Reviewer's report

Title: Clinical utility of PKD2 mutation testing in a polycystic kidney disease cohort attending a specialist nephrology out-patient clinic.

Version: 2 Date: 10 March 2012

Reviewer: York Pei

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The authors of this single-centre study report their experience in PKD2 mutation screening in 142 consecutive patients with ADPKD. They found that ~20% of their patients had a pathogenic PKD2 mutation and validated the use of family history of renal disease severity as a cost-effective means to selecting families with mild renal disease for PKD2 screening.

The strengths of this study include:

1. A well-defined prospective cohort of patients without advanced renal failure from a single centre
2. Its report of a higher prevalence of PKD2 using a more population based source is supported by two other recent single centre studies
3. Validation of the use of family history as a means of predicting the underlying gene type (i.e. "a history of one or more older affected family member who developed ESRD or remains renal sufficient at age older than 70" is highly predictive of PKD2)

Notwithstanding these strengths, there are also several issues that the authors need to address:

1. Their observation of 25.9 and 35.6 % of the probands without and with PKD2 mutations did not have a family history represents a very high rate compared to other series. They should expand on their discussion on why their observation appears to be discordant with the published series.
2. They should differentiate between single-centre vs. multiple centre studies in Table 1. Only single centre studies can provide results that estimates population prevalences of PKD1 and PKD2.
3. They should perform post-hoc sample size calculations which would likely show that the reason for a lack of differences in the three CKD stages between patients with the two gene mutation types is related to power.
4. Figure 3 is not really very useful and should be deleted.
5. There is an inconsistency in their recommendation that PKD2 mutation screening should be offered to all ADPKD patients except those whose family members developed ESRD under age 50 (line 9 from top of page 14) and whose family members developed ESRD before the sixth decade (lines 1 and 2 from the bottom of page 14).
They should update their references on PKD1 hypomorphic alleles as a potential cause of mild renal disease.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

No conflict of interest to declare