

## **General Response:**

We thank all the reviewers for the feedback and constructive suggestions. The comments are very helpful in improving the manuscript. We carefully provide point-by-point responses to the editor and reviewers' comments and list the associated revisions at the end of each comment.

### **Reviewer #1:**

Although the letter is interesting, I believe it requires a more extensive analysis of the literature. The authors state that therapeutic interventions such as TIPS can be considered in criteria of recompensation independent of clearance of the primary disease in future recompensation definitions in case it could not be achieved or sub-optimally achieved, as in many cases with non-alcohol and non-viral etiologies, however, they do not support their claims/suppositions with data from the literature.

**Response:** Thank you for your sincere advice. After a careful second review of literature we changed the suggestion to independently include TIPS in criteria of clearance of the primary disease in future recompensation definitions as this is not yet supported by data from literature. The letter's main concern now is the focus on inclusion of the data of etiological clearance in future studies of recompensation as this was not thoroughly discussed in the manuscript we commented on. We added the following parts to the manuscript to further show our point.

"The Baveno VII concept of hepatic recompensation requires fulfilment of all the following criteria:

- a. Removal/suppression/cure of the primary etiology of cirrhosis (viral elimination for hepatitis C, sustained viral suppression for hepatitis B, sustained alcohol abstinence for alcohol-induced cirrhosis)
- b. Resolution of ascites (off diuretics), encephalopathy (off lactulose/rifaximin) and absence of recurrent variceal haemorrhage (for at least 12 months)
- c. Stable improvement of liver function tests (albumin, INR, bilirubin) [1]."

"The concept of Baveno VII is novel and comparison of previous studies discussing hepatic recompensation is limited by the heterogeneity of the definition of hepatic recompensation. More studies are needed to accurately define the rate of recompensation under its criteria especially with different etiologies [3]. The criteria for recompensation for chronic hepatitis B patients were validated in a multicenter prospective study and the cut off values for stable improvement of liver function tests were explored [4]."

"There was no mention in the study of the specific viral etiologies, whether HBV, HCV, or coinfections, and the nature of the other diseases. It would have increased the value of the study if those specific details had been highlighted including follow up of the etiologic cause during the post intervention year to ensure the continuous state of suppression or cure. The follow up only included liver function tests, Child-Pugh score, and MELD score for 1 year which ensured stable improvement as per BAVENO VII criteria.

TIPS is a therapeutic intervention not aimed directly for clearance of the etiological factor of the liver cirrhosis. It has specific indications during chronic liver disease including bridging to liver transplantation, acute variceal bleeding, and refractory ascites. It has documented complications as well such as hemorrhage, encephalopathy, TIPS dysfunction, and liver failure [5]. To prove it carries additional benefits to achieve recompensation, it needs a controlled study where the isolated effect of TIPS is measured, but this poses an ethical challenge as mentioned in the study limitations.

Regarding the clearance of the etiologic diagnosis, the impact of therapy other than for viral and alcohol related liver disease remains to be further studied [3]."

### **Reviewer#2:**

**Specific Comments to Authors:** It is too long to be letter to editor Avoid terms like we , watching ... , New should be replaced by latest Will patients understand this topic , it is for clinicians would affect to be replaced by may improve or improve Authors should refer to Table 1 Where etiology of 42 patients is given There is etiological clearence evident on short follow ups in study.In your view , what is minimum

period for assessing etiological clearance.

**Response:** Thank you for your sincere advice. Regarding the length we tried to include only the relevant data that supports our point as requested by another reviewer for the same manuscript. We are willing to remove any part you could consider as irrelevant.

The words "watching" and "new" were removed when the whole first paragraph was rewritten. "would affect" has been replaced with "might improve".

"The topic of hepatic recompensation according to Baveno VII criteria is a novel and promising topic for patients with decompensated liver cirrhosis. It was previously thought that reaching the stage of decompensation in liver cirrhosis is a point of no return. This topic opens a new hope for patients with decompensated liver cirrhosis and **may improve** their clinical outcome if the appropriate therapeutic measures were taken."

Table 1 has been referred.

