Author's response to reviews

Title: Atrial Fibrillation in Chronic Dialysis Patients in the United States: Risk Factors for Hospitalization and Mortality.

Authors:

Kevin C Abbott (kevin.abbott@na.amedd.army.mil)
Fernando C Trespalacios (fernando.trespalacios@amedd.army.mil)
Dr Allen J Taylor (allen.taylor@na.amedd.army.mil)
Lawrence Y Agodoa (agodal@extra.niddk.nih.gov)

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Response to reviewers:

We appreciate the comments of the editors and reviewers, which were quite helpful. Our itemized response appears below:

Reviewer #1 (Dr. Zoccali)

1. We have described the DMMS 2 in somewhat more detail as requested. As shown, direct statistical comparison with the general population, such as with the National Hospital Discharge survey, would not be appropriate since the study is a weighted sample designed primarily to allow comparison between dialysis modalities. We hope that point is clarified.

2. Re propensity scores: this is often undertaken to assure comparability amongst strata. We agree that the observational nature of our study precludes conclusions re causation, particularly for medication use. Propensity scores are really a hybrid between matching and adjustment, and are in fact entered as covariates in multivariate analysis. They are usually calculated in logistic regression as the baseline factors independently associated with a treatment variable. Assessment of outcomes is then undertaken adjusted for this variable. This is essentially what is given in the last paragraph of page 12, "Because use of coumadin..." in which we perform this logistic regression analysis. We take a bit of pride in the thoroughness of this approach. For example, in the recent articles using this same database on the associations between HMG-CoA reductase inhibitors/Calcium channel blockers and survival (Kidney Int. 2002 Jan;61(1):297-304. and Kidney Int. 2002 Jun;61(6):2157-64.), no similar analysis was performed. Actually, I did the calculations myself and found the factor with the strongest association with use of HMG-CoA reductase inhibitors was renal transplantation (adjusted odds ratio 1.62, p≤. We originally referred to Dr. Herzog’s work in abstract form, although at the time our manuscript was submitted it had not yet been published in JASN. I did have a chance to talk with Dr. Herzog during a poster presentation. Dr. Herzog’s work looked at factors associated with mortality after atrial fibrillation but could not assess medication use. In addition, Dr. Herzog used atrial fibrillation as all-listed diagnoses, not just as a primary diagnosis. The raw survival scores were worse than we report, although the DMMS 2 population is weighted toward PD patients, who generally have somewhat better survival early in dialysis, which would be disproportionately important given the short followup of our study. However, since we don't have all the details of Dr. Herzog’s study, it would be premature to elaborate further.

Reviewer #2 (Dr. Fabbian)
1. We agree that digoxin use could be related to preexisting AFIB and so comment in the discussion.
2. We have added additional information from Vazquez’ paper in the first paragraph of the discussion re the rate of thromboembolic events after AFIB.
3. We have mentioned the univariate associations between cardiovascular comorbidities and AFIB in the discussion.
4. We have defined AFIB in the legend to Table 1, as well as shortened it. I did keep some of the demographic factors even where they were not significant, as well as the medications, since not all of these are described in other studies of DMMS 2.
5. We have resequenced the Tables and modified the references to them in the text.
6. We have corrected the errors mentioned in point #1 (relationship between LVH, "onorhematic")

Reviewer #3 (Dr. Korzets)

1. We agree that the observational nature of the study precludes assessment of causation. We hope that our findings finally spur prospective studies in this area.
2. We have added the risk factors of valvular calcification and hypokalemia as limitations in the discussion section.
3. We have changed the phrasing for "LV enlargement", "not uncommon" to "common,"
4. Table 2: We have added in the legend that N(%) refers to the N and percent of patients with that risk factor who were hospitalized for AFIB.
5. 20 patients with LVH were hospitalized for AFIB (of 123 total), which is correct.
6. We have resequenced the tables and references to them in the text, as above (point #5, reviewer #2).
7. We have added p values from Log Rank testing to Table #4
8. We have removed "chronic renal failure" from p 9, final paragraph
9. We have rephrased the sentence using the phrase "only the use of coumadin (now Fig 2)" to indicate a favorable association with survival.
10. analysis of cardioselective beta blockers was deleted.
11. We agree that embolic causes of death may be underestimated and have added this to the first paragraph of the discussion.
12. "might be much" changed to "is"
13. Changed Harnett to Foley
14. Changed phrasing of "Also hosp congestive heart failure...."
15. We have emphasized the findings of Wiesholzer as indicated.
16. The comparison group for blood pressure in multivariate analysis was 17. We have eliminated two of the figures. However, because of the confounded "U" shaped relationship between blood pressure and AFIB indicated by point #16 above, we would like to retain figure 1.

We would again like to thank the editors and reviewers for their thoughtful comments, time, and effort.