Author's response to reviews

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

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Author's response to reviews: see over
Dear Editor,

We thank both reviewers for their time in carefully reviewing our paper and for the helpful comments for improving our manuscript. We have responded to the comments below and have made highlighted changes to the text of the manuscript as suggested. Reviewer 2 did not suggest any changes.

Response to Comments of Reviewer 1:

1. With regards to patient recruitment, consecutive patients attending the Renal Outpatient Clinic were screened and recruited, including dialysis patients. Dialysis patients recruited into the trial were already on dialysis. This issue has been clarified in the Methods section.

2. The sentence has been changed as suggested “with patients at their dry weight within 24 hours after dialysis”.

3. We confirm that a 2 sided statistical significance level was used.

4. With regards to the multivariate model, age, sex, all major vascular risk factors including diabetes, history of MI, echo parameters and troponin level were entered into the model. The legend for Table 4 states that diabetes was entered in the model. Diabetes was not an independent predictor of mortality with the other variables entered. There was no significant change to the model after forcing diabetes into the model. We have clarified in the statistics section that all risk factors were adjusted for in the model.

With regards to use of ACEI/ARB, there was a non-significant trend towards lower mortality and adverse events in patients who were on these drugs. We felt that no conclusions could be drawn from these finding.

5. The setting of the study was the Renal Outpatient Clinic of a Public tertiary referral hospital with approximately 400 outpatients with GFR <30ml/min and 200 dialysis patients. This has been added to the manuscript. As this was intended as a long term study of CKD patients, we did not recruit patients with advanced malignancy who were not expected to survive more than 6 months. We do not know the number of patients in the clinic who were not invited to take part on the grounds of poor prognosis, as we did not keep a register of all potential subjects, but this number would be very small.

6. We agree that the differences between our mortality rate and those in SHARP and TREAT trials are likely due to sampling variation, but as we have mentioned our cohort was older and had more patients on dialysis and these factors may have also affected the mortality risk.

7. We have changed the text as suggested to “the associations between diastolic function, serum troponin and mortality were strong and independent of age, sex, and other factors adjusted for in the multivariate model.”
8. We agree that we have not shown any evidence for net clinical benefit or cost effectiveness of screening for diastolic dysfunction or troponin T measurement. We have changed the text to state that we suggest (rather than recommend) such evaluation for CKD patients. We have already stated that assessing any benefit in clinical outcome with this approach merits further study.

9. The number as well as percentage of patients has been shown in the abstract: Of 153 patients enrolled, 57 (37%) were on dialysis and 45 (78%) of these patients were on haemodialysis.

10. We did perform an analysis with MACE as the endpoint using Cox proportional hazards and the results were similar but not as significant as the model for mortality. We therefore decided to report the multivariate model for mortality.

11. We performed an analysis for a trend in mortality in 3 groups with diastolic function grade 0 vs 1 vs 2-4 as suggested. The p value for the trend between grade 0 vs 1 was 0.2 and the p value for grade 1 vs 2-4 was 0.03. Therefore we felt justified to use the 2 groups that we chose for analysis, namely grade 0-1 vs grade >1.

12. During the course of the PREDICT Study 24 patients progressed to maintenance dialysis. We did not analyse deterioration in renal function and progression to dialysis as this was not an endpoint in this study which focused on mortality and cardiovascular adverse events.

13. Heading for the first column of Table 2 has been changed to non-dialysis as suggested. We have also changed “pre-dialysis” to “non-dialysis” throughout the manuscript.

We thank the editors for their helpful comments and we feel that the suggested changes have enhanced the paper. We hereby resubmit the manuscript for consideration of publication.

Ahmad Farshid
On behalf of the Authors