The primary disease was referred in table 1 of the study as a collective viral hepatitis (32 patients), alcohol (10 patients) and others (22 patients).

We suggest that the etiological clearance follow up should accompany the other parameters in the post intervention year according to international guidelines per disease. It is tailored according to the etiology itself i.e. HBV PCR every 6 months for chronic hepatitis B patients but no follow up in cases with SVR for chronic HCV who received eradication.

We added the following part to the manuscript to highlight this idea.

"**It would have increased the value of the study if those specific details had been highlighted including follow up of the etiologic cause during the post intervention year to ensure the continuous state of suppression or cure. The follow up only included liver function tests, Child-Pugh score, and MELD score for 1 year which ensured stable improvement as per BAVENO VII criteria.**"

**Reviewer#3:**

Dear Author(s), 1/ I reviewed your efforts, but I saw that you presented personal ideas without proof from the ground, particularly on your part as researchers, as evidenced by what you claimed in the report about the study's author in Reference No. 2. I hope you will abandon this framework and elevate the scientific level by doing a real-world comparison using the available data and specific reasons. 2/ A linguistic corrector or a native English speaker is required to resolve various linguistic faults in the document. Good luck,

**Response:** Thank you for your sincere advice. We revised the manuscript and made sure it has no personal ideas in the revised section. We made sure that the new comments on reference no. 2 are backed with evidence from the literature. The language part has been taken care of in the revised manuscript.

**Science editor**

1Please add the author's contribution section. The format of this section will be as follows: Author contributions: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; Wang CL, Liang L and Fu JF wrote the paper. (2) Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. If there is no PMID or DOI, please provide the website address.

**Response:** Thank you for your sincere advice. Author contribution section has been added.

**Author contributions:**

Shaaban HE, Abdellatef A, and Okasha HH, shared equally in letter writing; Okasha HH revised the letter.

2- Citations were autocorrected and uploaded through the automatic editing offered by the manuscript revision interface.

1 **R. de Franchis**, J. Bosch, G. Garcia Tsao, T. Reiberger, C. Ripoll, J.G. Abraldes, et al [DOI:10.1016/j.jhep.2022.04.029]

2 Baveno VII - renewing consensus in portal hypertension

3 **Rabinowich L**, Grupper A, Baruch R, Ben-Yehoyada M, Halperin T, Turner D, Katchman E, Levi S, Houri I, Lubezky N, Shibolet O, Katchman H. Low immunogenicity to SARS-CoV-2 vaccination among liver transplant recipients. *J Hepatol* 2021; **75**: 435-438 [PMID: 33892006 DOI: 10.1016/j.jhep.2021.04.020]

4 **Gao L**, Li MB, Li JY, Liu Y, Ren C, Feng DP. Impressive recompensation in transjugular intrahepatic portosystemic shunt-treated individuals with complications of decompensated cirrhosis based on Baveno VII criteria. *World J Gastroenterol* 2023; **29**: 5383-5394 [PMID: 37900585 DOI: 10.3748/wjg.v29.i38.5383]

5 **Reiberger T**, Hofer BS. The Baveno VII concept of cirrhosis recompensation. *Dig Liver Dis* 2023; **55**: 431-441 [PMID: 36646527 DOI: 10.1016/j.dld.2022.12.014.]

6 **Wang Q**, Zhao H, Deng Y, Zheng H, Xiang H, Nan Y, Hu J, Meng Q, Xu X, Fang J, Xu J, Wang X, You H, Pan CQ, Xie W, Jia J. Validation of Baveno VII criteria for recompensation in entecavir-treated patients with hepatitis B-related [DOI:10.1016/j.jhep.2022.07.037]

7 **Suhocki PV**, Lungren MP, Kapoor B, Kim CY. Transjugular intrahepatic portosystemic shunt complications: prevention and management. *Semin Intervent Radiol* 2015; **32**: 123-132 [PMID: 26038620 DOI: 10.1055/s-0035-1549376.]

**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 at: <https://www.referencecitationanalysis.com/>, or visit PubMed at: <https://pubmed.ncbi.nlm.nih.gov/>.

**Response:** Thank you for your sincere advice. We included the latest literature in our manuscript.