Author’s response to reviews

Title: Layer-specific speckle tracking analysis of left ventricular systolic function and synchrony in maintenance hemodialysis patients

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Author’s response to reviews:

Dear Prof. Mohamed,

Thank you very much for your decision letter and additional advice on our manuscript (BCAR-D-19-00738) entitled, “Layer-specific speckle tracking analysis of left ventricular systolic function and synchrony in maintenance hemodialysis patients”. We also thank the reviewers for their review of our revised manuscript and further comments. We are pleased to have the opportunity to address their additional concerns, and as before, all amendments are indicated by red font in the revised manuscript. In addition, our point-by-point responses to the latest comments are listed below this letter.

This revised manuscript has again been edited and proofread by professional editors at Medjaden Bioscience Limited.

We hope that this further revised draft of the manuscript is now acceptable for publication in your journal and look forward to hearing from you soon.

With best wishes,
Yours sincerely,

Liu Chang
First, we would like to express our sincere gratitude to the reviewers for their constructive comments.

Replies to Reviewer 3

1.) The fundamental question is why we should measure layer-specific strain (LST) instead of using standard strains. The authors showed decreased strain values. What is the additional diagnostic value in using LST over the conventional strain?
Response: We thank the reviewer for the thoughtful comments. Anatomically, the left ventricular myocardium includes three layers: endocardium, middle myocardium, and epicardium. Standard strains can only provide indicators of global myocardial strain, while layer-specific strain (LST), which is an improvement on speckle tracking technology, can track and analyze the left ventricular myocardium to obtain the three-layer myocardial strain values. This approach can more accurately evaluate small changes in left ventricular function.

2.) LV strain values can be affected by preload and afterload (Voigt JU, et al. J Am Coll Cardiol Imag 2019;12:1849-63). In ESRD patients with MHD, preload can be changed from increased venous return as the result of arteriovenous fistulae. Also, increased total body water and toxic materials from decreased urinary excretion and altered cardiac geometry by increased afterload can affect the LV strain values. Thus, patients with MHD may have decreased strain values. However, the authors only showed the decreased strain values in these patients compared with controls. What is the meaning of decreased strain values in these patients? Do they have a higher mortality rate or increased clinical events?
Response: The reviewer brings up a valid point. Indeed, it has been reported that MHD patients have reduced left ventricular myocardial strain [1], which likely affects changes in pre- and post-load on left ventricular systolic function in MHD patients [2]. Few studies have measured the effects of changes in pre- and post-load on myocardial strain values in MHD patients, and we plan to perform these studies in our future directions. We are currently continuing to follow-up on the mortality and clinical event rates of the cohort of patients in our study, and will report these findings at appropriate times in the future. Accordingly, we have added several sentences in the Limitations section (Page17, Lines 4 - 9) to address these concerns in the revised manuscript.

3.) Because of the EchoPAC PC software set mid-myocardial strain value same as the global strain value including 3 layers. Thus, in table 3, the values should be rechecked.
Response: We thank the reviewer for this thoughtful comment. A similar study [3] averaged the three values, LSendo, LSmid, and LSepi, obtained by the EchoPAC PC software to obtain the GLS value. GCS can also be obtained using the average of CSendo, CSmid, and CSepi. In the present study, we performed a similar analysis. Another study [4] also used the EchoPAC PC software to obtain the value of LSmid, which was approximately equal to GLS, consistent with our observations. Accordingly, we have added several sentences in Data analysis of LV systolic function (Page 9, Lines 31 and 50) to address these concerns in the revised manuscript.
Replies to Reviewer 4

The authors have provided appropriate responses to the comments raised by other reviewers. I don't have anything else to add. There are limitations related to the small sample size and the strain measurements according to myocardial layers. These measurements have not been validated and they have limited application in clinical practice currently. However, there is potential and the hypothesis is interesting.

Response: We appreciate the reviewer’s favorable comments on our work.

References: