Author's response to reviews

Title: Polycystic Kidney Disease in Patients on the Renal Transplant Waiting List: Trends in Hematocrit and Survival

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Response to reviewers

Dear Editor:

We appreciate the thorough comments of all reviewers. We will respond by item. However, in response to reviewer #1's comment of the "salami effect," I hope it was clear from the introduction of our manuscript that we were responding directly to a concern raised by Dr. Fourtounas (Reference 2, now specified as a letter) re potential problems with the validity of previous analyses, and as such represented concerns that might be shared by a large number of nephrologists. Our response was in fact quite swift, if I may say so. Further, it would not have been possible to include all results and appropriate discussion in the typical 3000 words required by most journals; this is one key advantage of Biomed Central, in fact. In the future, we will certainly attempt to combine more information in the forum provided by Biomed Central.

Reviewer #1 (Dr. Locatelli):

1. We have used only hematocrit instead of both hemoglobin and hematocrit in analysis, consistent with most previously published studies. We certainly agree that lack of ability to follow hematocrit over time is a substantial limitation, and have added this to the discussion. However, this limitation is shared by all papers using USRDS data.
2. We have consolidated references #4 and 13.
3. We agree that residual confounding may persist beyond the ability of statistical adjustment to correct.
4. Limitations of the CMS Form 2728 in pre-dialysis EPO use have so far been reported only in abstract form. We show in Table 1, however, that there was no independent difference in pre-dialysis EPO use between patients with PKD and other causes of ESRD.
5. We agree that we were unable to correct for medication use. Since PKD accounted for 7% of patients on the waiting list, use of the USRDS special studies resulted in insufficient sample size for analysis.
6. We now give univariate and multivariate analysis of the odds ratios for transplantation for PKD in Table 1.

Reviewer #2 (Dr. Mehrotra):

1. The type of study design (historical cohort study) is explicitly stated in the abstract, in contrast to many published studies today. We have specified in the abstract and in discussion that the hematocrit levels were only available at the time of presentation to ESRD.
2. CMS 2728 tracks pre-dialysis EPO use, while DMMS 2 tracked the use of EPO 60 days after the start
of dialysis. It would be expected these numbers would be quite different. An alleged disparity between pre-dialysis EPO reported in form 2728 and Medicare claims has so far been published only in abstract form, not in peer-reviewed form. Further, Form 2728 has been considered reliable enough for other studies that have passed peer review, "Obrador GT, Roberts T, St Peter WL, Frazier E, Pereira BJ, Collins AJ. Trends in anemia at initiation of dialysis in the United States. Kidney Int. 2001 Nov;60(5):1875-84."

3. We have consolidated references 4 and 13 as above.
4. We have corrected the issue of the 90 day waiver.
5. Hematocrit levels increased significantly every year of the study in patients with PKD and with other causes of ESRD. Because of the confusion over the figures, these have been deleted. The median and standard deviations are given as text in the results section.
6. Table 3 has been eliminated.
7. The discussion for figures has been simplified. Figure 4, in retrospect, was superfluous and has been deleted.
8. We have changed "chronic kidney disease" to end stage renal disease.
9. In summary, we have tried to keep the terminology more consistent.

Reviewer #3 (Dr. Splendiani):

1. We have explicitly included renal transplantation as a covariate in both logistic regression and Cox Regression. The survival advantage of PKD persisted despite this, although the possibility of residual confounding is acknowledged as above.

We hope we have adequately addressed the concerns of the reviewers.

Sincerely,

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