Reviewer’s report

Title: Presence of Early CKD-Related Metabolic Complications Predict Progression of Stage 3 CKD: a Case-Controlled Study

Version: 2 Date: 11 August 2014

Reviewer: Carlos Poli de Figueiredo

Reviewer’s report:

Thank you very much for the opportunity of revising the manuscript entitled “Presence of Early CKD-Related Metabolic Complications Predict Progression of Stage 3 CKD: a Case-Controlled Study” by Herbert Chase et al.

The study presents a relevant subject in a well written paper, and contribute to the understanding of CKD progression. The model proposed was robust enough to reasonably discriminate groups of progressors and non-progressors.

1. Is the question posed by the authors well defined?
   The authors hypothesized that the risk of progression to CKD stage 4 is related to the degree of parenchymal damage present at the time of entry to stage 3, reflected in the presence (or absence) of metabolic complications of CKD (anemia, worsening acidosis and mineral abnormalities).

   This hypothesis demands the evaluation of kidney parenchymal damage, but the purpose of the study was to determine if the presence of metabolic complications were predictive of CKD progression.

   I believe the dissociation between hypothesis and aim is a major limitation that should be clarified.

2. Are the methods appropriate and well described?
   The authors used an electronic database to collect routine metabolic data from 481 stage 3 CKD patients, divided into progressors and non-progressors to stage 4 CKD. The mean age was high in both groups.

   Estimated GFR was not included in the predictive model, and one wonders if the inclusion of eGFR in the predictive model would have any influence on the results.

   Methods are appropriate and well described.

3. Are the data sound?
   Data is comprehensive, but in Table 1 (or in the text) I suggest that the CKD etiology should be reported.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data?

6. Are limitations of the work clearly stated?
Limitations are well described before conclusion.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes

8. Do the title and abstract accurately convey what has been found?
Yes, but I question (both in the abstract and in the main body of the text) the hypothesis mentioning the degree of parenchymal damage. Parenchymal damage has not been evaluated and no data has been provided to provide evidence that parenchymal damage can be assessed using metabolic data as surrogate marker.

9. Is the writing acceptable?
Yes

- **Major Compulsory Revisions**

  This hypothesis demands the evaluation of kidney parenchymal damage, but the purpose of the study was to determine if the presence of metabolic complications were predictive of CKD progression.

  I believe the dissociation between hypothesis and aim is a major limitation that should be clarified.

- **Minor Essential Revisions**

  Data is comprehensive, but in Table 1 (or in the text) I suggest that the CKD etiology should be reported.

- **Discretionary Revisions**

  Estimated GFR was not included in the predictive model, and one wonders if the inclusion of eGFR in the predictive model would have any influence on the results.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

I declare that I have no competing interests