Reviewer's report

Title: Diastolic function is a strong predictor of mortality in patients with chronic kidney disease

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Reviewer: Joseph Eustace

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Farshid and colleagues contribute to the extensive literature regarding the association of cardiac dysfunction with decreased survival in CKD with a single centre prospective descriptive study of 153 patients with CKD stage 4-5, with a comprehensive mean follow-up 2.6 years. Their report confirms earlier observations reported in large studies and is succinct and well written.

Minor essential suggested revisions:

Methods.
1. Despite the explanation in the text, I remain unclear as to how subjects were recruited, as stated ‘consecutive patients were recruited’. What does this mean for dialysis subjects? Were they incident (in which case why weren’t they enrolled into the study prior to dialysis at the CKD 4 stage) or prevalent –in which case what is meaning of ‘consecutive’. I would provide enrolment details of the CKD and dialysis patients separately.
2. Echocardiography: Line 5. Presumably should be ‘For patients on dialysis all studies were performed with patient at their dry weight within 24 hours after dialysis’ rather than “24 hours of dialysis”.

Statistical Methods:
3. Please confirm that a 2 sided type one error rate of 0.05 was used.
4. How were the variables used in the multivariate regression model selected. It surprises me that the model shown in table 3 is not adjusted for diabetes, as a major potential confounder. It would also be potentially of interest to see an adjustment for ACEI/ARB use though the interpretation may be difficult as a result of reverse causation.

Results
5. How many subjects declined to take part or were excluded on grounds of poor prognosis. It would also be interesting to the authors to provide some details of the setting in which the study took place, i.e. size of outpatient population, whether academic hospital based or private practise, size of the dialysis clinic.

Discussion
6. The differences between observed event rates and those in SHARP and TREAT as discussed are quite likely the result of sampling variability, especially given the far smaller size of the current study.
Limitations.

7. ‘As in all observational studies, no conclusions can be drawn regarding causality, even though the associations between diastolic function, serum troponin and mortality were strong and independent.’ I would suggest leaving out the latter part of the above sentence or alternatively state that it was ‘independent of the 6 variables adjusted for in the multivariate model’. Given the limited nature of the multivariate model -especially in absence of adjusting for diabetes- there is a substantial potential for residual confounding; and regardless of the quality of the multivariate model this still cannot address causality.

Conclusions.

8. The conclusions overstate the evidence provided by the study. The data provided certainly supports the hypothesis that the evaluation of diastolic function and TnT measurement may potentially be useful screening method for vascular disease but clearly provides no evidence regarding either the net clinical benefit or cost effectiveness of using these tests in a formal screening program.

Discretionary revisions:

Abstract:

9. It is difficult to follow the embedded percentages (i.e. 78% of 38% of 153 were on hemodialysis), providing both the actual number and associated percentages may be clearer.

Results

10. A model examining the associations with MACE in addition to the reported model shown in Table 3 would be of interest and given the greater number of event would be more powerful.

11. It may be of interest to examine for a test for trend between Grade 0 vs. Grade 1 vs. Grade 2-4 diastolic dysfunction in its association with death or MACE.

12. Do the authors have any data of the number of initial CKD 4 subjects that progressed to dialysis during study and what was the median decrease in eGFR at last follow up with independent renal function. What proportion of the CKD patients had stable renal function vs. progressive disease.

13. Table 2 given the mean eGFR in column 1 is 22 with a sd of 7 ml/min, I think the heading for first column as ‘pre-dialysis’ is misleading, ‘non dialysis’ may be a preferable alternative.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

'I declare that I have no competing interests' below