Author’s response to reviews

Title: Abdominal aortic calcification is superior to other arteries calcification in predicting the mortality in peritoneal dialysis patients – a 8 years cohort study

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Author’s response to reviews:

Dear Nada Dimkovic:

Thank you very much for your advices. Thank you for your guidance in terms of professional knowledge. Your opinion is pretty good, it is worth learning, and we have gained a lot. We have modified the article based on your suggestion, and answered your questions. See below for details. If there is any change that you think is inappropriate or does not meet your requirements, please point out that we will definitely modify it again.

Thanks again for your guidance, this is a great improvement in the quality of our articles.

Answers see below:

1. Secondary end points need to be clearly defined without statement 'so on'.

Our answer: we have carefully revised this part and dropped ‘so on’, see ‘Materials and methods’ part.
2. It is important to know if patients were treated with the same method and solutions (CAPD/IPD/APD, use of icodextran.)

Our answer: There is no icodextran solution in China. All of our patients were used glucose-based solution. In order to make the methodological part clearer, we added this sentence in the part pf Results "All the patients used conventional glucose-based, lactate-buffered PD solutions (Ultrabag; Baxter Healthcare, Guangzhou, China; Mg2+ 0.25 mmol/L, Ca2+ 1.25 mmol/L or 1.75 mmol/L, Na+ 132 mmol/L, and Cl– 96 mmol/L). The daily dialysate exchange dose was more than 6 L, received either by continuous ambulatory PD (CAPD) or intermittent PD."

3. Note if some patients were switched from initial HD to PD.

Our answer: There was no patient who was transferred from HD. We added exclusion criteria in the method part to explain this issue. ‘Exclusion criteria: patients transformed from HD or received kidney transplantation; patients withdrew during the follow-up period (transfer to hemodialysis, receive kidney transplantation or move to other centers).’

4. Therapy is very important: frequency of use of calcium-based phosphate binders and, if possible, vitamin D metabolite and calcimimetics

Our answer: The situation in China may be different from other countries. Non-calcium phosphorus binder entered the Chinese market at the end of 2015 and are self-funded, which is expensive for CKD patients. Until the end of 2018, sevelamer and lanthanum carbonate were included in China’s public health insurance reimbursement list. So before the end of our study, few of our patients took non-calcium phosphorus binders, which is very clear. Due to our long follow-up period, almost all patients used calcium-based P binder during this period. And the dose and frequency used were adjusted according to the patient’s serum Ca, P, PTH level. Therefore, we didn’t include the use of calcium-based P binders into our analysis. We hope you can understand this situation of our patients.

Then, patients in China tend to have lower PTH level, so there are little patients need to use calcimetics, such as cinacalcet. In our center, there is 1 or 2 patients need to use it. So we didn’t include this part in text.

However, we reviewed patients’ outpatient medical records and added the information of using of vitamin D in table 1.

5. Note intra-observer variability of radiologists.

Our answer: For this issue, we revised the text as ‘The radiographs were reviewed by 2 radiologists blindly. For the inconsistent results, 2 radiologists re-scored and discussed together and then gave a unified result.’

6. Numeration of tables need to be consecutive. Therefore, Table 2 cannot be after Table 3.

I believe that there are a lot of figures. Also, in the headings of figures 5 and 6 adjusting variables should be noted.

Our answer: We reordered tables and added adjusting variables to the headings of fig 3,4,5,6.

Our answer: We quoted this citation in the text and discussed a little bit about the reasons for different calcification process. See Discussion paragraph 2 and 3.

Reviewer 2#:

Dear Fellype C. Barreto:

Thank you very much for your advice. It can be seen that your review of the manuscript is very careful and the suggestions that you mentioned are very helpful. We have modified the article based on your suggestion, and answered your questions. See below for details. If there is any change that you think is inappropriate or does not meet your requirements, please point out that we will definitely modify it again.

Thanks again for your guidance, this is a great improvement in the quality of our articles.

1. The authors must clarify if the patients who changed to a different renal replacement therapy modality, hemodialysis or kidney transplant, or moved to a different dialysis centre were withdrew of the study. According to the method section, it seems that those patients were still followed up and had their data included in the final analysis. If so, analysing data of these patients imposed a huge flaw to the study because their exposition to completely different factors related to their new treatment modality may have influenced their outcomes. In addition, patients who moved to a different dialysis centre should had been excluded of the study as well. Please, clarify.

