

Response to reviewers

Dear Editor and Reviewers,

We gratefully thank all editors and reviewers for their constructive remarks and useful suggestions concerning our manuscript entitled “A skeletal muscle index-based model to predict disease progression in cirrhotic patients after transjugular intrahepatic portosystemic shunt implantation: a sex-stratified analysis” (Manuscript NO. 87580, Observational Study) since these remarks and suggestions have significantly raised the quality of the manuscript and have instructed us to modify the manuscript. We have revised the article according to each suggestion and comment proposed by the reviewers, with the revisions labeled, and have responded to the comments of the reviewers point by point. We hope you will accept the revised manuscript and look forward to hearing from you soon. Moreover, we will be glad to respond to any further questions and comments you may have.

Yours sincerely,

Rongpin Wang

Responds to the reviewer's comments:

Reviewer #1:

Some minor comments:

1. in the abstract, please spell out SMI.

Response: Thank you for your reminder. We have defined SMI at its first appearance in the method section of the abstract, with the revision highlighted in yellow.

2. general proof-reading is required

Response: Thanks for your valuable suggestions. We have sent our revised manuscript to a professional English language editing company to carefully check and revise the manuscript.

3. please improve quality of artwork

Response: We are grateful for your constructive suggestion. We have enriched the color and content of our figures to improve the quality of artwork.

Reviewer #2:

1. It seems that only selected variables were used in the regression analysis. Many important variables, including serum bilirubin, INR, age, BMI, etc, did not appear to have been taken into account, leaving the risk of significant bias.

Response: We appreciate you for your careful review. Considering that the CTP model involves serum bilirubin, INR, and Alb, there may be collinearity if the above parameters are included in univariate and multivariate regression analyses, respectively. Therefore, the above indicators were not analyzed separately. In our previous analysis, statistically different indicators in the univariate analysis were included in the multivariate analysis. Accordingly, age, a key indicator, was analyzed. The multivariate analysis showed that age was not an independent risk factor for the long-term outcomes of cirrhotic patients. However, BMI was indeed not analyzed in the multivariate analysis. Hence, BMI has been included in the multivariate analysis this time, and the result was consistent with previous findings, indicating that BMI was not an independent risk factor for the long-term outcomes of cirrhotic patients after TIPS implantation.

2. It may be inappropriate to include post-TIPS complications (such ACLF and HE) in a model used to predict the prognosis of patients who have had TIPS implanted. As clinically relevant factors, only pre-TIPS parameters should be used.

Response: We are grateful for your kind reminder. However, we believe that it is necessary to include short-term complications after TIPS in the model for the assessment of the long-term prognosis based on two considerations. First, the model constructed in our study was used to assess the long-term prognosis of patients (30 months). Therefore, the inclusion of short-term postoperative complications is more conducive for clinicians to pay attention to this subset of patients and provide interventions when necessary, which may potentially change the outcomes of patients. Second, post-TIPS ACLF occurrence is associated with the increased blood flow of the systemic circulation after stent implantation, resulting in hepatic ischemia and hypoxia. The occurrence of HE after TIPS implantation is also associated with the increased shunting of blood without liver metabolism and detoxification. Both complications suggest that the excessive shunt volume of blood after TIPS is associated with poor long-term outcomes. Overall, we believe that short-term postoperative complications should be taken into account when a long-term prognostic model for TIPS is constructed.

3. What was the basis of sample size selection?

Response: We sincerely thank you for your valuable feedback. The study was a retrospective observational study, and the sample size was selected based on the number of TIPS implantation annually performed at our hospital and the number of cases included according to the inclusion and exclusion criteria. Thank you for reminding us of the need to be more rigorous about sample size. The two-sided test (α) and tolerance (D) were set at 0.05 and 10%, respectively, to calculate the sample size based on the calculation of the sample size in the diagnostic test study and the sensitivity and specificity of the model obtained in our study. The sample size was calculated as 88 cases. Considering the possibility of 20% of patients who were lost to follow-up and refused to visit the hospital, at least 106 cases need to be included in the study. Therefore, the inclusion of 186 patients in our study met the need of the sample size for this type of study.

4. It would be better to have a flow diagram showing how eligibility was decided and reasons for exclusion at different stages.

Response: We feel great thanks for your reminder. We have added a flow diagram in the methods section based on the inclusion and exclusion criteria, with the revision highlighted in yellow.

5. In the abstract, some non-standard abbreviation (SMI, FIPS, etc) have been used which need to be expanded.

Response: We appreciate your constructive comment. We have defined abbreviations at their first appearance in the abstract, with the revision highlighted in yellow.

6. How BMI was calculated in cirrhosis patients with ascites?

Response: We would like to express our sincere gratitude for your professional review. Indeed, it is difficult to accurately calculate BMI in cirrhotic patients with ascites. Therefore, patients in our study were classified into patients with mild, moderate, and severe ascites based on the data of fluid dark areas shown by ascites ultrasound. Meanwhile, considering the possibility of peripheral edema in cirrhotic patients, the BMI of patients with mild, moderate, and severe ascites was roughly calculated with the weight loss of 5% , 10% , and 15% , respectively.

7. What is the relevance of figure 2 in the current study?

Response: Thank you for your valuable question. In this study, the association between SMI and CTP scores in patients undergoing TIPS was analyzed to demonstrate that decreased SMI was associated with the severity of cirrhosis. SMI levels were lower in patients with CTP grades B and C than in patients with CTP grade A, indicating that patients with worse liver function have poorer nutritional status and may also be at higher risk of long-term adverse outcomes after TIPS.

Responds to the company editor-in-chief's comments:

1. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...” .

Response: We are grateful for your valuable comment and have carefully revised the legends strictly according to your suggestion for uniform presentation.

2. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: We think this is an excellent suggestion. We have organized decomposable Figures into a separate PowerPoint file as required.

3. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thanks for your constructive suggestion. We have carefully re-checked and revised our tables to meet the requirements of the journal.

4. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is ‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Response: We feel great thanks for your valuable comments. We have confirmed that our figures are original and have added the copyright information, Copyright ©Zhang Q et al. 2023, to the bottom right-hand side of the picture in PowerPoint (PPT) as required.

5. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Response: Thanks for your kind reminder. Thanks for your kind reminder. We have rearranged our highlights to meet the requirements of the journal and the editor.

6. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company

Response: Thanks for your valuable advice. We have sent our revised manuscript to a professional English language editing company to carefully check and revise the manuscript and have uploaded the relevant English Language Certificate to the system as required.