Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: I would like to thank for the opportunity to revise this manuscript. This was a paper which proposed a modified classification for ACLF, based on EASL-CLIF Criteria. The Authors retrospectively evaluated a large number of patients who were listed for transplantation in the UNOS database. The Authors modified INR and serum creatinine levels from the original EASL-CLIF criteria. Therefore, a non irrelevant number of patients, previously without diagnosis of ACLF according to original criteria, now fulfilled criteria of ACLF. The second improvement of this study was the creation of a smooth definition of ACLF grades (deleting previosly definition of ACLF grade 1b). The paper is of interest, in my opinion. Statistical analysis is good, as well as references. The Authors adequately discussed their findings in the appropriate section. No typos are present. I have only two comments. - First, mechanical ventilation should not be considered a surrogate of respiratory failure in all patients with ACLF (for instance, a patient with hepatic encephalopathy grade IV must be intubated without respiratory failure). This point should be discussed in the appropriate section. - Second, the use of "presence of vasopressors" (Table 1) without including MAP is another important difference form previous EASL-CLIF criteria. This point should be better discussed.

Comments:

First, mechanical ventilation should not be considered a surrogate of respiratory failure in all patients with ACLF (for instance, a patient with hepatic encephalopathy grade IV must be intubated without respiratory failure). Second, the use of "presence of vasopressors" (Table 1) without including MAP is another important difference form previous EASL-CLIF criteria. This point should be better discussed.

Answer:

A discussion about the limitation of the UNOS data set, lacking information about PaO2, FIO2 or mean arterial pressure (MAP), has been added to the discussion section.

Reviewer #2:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: The subject of improving the diagnostic criteria for ACLF is of great importance, especially considering the need of a universal definition for this condition. Nevertheless, some considerations on this study are in order. Minor comments: -Please avoid abbreviations in the title. The title should not begin with "A" as per journal style. -Please avoid long expressions as key words. -The Abstract must have at least 350 words as per journal style. Please also see the length recommended for each section. It is not clear in the Abstract why the authors consider mEACLF easier to use than EASL-ACLF (in the Abstract, there only seems to be a change in cutoff points). Nevertheless, even after understanding the simplification suggested for ACLF grade 1, it does not seem to make much of a difference in terms of easiness to use. -In Introduction, page 3, lines 3-4, ACLF is spelled out incorrectly. In the same page, APASL also is spelled out incorrectly (Asian x Asia) and there is a parenthesis symbol missing. -In Results, page 7, lines 21-22, the sentence is not clear and should be rephrased. -The references list should meet journal style. -In Table 1, "T" is standing for "circulatory failure". Authors should amend this. Major comments: -The definition of ACLF implies the presence of acute decompensation of cirrhosis, associated with organ failures and high short-term mortality. A database of outpatients is probably not appropriate for denifing a condition requiring the presence of acute decompensation of cirrhosis. Considering that most of their patients probably were not hospitalized, authors should discuss this limitation of their study. This might even explain why 30-day mortality rates for EASL-ACLF were lower than in other studies. -Since the concept of ACLF implies a high short-term mortality, authors should justify the diagnosis of ACLF by mEACLF criteria in patients with a 30-day mortlity <15% (for mEACLF grade 1, the mortality was only 4.7%). -If authors are suggesting that any single organ failure would lead to the diagnosis of ACLF, they should inform the mortality rate of ACLF grade 1 patients according to the different organ failures. -Authors must ackowledge the limitations of working with a large administrative database, which was not developed with the purpose of this study and which lacks the granularity for obtaining important information. The lack of data on

PaO2/FiO2 (or SpO2/FiO2) probably impaired the performance of the EASL-ACLF criteria. - Moreover, using such a large database comes with certain drawbacks, as the fact that clinically irrelevant differences might reach statistical significance. Authors should explain if they believe there is a clinically relevant difference in the prognostic performances of both criteria (for instance, 0.842 x 0.835 or 0.859 x 0.851, including an intersection of confidence intervals). - Furthermore, it is expected that cutoff points derived from a given population would perform better in that population than cutoff points derived from different populations. Therefore, the results of this study must be validated in other populations before mEACLF could be considered better than EASL-ACLF.

Minor comments:

1. Please avoid abbreviations in the title. The title should not begin with "A" as per journal style.

Answer: The abbreviation has been removed from the title.

2. Please avoid long expressions as key words.

Answer: The long expression in the key words has been shortened.

3. The Abstract must have at least 350 words as per journal style. Please also see the length recommended for each section. It is not clear in the Abstract why the authors consider mEACLF easier to use than EASL-ACLF (in the Abstract, there only seems to be a change in cutoff points). Nevertheless, even after understanding the simplification suggested for ACLF grade 1, it does not seem to make much of a difference in terms of easiness to use.

