

Jin-Lei Wang
Science Editor
Editorial Office
Baishideng Publishing Group Inc

12/06/2019

Dear Editor,

Re: Response to Reviewer's Comments

We would like to thank the editorial team and reviewers for their comments in improving the quality of the manuscript. All comments and suggestions have been addressed carefully and responses are listed below. We hope that this is satisfactory and that the manuscript will pique the interest of your readership. We have verified the accuracy of general information for our manuscript. The changes made in the manuscript have been highlighted as advised. We have provided a separate file with the figures in Powerpoint format.

Following docs have been submitted except number 6, 7, 8, 10:

- (1) 48967-Manuscript File
- (2) 48967-Answering Reviewers
- (3) 48967-Audio Core Tip
- (4) 48967-Conflict-of-Interest Disclosure Form
- (5) 48967-Copyright License Agreement
- (6) 48967-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s): not submitted as not relevant
- (7) 48967-Non-Native Speakers of English Editing Certificate: :not applicable to this manuscript, all authors are native speakers.
- (8) 48967-Video : not applicable to this manuscript
- (9) 48967-Image File
- (10) 48967-Supplementary Material :not applicable to this manuscript

Please do not hesitate to contact us if any further clarification or documentation is required.

Yours sincerely,

Dr. Lavanya Athithan
Corresponding Author

Response to Reviewer 1 (Reviewer's code: 02446627)

We thank the reviewer for his time and kind comments. We have reviewed the language within the text and addressed as appropriate. We hope this is satisfactory.

Response to Reviewer 2 (Reviewer's code: 03460306)

We thank the reviewer for his time and comments. Our response is as follows in point form.

1. The manuscript was focused on the pathophysiology such as metabolic, structural and functional changes in patients with T2D. On the other hand, section regarding therapeutic strategy seems a little short. They mentioned SGLT2 inhibitors and GLP-1 agonists but the other possible therapeutic strategies for diabetic cardiomyopathy based on the pathophysiology should also be mentioned.

Response: Thank you for highlighting this. We have now expanded the section on therapeutic strategies. This includes other drug categories and specifically DPPV inhibitors within diabetic treatment. We have also included the outcomes from the recent PIONEER-6 trial.

2. Mechanisms by which GLP-1 agonists improve CV outcomes should be discussed.

Response: The effects of GLP-1 agonists on improving CV outcomes via glycaemic control, blood pressure, effects on the vascular endothelium, atherosclerosis progression and inflammation, myocardial ischaemia and heart failure have been elaborated on.

3. Page 20. DECLARE-TIMI 58 trial included both primary and secondary prevention of CVD. Thus, the sentence "the patients in these studies had established cardiovascular disease" should be corrected.

Response: This has now been corrected to read "the patients in these studies either had established cardiovascular disease or multiple risk factors for

atherosclerotic cardiovascular disease risk factors” which is as per the trial inclusion criteria. Thank you for pointing this out.

4. The authors limited the topics on T2D. It will be useful if the authors could briefly mention common and distinct mechanisms of cardiomyopathy between T1D and T2D.

Response: We have now added a paragraph with an overview of the mechanisms in T1D, but have further specified that this review will be focusing on T2D.

5. Page 19. A reference should be needed for the sentence “A meta-analysis of 37,299 people with T2D data from ... on HF related outcomes”.

Response: We apologise for this oversight and this has now been appropriately referenced within the text as follows: Castagno D, Baird-Gunning J, Jhund PS, Biondi-Zoccai G, MacDonald MR, Petrie MC, Gaita F, McMurray JJ. Intensive glycaemic control has no impact on the risk of heart failure in type 2 diabetic patients: evidence from a 37,229 patient meta-analysis. *Am Heart J*. 2011; **162**: 938-948 e932 [PMID: 22093212 DOI: 10.1016/j.ahj.2011.07.030]

6. There are misspellings in the figures. Please check and correct.

Response: We have checked and corrected this. Thank you.