Reviewer's report

Title: Association between Extracellular Volume Excess and Renal Outcomes in Patients with Chronic Kidney Disease: Retrospective single-center cohort study

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Reviewer: Folkert W Visser

Reviewer's report:

Firstly, I like to congratulate the authors with the accomplishment of greatly improving the manuscript in short notice, with thoroughly replies to the reviewers comments. The study question is very important, the data (with its correctly stated limitations) very interesting and soundly derived. The article is well written. However, I have still two major concern and some minor concerns.

Major Compulsory Revisions:

Major concern remains the main study parameter. It is extremely difficult to ‘normalise’ the measured parameter of volume status. We agree that volume overload should be assessed by comparing a measured volume compared to the expected volume. For this you chose ECW-measured compared to TBW-calculated.

In your introduction you state that ECW/TBW is commonly used to assess overhydration (this is correct for reference 2-3-4-5 and 7, however all being hemodialysis patients; in reference 6 however, measure of overhydration is ECW/BW). Next you- correctly- state that the ratio ECW/TBW is not only influenced by increasing ECW, but also by a drop in ICW (under influence of aging, malnutrition-also in ref6- etcetera). Therefore, I suggest you state that ECW/TBW is better not used as an ideal measure of volume overload.

When in the end using ECWbia/ TBW-watson you still are using these parameters, while you probably mean something else. Therefore I believe your article should advocate ECWbia/ ECW-calculated (or other possibility is normalizing for calculated BSA of lean body mass- see for example Peter AM et al NDT 2012 for some considerations). When changing this parameter you stop suggesting that you are studying the relation between ECW-ICW and TBW, which you don’t do in this analyses (you are doing that very interestingly in supplementary data, but NOT for your main study parameter).

- This suggestion (of studying the relation of ECW to TBW) is strengthened in the second paragraph on page 15, where you (in my opinion wrongly) translate your results to ECW/ICW ratios. Please revise.

The second major concern is the relation you describe between fluid overload and BMI. The only result you show in the main article is a negative correlation between BMI and ECWbia/TBWwatson. This correlation is probably not valid as body weight and height are both in the formula for calculating BMI and
TBW-watson.

(Watson formula: Male TBW = 2.447 - (0.09156 x age) + (0.1074 x height) + (0.3362 x weight)

Meaning: an increase in weight increases TBW-watson, thus decreasing ECW/TBW-watson (since fat contains less water than other tissues, measured ECW is probably increased in a lesser amount). An increase in weight increases BMI. Thus: the negative correlation between BMI and ECW/TBW is mathematical and not any conclusion should be drawn from this analyses. I believe this analyses should not be part of the manuscript.

Your discussion paragraph concerning this issue is very interesting, but would better be based on relations comparing measured ECW, ICW and TBW in relation to BMI (but as supplement figure 4 shows you don’t have significant correlations comparing BMI to ECWbia/TBWbia).

Minor Essential Revisions:
- when changing main study parameter; change figure 1 (using the altered main study parameter)
- although the manuscript is written in clear English, some typical errors do occur, please correct.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests