

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 53709

Title: LIV-4: A novel model for predicting transplant-free survival in critically ill cirrhotics

Reviewer's code: 02511796

Position: Peer Reviewer

Academic degree: FRACP, FRCP (C), FRCPA, MBBS

Professional title: Doctor, Senior Lecturer

Reviewer's Country/Territory: Australia

Author's Country/Territory: United States

Manuscript submission date: 2020-01-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-01-26 05:00

Reviewer performed review: 2020-01-28 00:58

Review time: 1 Day and 19 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input type="radio"/>] Yes [<input type="radio"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No



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SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to view the manuscript. My comments on paper are as follows. 1. Please consider expanding the methods (i.e. detail so can be replicated) and breaking down the methods into subsections e.g. aims/ hypothesis; study design (inc/exclusion), etc. 2. Limitations and conclusion expand to cover these points [e.g. this from BPG publishing - (what are the limitations of the study and its findings? What are the future directions of the topic described in this manuscript? What are the questions/issues that remain to be solved? What are the questions that this study prompts for the authors to do next? How might this publication impact basic science and/or clinical practice?)] 2. Apart from this I don't not have any major criticism of the article from the title, abstract, intro, method and discussions. My comments to authors: 1. I note that looking at a retrospective angle and then testing prospectively is a strong method to study this problem - however this concept has still a way to go before making it into mainstream clinical use 2. I however feel the strength of this paper can be enhanced by a) Editorial on scoring systems in medicine (even from your group or another); b) defining the future pathway you propose to study in greater clarity.

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 53709

Title: LIV-4: A novel model for predicting transplant-free survival in critically ill cirrhotics

Reviewer's code: 02904354

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Chief Physician, Associate Professor, Doctor, Postdoc

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2020-01-26

Reviewer chosen by: Ruo-Yu Ma

Reviewer accepted review: 2020-02-20 08:43

Reviewer performed review: 2020-02-21 11:33

Review time: 1 Day and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This paper deserves the publication in this journal. Some comments are listed as follows.

In the introduction section, when the authors introduced the previous prognostic scoring system, do not forget the MELD and Child-Pugh score. There are some important systematic reviews published regarding this topic. Some recently established prognostic scores for liver cirrhosis, such as ALBI (PMID 29264426) and CAGIB (PMID: 31512140), should be statistically compared and discussed. Give the full names for some abbreviations, such as CPS. In the Results section, the authors said "... CPS of 10.2 (B) ...". Are you sure CPS 10.2 points = CPS class B? In the Results section, the authors said "Survivors had more compensated liver disease than patients who did not survive". Please improve your words. Indeed, your patients are critical, so please avoid the words "compensated liver disease". In the Results section, when the authors said "the SOFA scored performed with an AUC of 0.78", "scored" should be revised as "score". Language and grammar mistakes should be carefully checked. Please improve your words throughout the text. Avoid the use of abbreviations as possible as you can.

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 53709

Title: LIV-4: A novel model for predicting transplant-free survival in critically ill cirrhotics

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: 2020-01-26

Reviewer chosen by: Ruo-Yu Ma

Reviewer accepted review: 2020-02-21 15:13

Reviewer performed review: 2020-02-26 14:11

Review time: 4 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input checked="" type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Unfortunately, the manuscript file is incomplete, making it impossible for a proper review.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Hepatology

Manuscript NO: 53709

Title: LIV-4: A novel model for predicting transplant-free survival in critically ill cirrhotics

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: 2020-01-26

Reviewer chosen by: Jie Wang

Reviewer accepted review: 2020-04-16 14:20

Reviewer performed review: 2020-04-17 13:03

Review time: 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Studying critically ill patients with cirrhosis is highly important. Nevertheless, some issues regarding this manuscript deserve attention. In the Abstract, the sentence “Area under the receiver operating characteristic (AUROC) curve was calculated for different scores regarding prediction of in-hospital mortality.” should substitute for “Area under the curve receiver operator characteristics (AUCROC) analysis was performed to assess the value of various scores in predicting in-hospital mortality.” AUROC should substitute for AUCROC throughout the text (in some parts of the text, AUROC already is the used abbreviation). The authors should evaluate CLIF-C AD and CLIF-C ACLF scores and compare them to LIV-4 score. CLIF-C AD and CLIF-C ACLF scores performed better than other prognostic scores in the original publications, were externally validated and can be easily calculated on-line. In the original publication, CLIF-SOFA was not primarily used for prognostication, but for diagnosis of ACLF. CLIF-C AD and CLIF-C ACLF are the prognostic scores recommended by the CLIF Consortium. Authors refer to their hospital as a tertiary care center in the Abstract and as a quaternary one in Methods. They should choose either one or the other. Authors should confirm if they evaluated FiO₂/PaO₂ (as it is stated in Methods) or PaO₂/FiO₂ (which is the usual parameter). Using prothrombin time instead of INR could be a problem, since there is high variability for prothrombin time among different laboratories. This might impact the external validity of LIV-4 score. Authors should comment on this. In the 1st paragraph of Results, authors should revise the sentence “In total, 436 patients cirrhotic patients, aged 57 ± 10.6 years...”. In Results, authors should revise the sentence “A trend toward significance was seen was seen when comparing the LIV-4 score to both the SOFA and CLIF-SOFA scores (Table 3).”. In the last paragraph of Results, authors comment on the cut-off of 26.5, but they do not comment on the cut-off of 45.8. They should comment on it. Moreover, authors use both “cutoff” and “cut-off” throughout the text; they should also revise this. Besides, the performance of

the LIV-4 score for both cut-off points shown in Table 6 is different than that described in the main text, which must also be revised. In the 1st paragraph of Discussion, authors should not state that LIV-4 score performed better than SOFA and CLIF-SOFA in the training cohort, since the differences were not significant according to what they informed in Results. Authors should discuss the fact that, in the validation cohort, LIV-4 performed quite similarly to the other scores and actually numerically worse than CLIF-SOFA. Authors should not conclude that LIV-4 score performs better than other scores, since this was not true for SOFA and CLIF-SOFA in the training cohort and since this was only true for RFH in the validation cohort.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Hepatology

Manuscript NO: 53709

Title: LIV-4: A novel model for predicting transplant-free survival in critically ill cirrhotics

Reviewer's code: 02904354

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Chief Physician, Associate Professor, Doctor, Postdoc

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2020-01-26

Reviewer chosen by: Jie Wang

Reviewer accepted review: 2020-04-15 08:24

Reviewer performed review: 2020-04-25 03:46

Review time: 9 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

There are lots of scores established. It is necessary to discuss the difference between your new score with others. ABLI is a score broadly used in different liver diseases. It is necessary to discuss its prognostic role.