Author's response to reviews

Title: Risk Of Intracranial Hemorrhage Associated With Autosomal Dominant Polycystic Kidney Disease In Patients With End Stage Renal Disease

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Response to Reviewers:

We appreciate the comments of the reviewers and attach our responses:

Reviewer (Dr. Irazabal)

We appreciate the general comments.

We have added the hypothesis to the abstract.

We have expanded the introduction (we hope not too much!) and include citations on the pathogenesis of the polycystin genes on vascular aneurysm formation.

Rather than a list of exclusions, we expand the list of inclusionary criteria. We appreciate the opportunity to add greater clarity on our use of the prior history of stroke, as documented by the USRDS, both excluding it and accounting for it in adjusted analysis, which we think provides additional information.

We have spelled out NOS and replaced AF with AA, and spelled out BMI, as well as indicated our non-parametric tests (Kruskal-Wallis).

P value added for page 8.

We have revised the discussion as requested. We have elaborated on the difficulty of screening for ICA in this population, both due to the low incidence despite increased relative risk, and the fact that the majority of aneurysms do not rupture. Since we do not have family history as part of the data, we are unable to conclude how much that would improve the utility of screening in this population.
Reviewer (Dr Dahl).

We appreciate the general comments.

We have revised the introduction to account for family history in the upper end of prevalence for ADPKD. We have expanded discussion of the natural history.

We reemphasize that ICH is still rare and add the number of patients with ADPKD who would need to be observed for one additional case of ICH (51.5), which may make the point better.

We have added discussion on the time to development of ICH. This is likely related to the older study population in whom patients who suffered adverse consequences of earlier ICH are not included.

We expand comments on the significance of the lower ICH incidence in the transplant patients.

We have reworded the discussion on the possible prevalence of PKD2 vs. PKD1.

We indicate that lack of family history is a key limitation.

We have reworded the discussion to indicate that we are looking at a lower risk population due to the older nature and exclusion criteria of the study.

We have revised the figure legends and changed AF to AA.