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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 72746

Title: A modified EASL-CLIF criteria that is easier to use and perform better to prognosticate ACLF

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00199582
Position: Editorial Board
Academic degree: MD, MSc, PhD

Professional title: Adjunct Professor, Attending Doctor, Doctor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: United States

Manuscript submission date: 2021-10-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-27 10:32

Reviewer performed review: 2021-10-27 13:17

Review time: 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [Y] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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%

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(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.

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Reviewer's code: 03668558
Position: Editorial Board
Academic degree: MD

Professional title: Consultant Physician-Scientist, Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2021-10-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-11 05:32

Reviewer performed review: 2021-11-12 05:52

Review time: 1 Day

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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.