Coefficient of variations?

14) I appreciate if further efforts are made to improve this manuscript grammatically correct. Please do spell check.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.
Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.
Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
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Acceptable

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