

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10307-Edited.doc).

Title: CLIF-SOFA is better than the apasl criteria for defining ACUTE-ON-Chronic Liver Failure and Predicting Outcome

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Name of Journal: World Journal of Gastroenterology

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The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated as per Journal requirements

2. Revisions have been made according to the suggestions of the reviewers as below:

REVIEWER NO. 507910:

Query:

This is an outstanding paper! Editorial suggestions are as follows: insert into the article under Materials and Methods the APASL and CLIF-SOFA criteria for classification of ACLF for the benefit of the readers. In the Materials and Methods section the first sentence should be rewritten as "Consecutive cirrhotic patients with..." The third sentence should be changed to read "patients were followed up for 3 months from inclusion or until mortality, whichever was earlier." in the section entitled "Characteristics of patients with acute decompensation, change the word once to "...one acute precipitating cause..." on page 14 at the end of the first paragraph insert "to " into "hence fails TO identify many patients at high risk of mortality" after that, it is ready to go! :-)

Answer:

We thank reviewer for appreciating the study and positive comments.

The line "consecutive patients with cirrhosis with acute decompensation...." is already mentioned in the 4th line of the Materials and Methods section. We have mentioned the study design, period of the study and the cohort of patients from whom the study population was derived as the first 3 lines of the materials section which we feel should remain.

Statement regarding follow-up of patients has been added to the beginning of the materials section and removed from the end of the management section as suggested.

"Once" changed to "one" in the section entitled "Characteristics of patients with acute decompensation"

“To” added to the line “hence fails identify many patients at high risk of mortality”
in discussion section

REVIEWER NO. 742516:

Query:

Moreau et al. established a diagnostic criteria for ACLF using CLIF-SOFA score and high 28-day mortality rate (2013 Gastroenterology). With great interest, I read the paper “CLIF-SOFA IS BETTER THAN THE APASL CRITERIA FOR DEFINING ACUTE-ON-CHRONIC LIVER FAILURE AND PREDICTING OUTCOME” by Radha K Dhiman et al. In this work, the authors compared the CLIF-SOFA criteria and the APASL criteria for defining ACLF and concluded that the CLIF-SOFA criteria was better when predicting the 28-day mortality. However, the authors just showed that the mortality rate was significantly different between ACLF and Non-ACLF as per CLIF-SOFA criteria and was not significantly different as per APASL criteria. Can this prove that one criteria is really better than the other criteria in identifying who will die within 28 days? I think more analysis will be needed. The authors should prove that the two filters are different not by chance.

Answer:

In the discussion we have mentioned that practically objective of defining ACLF in the real world setting is to differentiate the subset of patients who are at high risk of

mortality from those with a good expected outcome at time of admission. This study has conclusively demonstrated that there is no difference in the mortality with and without ACLF as per APASL criteria, thus the purpose of calling some of these patients ACLF and some non-ACLF is defeated. However, with the CANONIC criteria, there is a marked difference in mortality in patients with ACLF versus without ACLF. Hence, we have concluded that further studies should prefer the CANONIC criteria to define ACLF for including patients for interventional trials in the research settings and for considering liver transplantation in the clinical setting.

There is always a possibility of a falsely positive or negative finding in any statistical analysis due to effect of chance, especially when sample size is small. However, we have conclusively demonstrated that the finding of increased mortality in CANONIC criteria ACLF is not by chance as we have also shown that the mortality increases with increasing grades of ACLF, and moreover that the CLIF-SOFA score related to the same CANONIC criteria is an independent predictor of mortality. Hence, we would like to keep the same conclusion of our study.

REVIEWER NO. 2444883:

Query:

In the current manuscript, Radha K Dhiman et al compared the CLIF-SOFA criteria and the APSAL criteria in predicting short-term prognosis of patients with ACLF (acute on chronic liver failure). They conclude that the CLIF-SOFA criteria is better

that the APASL criteria in predicting the outcome of ACLF patients. The study is interesting and well written and no major criticism can be raised.

Answer:

We thank reviewer for appreciating the study and positive comments.

3. References have been checked and DOI numbers and PMID added.

Thank you for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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