Re: Manuscript ID: 53709

Dear Editorial Board and Reviewers,

Thank you for your thoughtful review of our manuscript, "The LIV-4 Score: A Novel Model for Predicting Transplant-Free Survival in Critically Ill Patients with Cirrhosis".

Below are our responses to review and explanation of manuscript alterations. Changes to the manuscript and tables are highlighted in tracked changes. We hope you agree with us that the revised manuscript incorporating the reviewer's comments makes for a much better report.

Sincerely,

Christina Lindenmeyer, M.D.

Response to Reviewer 1:

Thank you for the opportunity tr 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.

Thank you for your kind and thoughtful feedback. We respectfully have revised the manuscript as outlined below:

1) Thank you for your suggestion regarding our Methods section. We have expanded the Methods section in detail and divided the text into subsections so as to facilitate replication and validation of the data.

2) Thank you for your suggestion regarding commenting on limitations of our study. We have reviewed the text to ensure that all of these points have been appropriately addressed.

2) We agree with your assessment regarding our study design (retrospective modeling with prospective validation). We suggest in our final concluding sentence that external study be undertaken in an effort to widely validate this novel model. We also suggest the LIV-4 score be used in the future as a means of stratifying cirrhotic ICU patients in clinical research studies.

Response to Reviewer 2:

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.

Thank you for your kind and thoughtful feedback. We respectfully have revised the manuscript as outlined below:

1) Thank you for your suggestion on improving our Introduction. We have expanded our Introduction to specifically comment on liver-specific scoring systems.

2) Thank you for referencing the ALBI score and the CAGIB score and for your kind suggestion. We have intentionally included only scores in this analysis that have been previously validated broadly in diverse cohorts in an effort to develop and test a widely-applicable and universal survival analysis tool. While the ALBI score has been proposed as a model to predict in-hospital death for cirrhotic patients, it has not yet been shown to be equally applicable across the spectrum of etiologies of chronic liver disease and has not yet been externally validated. Similarly, the CAGIB score has been proposed as a model for prognosticating death in cirrhotic patients who present specifically with acute gastrointestinal hemorrhage, rather than all-cause mortality.

3) We have minimized our use of abbreviations and have carefully reviewed the manuscript to correct all grammatical errors.

4) Thank you for clarifying our error. The Child-Pugh Score of 10.2 in the Results section has been changed correctly to C.

5) Thank you for noting our incorrect use of "compensated liver disease." We have revised this section.

6) Thank you for noting the following grammatical error: ..."scored performed with...". This has been corrected.