Reviewer’s report

Title: Large kidneys predict poor renal outcome in subjects with diabetes and chronic kidney disease

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Reviewer: Scott Thomson

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The question answered by this study is well-defined by the authors. It is generally accepted that those kidneys that become large during the early stages of diabetes are more likely to develop diabetic kidney disease 10-20 years later and to fail some years after that. The present study reveals that the same prognostic significance applies to kidneys that are found to be large after 17 years of diabetes. The present finding could not have been predicted with intuition alone, since CKD generally makes kidneys smaller and a more damaged (to wit smaller) kidney has already revealed itself to be vulnerable to disease. Hence, one might imagine that, at the 17-year time point, small kidneys would include those that were formerly large, but have shrunk on their way to failing, while those that remain large represent a subset of the originally large kidneys that are somehow resistant to injury.

The methods are also adequately described. The data appear sound in most respects and support the main conclusion with certain caveats:

Major "compulsory" revisions

Under Results, the baseline characteristics are described as continuous variables, but everything becomes categorical when the outcomes are reported. It would be instructive to see continuous data presented as such for outcomes as well. For example, scatter plots showing rate of change in GFR vs initial kidney size, rate of change in GFR as function of AER, etc. Key associations may be revealed to the human eye from scatter plots that are concealed by treating all the outcomes as categorical variables. Categories can still be shown by drawing vertical and horizontal lines on a scatter plot and are still shown in the tables. For example, see figure 1 in Ref 33.

The authors previously found that AER strongly predicts progression to ESRD in a similar (possibly the same?) population of diabetics with CKD (ref 35). It is presently reported that kidney size predicts progression to ESRD and that AER and kidney size are uncorrelated. But if kidney size and AER are both greater among those that progress, then kidney size and AER should be correlated, by virtue of their mutual connection to cases that progress. So there is a burden here for the authors to reconcile their conclusions in ref 35 about the role of AER with the present conclusions about kidney size if AER and kidney size are uncorrelated. I’m not arguing that this is impossible to explain, only that some cogent explanation is warranted.
In the prior study (ref 35), as in most similar studies, a distinction was made between micro- and macroalbuminuria. Why was this not done here? There is a case to be made that the distinction between macro- and microalbuminuria is more germane to the progression (as opposed to the existence) of diabetic CKD, than is the distinction between microalbuminuria and no albuminuria.

The authors point out that proteinuria is no longer an obligatory predictor of CKD in diabetes. The inference is that large kidney size can be used to predict ESRD in diabetics without proteinuria. Here, the authors don't overtly mis-represent the literature, but they facilitate mis-interpretation by the reader. The literature cited to validate the existence of nonproteinuric CKD in diabetes does not actually suggest that this type of kidney disease is likely to progress to ESRD.

Minor essential revisions
p6: change 'the correlations with age..." to "the correlations of kidney size with age..."

p9: change pronostic to prognostic.

p9: change "patients with CKD require an ultrasound..." to "patients with CKD are likely to undergo ultrasound..."

P9: "...hypertrophy (17,27-29), but it has yet to be reported in advanced stages of diabetic renal disease..." Awkward wording makes it ambiguous what "it" refers to.

If this is the same population studied in Ref 35, this should be stated.

Discretionary revisions
The point is made that there is value to measuring kidney size in CKD clinic. This should be reinforced by presenting the positive and negative predictive values of kidney size. The large overlap of the kidney size distributions of progressors vs non-progressors (116±19 vs 107±12 mm (mean±SD)) suggests there might not be much power here.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**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.