Answer: We believe that compared to the original EASL-CLIF criteria, the modified EASL-CLIF, that simplify the EASL-CLIF ACLF definition criteria, is easier to use and has a better performance.

4. In Introduction, page 3, lines 3-4, ACLF is spelled out incorrectly. In the same page, APASL also is spelled out incorrectly (Asian x Asia) and there is a parenthesis symbol missing.

Answer: These errors have been corrected.

5. In Results, page 7, lines 21-22, the sentence is not clear and should be rephrased.

Answer: The sentences have been updated.

6. The references list should meet journal style.

Answer: The style of the references has been updated to the WJH style.

7. In Table 1, "T" is standing for "circulatory failure". Authors should amend this.

Answer: It has been changed to "Heart".

Major comments:

1. The definition of ACLF implies the presence of acute decompensation of cirrhosis, associated with organ failures and high short-term mortality. A database of outpatients is probably not appropriate for denifing a condition requiring the presence of acute decompensation of cirrhosis. Considering that most of their patients probably were not hospitalized, authors should discuss this limitation of their study. This might even explain why 30-day mortality rates for EASL-ACLF were lower than in other studies.

Answer: The limitation of UNOS data set has been expanded in the discussion section. We believe that our study population truly reflected the transplant population with ACLF since it included all available liver transplant data from the entire country.

2. Since the concept of ACLF implies a high short-term mortality, authors should justify the diagnosis of ACLF by mEACLF criteria in patients with a 30-day mortlity <15% (for mEACLF grade 1, the mortality was only 4.7%).

Answer: The 30-day all-cause mortality of the mEACLF grade 1 was slightly less than the original EASL-CLIF grade 1 (4.7% vs. 6.1%). The lower short-term mortality (< 15%) could be due to the UNOS data set which includes only patients listed for liver transplant with ACLF.

3. If authors are suggesting that any single organ failure would lead to the diagnosis of ACLF, they should inform the mortality rate of ACLF grade 1 patients according to the different organ failures.

Answer: Due to the lack information about the order in which organ failures in the UNOS data set, we cannot answer this question objectively. We do not think it will provide too much useful information by further stratifying the mortality of ACLF grade 1 patients with different organ failures since ACLF is a very broad clinical concept.

4. Authors must ackowledge the limitations of working with a large administrative database, which was not developed with the purpose of this study and which lacks the granularity for obtaining important information. The lack of data on PaO2/FiO2 (or SpO2/FiO2) probably impaired the performance of the EASL-ACLF criteria.

Answer: A discussion about the limitation of UNOS data set, lacking information about PaO2, FIO2 or mean arterial pressure (MAP), has been added to the discussion section.

5. Moreover, using such a large database comes with certain drawbacks, as the fact that clinically irrelevant differences might reach statistical significance. Authors should explain if they believe there is a clinically relevant difference in the prognostic performances of both criteria (for instance, 0.842 x 0.835 or 0.859 x 0.851, including an intersection of confidence intervals).

Answer: It seems like there is an intersection of the two confidence intervals. However, the 95% Wald confidence limits of the difference between these two models (mEACLF AUROC - original EASL-CLIF AUROC; AUROC contrast estimation 0.0072, 95% CI 0.00208 - 0.0123, p=0.006, 30-day all-cause mortality; AUROC contrast estimation 0.0085, 95% CI 0.00329 - 0.0136, p=0.001, 30-day transplant-free mortality) do not include zero. The difference between the two models is statistically significant.

6. Furthermore, it is expected that cutoff points derived from a given population would perform better in that population than cutoff points derived from different populations. Therefore, the results of this study must be validated in other populations before mEACLF could be considered better than EASL-ACLF.

Answer: The derived cutoff points were based on all available information from the UNOS data set. The mortality rate comparison of mEACLF and EASL-ACLF was based on all patients in the UNOS data set. It is unlikely that the performance of mEACLF in some subpopulation will affect the comparison of mEACLF and EASL-ACLF for all the patients in the UNOS data set.

(1) Science editor:

The manuscipt entitled "A modified EASL-CLIF (mEACLF) criteria that is easier to use and perform better to prognosticate ACLF" is based on the results of original study. It is well-written, and bring new to the field. There are no major flaws with the study design, methods, results and interpretation. The manuscript is not arranged in accordance to the Journal requirements yet, however it does not impact its scientific quality. I would suggest either to add formal evaluation of simplicity compared to the standard criteria or skip the related mentioning in the title.

Answer: The title has been updated by removing the abbreviation.