Reviewer's report

Title: Cardiac Function Assessed by Myocardial Deformation in Adult Polycystic Kidney Disease Patients

Version: 0 Date: 23 Jan 2019

Reviewer: PETER JANSSENS

Reviewer's report:

This study evaluates early cardiovascular manifestations of ADPKD patients by measuring ventricular global longitudinal strain, a relatively new echocardiography technique. This has not been studied yet in ADPKD patients and as the study looks at a relatively large cohort of 110 ADPKD patients this has certainly his merits. However, there are several methodological problems. First, the study population already presents a relatively advances disease stage, with significant CKD. The aim of the study is to investigate the distribution of GLS in ADPKD subjects. Also, especially in view of the high inter-ventor variability of this technique, the absence of a healthy and/or CKD control group is problematic. To identify clinical variables associated with higher strain, the authors subdivided the cohort in a low and high strain group based on the median GLS of 17.8%. However, in one study (Russo et al, European Journal of Heart Failure (2014) 16, 1301-1309) mean GLS in a healthy reference sample was -18.1% and an abnormal GLS was defined as > -14.7%. Also, the authors make several ADPKD-specific claims but describe anomalies in a population with CKD without a CKD control group.

Abstract:

P2 Line 4: Many patients with autosomal dominant polycystic kidney disease (ADPKD) die from complications of cardiovascular (CV) disease -> this statement is too vague

P2Line 7-12: It is unclear from this phrasing if GLS is a predictor in ADPKD patients on dialysis or rather in a general dialysis population, please specify.

P2Line 28: E/SRe was not introduced

P3Line 1: that GLS and E/SRe are common: compared to what? Please consider adding a control population
Introduction: Death due to cardiovascular disease has been reported to be as high as 33% in ADPKD patients with end-stage renal disease (ESRD), primarily due to ischemic heart disease (IHD) and congestive heart failure (CHF). How does this compare to other CKD populations? Is this ADPKD specific?

P4 40: More sensitive echocardiographic techniques could not describe the CV risk but rather be used to be correlated to CV risk

Methods:

The enrollment period was 5 years. It is mentioned that this is a prospective cohort study. No information is given on the time relation between the echocardiography measurement and the clinical variables. Isn't this study cross sectional?

The median GLS is was used to discriminate two groups, higher and lower; however, this cuts the groups over the normal value. How many had an "abnormal" GLS e.g. >-14.7%?

One of the inclusion criteria is eGFR >15 ml/min; this is already severe CKD. Although the two groups do not differ statistically significant in eGFR there is a clinically significant difference of almost 10ml/min between the groups. The authors do not address the possibility that the differences are driven by kidney function rather than PKD.

The authors claim to have looked at a population with no history of cardiac disease. However, in this high risk population, it is not mentioned in the methods how the absence of CV disease was addressed.

The images were obtained by multiple operators. Although they are processed semiautomatic they can be manually adjusted; potential interoperator variability is not addressed.

Considering E/e's: The investigator could exclude segments, if considered untraceable. In how many subjects exclusions were made?
Results:

Odds ratios all small except for gender and beta blockers; the authors suggest advising against beta blockers as a second antihypertensive agent in the ADPKD population. Has the effect of beta blockers on GLS measurements been studied or described in other populations? Is this linked to the pharmacological effect of Beta-blockade?

Is a (technical-physical) interference of hemoglobin with GLS measurements described?

Why is the linear regression with eGFR done per per 10 mL/min/1.73m^2?

Discussion:

P10 line 14: without control population is difficult to state that GLS is an early and sensitive marker in this ADPKD population

Line 49: Is the association of TKV with GLS also independent of kidney function?

Line 41:

More sensitive echocardiographic techniques don't describe CV risk but could be associated with CV risk

Are there any publications validating the specific used technique? What is prevalence of increased strain in this ADPKD group compared to the normal population and other CKD populations?

The authors should try to explain to the readership more in detail mechanistically what GLS means

P11 line 33: The sentence "This is consistent with reports that CV disease in men with ADPKD is more severe (3) and it is well known that women have higher LVEF and GLS than men" is contradictory. Does it mean that despite that woman have worse GLS in the general population this is inverse in ADPKD? This would be a interesting finding that could be more highlighted by the authors.
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