Reviewer’s report

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

Version: 2 Date: 17 December 2013

Reviewer: Neera Dahl

Reviewer’s report:

The paper contributes to our understanding of ICH in ADPKD, and should be published.

Most of my comments below are regarding the abbreviated discussion of the natural history of ICH in ADPKD, the need to emphasize the importance of family history, and the need to include in the discussion that this is a study done in a low risk population (who did not develop ICA prior to the age of 65).

The study is well designed and the data are nicely presented.

Major Revisions:

In the introduction on page 3, the authors state that the prevalence of aneurysm is 4% to 41%. The value of 41% seems high. The numbers should be put in the context of family history as prevalence is clearly higher with a family history. The introduction section for ICAs in ADPKD needs to be better documented, with more discussion of the natural history.

Conclusions: the authors should point out that even in ADPKD, the development of ICH remains a rare event (affecting <2% of the older ESRD population captured in this study). This is important as it clearly has implications for screening (or rescreening) prior to transplant.

Figure 1 suggests that time with ESRD is important in the development of ICH. The 2 curves do not separate until about year 3. This needs to be better discussed in the text and conclusions.

The authors discuss screening in the conclusions. In this context they could discuss the data that shows that patients with a previous transplant are at lower risk for ICH. This previously transplanted group is the most likely to have previously screened for ICA, which may explain the finding.

Under limitations: pg 12, the authors speculate that they have enriched for a PKD2 population. I don’t think this is correct. For patients with ESRD at age 65, a PKD1 mutation still remains most likely (given that about 80% mutations are PKD1, and that the age of onset of ESRD in PKD2 is later—early 70s). The last sentence of the limitations paragraph—As such.................once they have started dialysis should be removed unless it can be more fully referenced.
Page 12: Prevalence of ICH is again discussed. Please include family history in this discussion as prevalence is clearly higher in those patients with a family history.

Page 13: the second to last paragraph states that the study cohort was older than 41 yrs, the mean age of aneurysm rupture. These numbers cannot be compared directly without discussion. The mean age of rupture of 41 includes those families at highest risk. This study looks at a low risk population (defined as not having ICA prior to the age of 65). This part of the discussion should be revised.

Minor Revisions:

The figure legends could be improved for clarity. For example, in Figure 1, APPKD =0 could be replaced with non-ADPKD, and ADPKD =1, with ADPKD. This would be more consistent with the language in the title. In addition to these changes for Figure 2 and 3, a title over the graphs would be helpful.

Suggested Revisions:

I am used to seeing African-American abbreviated as AA, not AF.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I am a consultant for Otsuka. I declare that I have no competing interests in reviewing this paper.