Reviewer’s report

Title: Plasma metabolites and lipids associate with kidney function and kidney volume in hypertensive ADPKD patients early in the disease course

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Reviewer: Valeria Padovano

Reviewer's report:

The study by Kim et al reports a non-targeted GC-TOF/MS-based metabolomics approach to investigate the predictive role of plasma metabolites on hypertensive ADPKD patients. The authors identified 12 metabolites that were significantly associated with eGFR and 2 triglycerides that were significantly associated with ht-TKV. None of the metabolites and triglycerides showed significant effect modification by sex or genotype. Interestingly, these metabolites were altered in individuals with preserved renal function, suggesting that early metabolic derangements occur before significant loss of renal function and might prove helpful for the development of diagnostic and/or prognostic tools.

Although further investigation is needed to identify metabolites that can be used as prognostic indicators of slow and rapid disease progression, these data indicate that analysis of plasma metabolites in ADPKD can reveal predictors of early kidney dysfunction.

The paper is well written and the conclusions are well supported by the analysis. Some minor concerns need to be addressed.

The background section is missing references to the disease genetics, progression and environmental factors that can affect it.

Altered metabolism has emerged as a key feature in ADPKD and many papers have been published in recent years reporting such alterations. The discussion would benefit from more extensive comparison to other metabolomics data already published.
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