Our answer: Your suggestion is very reasonable, so we decided to modify the article as your suggestion. We excluded these patients who transferred from HD or received kidney transplantation or moved to other center in the statistical analysis and survival plots. And we revised the discretion in the method and result parts. And we added exclusion criteria in the method part to explain this issue. “Exclusion criteria: patients transformed from HD or received kidney transplantation; patients withdrew during the follow-up period (transfer to hemodialysis, receive kidney transplantation or move to other centers).”

See details in method part.

2. In contrast to the description of the Adragao score, it does not include lateral abdominal X-Ray, but only of the hips and hands. Moreover, the method commonly used to evaluate abdominal aorta calcification by X-Ray is the Kauppila score, which is quite different form the one described in the method section (page 4; lines 55 - 60). The authors must (i) clarify from which study the method used for evaluating abdominal aorta calcification comes from to demonstrate that it is a valid method for quantifying abdominal aorta calcification and (ii) use the appropriate description and reference to the Adragao score.

The method we used was an improvement based on the method described by Adragao, which was described in 2 papers about assessing vascular calcification in dialysis patients. Now, we added the citations and explained it. As “This method was described by WANG Mi and WANG Mei et al previously[24-26], and it was an improvement based on the method
described by Adragao et al[19]. In Adragao’s method, radiographs of the pelvis were divided by 2 lines: a horizontal line just above the femoral heads and a median vertical line; and radiographs of each hand were divided by a horizontal lone over the proximal end of the metacarpals, with total 8 points. The method of WANG Mi and WANG Mei was also added the score of abdominal aorta: the lateral abdominal radiographs were divided into two sections by a horizontal line over the intervertebral space between L2 and L3, and the presence of calcification was given 1 point for each part. Scores from all parts summed up to a total score, which ranging from 0 to 10.”. see details in method part.

3. It would be interesting to perform statistical analysis to identify the risk factors associated to the presence of vascular calcification in the different arterial sites evaluated in the study.

Our answer: Your suggestion is very professional, and we also have thought of this, but consider that if add relevant results in this article, the content is too much and the focus is not prominent. The part you mentioned is included in another article and has been published, we have talked about this in the introduction part.

4. As correctly reported by the authors in the discussion section, previous studies have reported that AAC is a good predictor of cardiovascular outcomes in PD patients. Thus, which novelty the current study brings in comparison to the other studies? Only the longer follow up?

Our answer: First, our study validated the predictive effect of AAC on all-cause mortality and cardiovascular mortality in PD patients. Previous studies on the mortality of patients with vascular calcification have focused on coronary artery calcification, and less about AAC, especially in PD patients. Second, vascular calcification in other areas has received little attention and assessment of the predictive value of death. we followed up and analyzed the predictive effects of vascular calcification in different parts of PD patients. Some scholars have paid attention to the problem of vascular calcification in different parts in ESRD patients, but have not specifically clarified its impact on death. We found that femoral artery calcification can also predict the increasing risk of all-cause mortality and CV mortality in patients. Third, in addition to assessing AAC, X-ray films have an additional value to PD patients. Through abdominal X-ray or CT, doctors can observe the position of the PD catheter and the intra-abdominal condition. Therefore, in clinical work, in assessing patients' vascular calcification and status of CKD-MBD, and predicting patients’ prognosis, vascular calcification of the abdominal aorta and femoral artery can be combined to make a more accurate and meaningful assessment of patients. In text, we also added some content to illustrate the innovation and significance of this work.

5. The finding that femoral artery calcification is an independent predictor of mortality should also be discussed in the article.

Our answer: We added this part in discussion. As ‘However, VC in other areas has received little attention and assessment of the predictive value of mortality. Femoral artery is a medium-sized artery. We found that femoral artery calcification is a good predictor of risk of all-cause mortality and CV mortality in PD patients. Moreover, it is easy to know whether or not the femoral artery is calcified by X-ray film. For patients with high risk of VC, the calcification of the abdominal aorta and femoral artery can be evaluated simultaneously, and the VC burden caused by CKD-MBD and the effect of prognosis can be more accurately
understood.’ And in the conclusion part, ‘If necessary, the risk of CVD and mortality can be assessed based on the calcification of the abdominal aorta and femoral artery.’

# Minor remarks:

1. The term "prognosis" should be changed for "mortality" in the title.

Our answer: we replaced ‘prognosis’ with ‘mortality’. And revised relative part in the whole text.

2. The variables age, TG and BMI should be shown as both continuous and dichotomous variables in table 1.

Our answer: yes, we added them in table 1 now.

The text requires thorough English revision.

Our answer: A native English-speaking expert has revised this article. And for the content of the article, modified some content, to make the article more fluent and more reasonable.

Your sincerely,

QINGYU NIU and HUIPING ZHAO