

Point-by-Point Response

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Notes on the manuscript:

- 1- Title: the authors tries to present the new term in the title but as they described in the abstract it is mainly caused by liver cirrhosis, this should be stated by the title.

Thank you for your review and comments. We have now reworded the title to "Hepatocardiorenal syndrome in liver cirrhosis: Recognition of a new entity?" as recommended.

- 2- In the abstract and the main text the word "temporality" is repeated many times although it is vague in meaning, because it is a noun, if the authors mean a short or temporal state of the disease it should be clarified.

We have used the word "temporality" in context of highlighting the temporal state of the disease.

To define what we meant clearly, we have now included the word "prior onset" in brackets next to "temporality" when this vocabulary is used for the first time in the abstract and main manuscript.

- 3- In the keywords the authors wrote the new term "Hepatocardiorenal syndrome" this should not be in the keywords as it is not presented previously in the literature. Kindly omit.

We have now omitted "Hepatocardiorenal syndrome" from the keywords as recommended.

- 4- The figure contains a lot of writing like a text of the manuscript, please use abbreviations and small words illustrations.

We have now reduced the wordiness of the revised figure by including more frequent use of abbreviations.

- 5- The table contains simple information that could be presented on the text, I suggest modification with adding the referenced studies on the topic and the exact pathophysiological mechanism examined.

The table provides summary points of key areas within the topic that are known and those that is still in debate and require more extensive investigation, as discussed in detail throughout the main text of our manuscript. For each summary point, we have now included references referring to the studies that describe the exact pathophysiological mechanisms or clinical aspects that underpin the summary point stated.

- 6- the authors mention "These observations highlighted a temporal pattern of cardiac and kidney dysfunction in HRS, suggesting perhaps there is pathophysiological involvement of the heart in the manifestation of HRS and cardiac dysfunction is not simply just the consequence of a HRS-associated complication" >> you could reference the studies where liver transplantation reversed the cardiac condition and the residual cardiac function after and before the operation.

Thank you for your comment. We have now considered this point and added discussion on the impact of liver transplantation on reversing cardiac dysfunction and improving hemodynamic status in HRS patients. We have now added two references to support the added points here (see references 35 and 36 in revised manuscript)

- 7- the authors state that "they demonstrated lower renal artery flow compared to non-HRS groups.[9] These findings indicate that even with a hyperdynamic resting cardiac output there was inadequate kidney perfusion in early stages of HRS" >> this is explained by the rise in the RAAS system, please add to this paragraph.

We have now highlighted this point in the text, that it is "triggered by activation of the renin-angiotensin-aldosterone system".

- 8- this review lacks the data from transplanted patients, and the relation to the Child Pugh or MELD clinical staging, which makes the term lacking important factors, please add with referencing the studies.

We have now added two paragraphs under the section "Clinical and Therapeutic Implications of Hepatocardiorenal Interactions in Hepatorenal Syndrome" which reviewed current evidence surrounding liver transplant

recipients, in terms of strategies advocated for pre-transplant cardiac investigation to determine operative risk, and cardiac risk factors which may indicate adverse cardiac and overall outcomes post-transplantation with reference in relation to Child-Pugh and MELD classification systems. We have also discussed post-transplant management to optimize recovery of cardiac function and the current unknowns surrounding potential post-transplant cardiac complications and its utility to prognosticate cardiac and overall clinical outcomes over the longer term. References 68 to 78 were added in the revised manuscript to support the additional content.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The review summarized the current progress of hepatocardiorenal syndrome. I recommend that it can be accepted for publication.

Many thanks for your review and comments.

(1) Science editor:

1 Conflict of interest statement: Academic Editor has no conflict of interest. 2 Academic misconduct: No academic misconduct was found. 3 Scientific quality: The authors submitted a study of hepatocardiorenal syndrome. The manuscript is overall qualified. (1) Advantages and disadvantages: The reviewers have given positive peer-review reports for the manuscript. Classification: Grade B and Grade C; Language Quality: Grade A and Grade B. The review summarized the current progress of hepatocardiorenal syndrome. The authors tries to present the new term in the title but as they described in the abstract it is mainly caused by liver cirrhosis, this should be stated by the title. This review lacks the data from transplanted patients, and the relation to the child Pugh or MELD clinical staging, which makes the term lacking important factors, please add with referencing the studies. There are some contents in the manuscript that need to be clarified for clearer expression. (2) Main manuscript content: The author clearly stated the purpose of the study and the research structure is complete. However, the manuscript is still required a further revision according to the detailed comments listed below. (3) Table(s) and figure(s): There are 1 Figure and 1 Table should be improved. Detailed suggestions

for each are listed in the specific comments section. (4) References: A total of 67 references are cited, including 18 published in the last 3 years. 4 Language evaluation: The English-language grammatical presentation needs to be improved to a certain extent. There are many errors in grammar and format, throughout the entire manuscript. Before final acceptance, the authors must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>. 5 Specific comments: (1) Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A,B, arrows, etc. With respect to the reference to the Figure, please verify if it is an original image created for the manuscript, if not, please provide the source of the picture and the proof that the Figure has been authorized by the previous publisher or copyright owner to allow it to be redistributed. All legends are incorrectly formatted and require a general title and explanation for each figure. Such as Figure 1 title. A: ; B: ; C: . (2) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published, and correctly indicate the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. (3) Please don't include any *, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as aP < 0.05, bP < 0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP < 0.05 and dP < 0.01 are used, and a third series of P values is expressed as eP < 0.05 and fP < 0.01. (4) The "conclusion" section is missing at the end of the manuscript. 6 Recommendation: Conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Thank you for your review and comments. We have now responded to and addressed the reviewer comments in relation to content and English Language of the initial manuscript in our revised submission. We have now reviewed the entire manuscript to ensure that the language is polished and grammatically correct, and expression of content is as clear as possible. We have now reviewed the BPG author guidelines in revising the formatting of our figure. The figure is now in editable form in a PowerPoint file. Our figure is original with no copyright issues. We have inserted the copyright statement in the format as recommended by BPG guidelines alongside the figure. The title of the final section in our revised manuscript is now changed to simply "Conclusion" as requested, clearly noting that this is the conclusion section of the paper.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. When revising the manuscript, it is recommended that the author supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply PubMed, or a new tool, the RCA, of which data source is PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information

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Thank you for your review and comments. We have now attended to the reviewer comments as well as the comments from the Science Editor. We have reviewed the BPG author guidelines to ensure we fulfilled the specified requirements in our revised manuscript submission.