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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75460

Title: Development and validation of a nomogram for predicting overall survival in cirrhotic patients with acute kidney injury

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03555502
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2022-02-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-07 11:07

Reviewer performed review: 2022-02-09 13:05

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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 [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

The manuscript attempted to identify predictors of mortality in patients with cirrhosis and acute kidney injury and establish a nomogram for predicting overall survival in cirrhotic patients with AKI. A nomogram incorporating predictors including presence of diabetes, HE, INR, serum sodium and peak SCr levels were developed and showed good predictive discrimination and calibration for the mortality of such patients. The idea of the manuscript is novel, and the research results have certain clinical value. Although I appreciate the authors' effort on this study, there are still some unaddressed issues in the work. My detailed comments are as follows: 1. How about the Child-Turcotte-Pugh (CTP), the model for end-stage liver failure (MELD) and MELD-Na score exhibited in predicting mortality in previous studies? 2. A nomogram incorporating predictors including presence of diabetes, HE, INR, serum sodium and peak SCr levels were developed and showed good predictive discrimination and calibration for the mortality of patients with cirrhosis and acute kidney injury. Please explain the possible reasons why every factor could play a role to predictive discrimination. 3. Figures and tables should be improved to make it easier for readers to understand and make the manuscript look better. What is the x-coordinate of Figure4 d? 4. In this manuscript, INTRUDOCTION and DISCUSSION should be well organized, and the logic is not good. The authors need to cite and discuss some recent findings as follows in the discussion and introduction to enhance my above concerns: 1. Hu L, Gao L, Zhang D, Hou Y, He LL, Zhang H, et al. (2022). The incidence, risk factors and outcomes of acute kidney injury in critically ill patients undergoing emergency surgery: a prospective observational study. BMC Nephrol, 23:42. 2. Sun D, Wang J, Shao W, Wang J, Yao L, Li Z,

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et al. (2020). Pathogenesis and Damage Targets of Hypertensive Kidney Injury. J Transl Int Med, 8:205-209. 3. Martins CB, De Bels D, Honore PM, Redant S (2020). Early Prediction of Acute Kidney Injury by Machine Learning: Should We Add the Urine Output Criterion to Improve this New Tool? J Transl Int Med, 8:201-202. Once the authors revise the manuscript according to my concerns, and cite and discuss those studies in the revised version, I am happy to re-evaluate it. I am looking forward to getting a revised version based on my above suggestions.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

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Reviewer's code: 06151472
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: Italy
Author's Country/Territory: China

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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 [Y] Major revision [ ] 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

I would like to thank for the opportunity to revise this manuscript. This was a retrospective, single center study which investigated the prognostic role of AKI in patients with cirrhosis admitted to the hospital. The Authors consecutively considered 250 patients, who were further divided in a training and a validation cohort. A nomogram was created from the training cohort to predict mortality in patients with AKI. The paper is of interest, well-written and easy to understand. The topic in of interest, although not novel. Major comments - I do not understand why the Authors used many different criteria for diagnosis of AKI. This point does not make, in my opinion, these data suitable for reproducibility in other centers. As the Authors stated, there are several definitions of AKI in cirrhosis. I suggest to revise this paper using one of these definitions (e.g., ICA classification). - I do not understand the role of liver transplantation: how many patients underwent LT? All of these were at least evaluated for transplant? This is an important point, in my opinion, because transplant can be considered a competing event with death in such patients, if they were suitable for transplant. -The study focused on AKI at any stage. Therefore, the nomogram could be useful both for AKI I and III. Furthermore, this nomogram can be used for any type of AKI (ATN, HRS, pre-renal AKI), even if, as the Authors said, the outcome of these types of AKI significantly differs. I suggest more granularity about these points. - Similarly, it would be interesting to see if patients died of renal-related causes or not. How many patients were discharged within 180-d? - I do not understand if patients admitted to ICU for CVVH or patients undergoing CRRT due to AKI were included or not. - When was diagnosed HE? At time of AKI, during hospitalization? - Discussion section. The

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Authors said that they included patients with compensated and decompensated cirrhosis. Nevertheless, the mean CHILD Pugh was 10, reflecting patients with decompensated disease. Moreover, the short-term outcome mirrors the outcome of a cohort of decompensated patients more than compensated ones. - I agree with the Authors when they said that this nomogram could be useful to select those patients who are at highest risk of death. What could be the best treatments to be offered to these patients? Early RRT? Minor comments - There are some typos to be corrected (Table 1: live-→ liver) - Table 1: not all patients had Hep B cirrhosis.

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Title: Development and validation of a nomogram for predicting overall survival in cirrhotic patients with acute kidney injury

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02567669
Position: Editorial Board
Academic degree: MD

Professional title: Emeritus Professor

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] 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 [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

This is a very interesting manuscript that deals with prognosis of patients with liver cirrhosis who have acute kidney injury. My concern is the following: Acute kidney injury is caused by numerous different factors, e.g. nephrotoxic antibiotics, X-ray contrast media, diuretics, among others. 1. How is the underlying cause of AKI considered in the present mansucript? 2. The "functional kidney failure" - the hepato-renal syndrome is categorized in type 1 (bad prognosis) and type 2 (better prognosis). Does the nomogramm reflect this difference. 3. There are many measures to treat AKI in liver cirrhosis. The high rate of patients with ascites suggests that diuretics were given to the patients. What's about terlipressin? Influence on the nomogramms?

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Manuscript NO: 75460

Title: Development and validation of a nomogram for predicting overall survival in cirrhotic patients with acute kidney injury

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02541712
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Associate Professor, Chief Physician
Reviewer's Country/Territory: Slovakia
Author's Country/Territory: China

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Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

1. I read with interest the manuscript entitled "Development and validation of a nomogram for predicting overall survival in cirrhotic patients with acute kidney injury". The findings of the study are original and I think that they would be of interest for the readers of the Journal. 2. The concept they propose could be used in clinical practice to help clinicians in identifying high-risk vs. low-risk patients with cirrhosis and AKI. 3. Limitations are well described. I have come comments and questions: 1. It is not clear to me, if all patients were hospitalized or not. At some point in the discussion authors state, that they also included patients with "compensated cirrhosis", which was surprising since AKI (and 60% ACLF) is usually diagnosed in the context of acute decompensation and highly likely a hospitalisation. Authors should elaborate on the inclusion criteria, routine controls, or hospital admissions? 2. What was the principle etiology of AKI in these patients, are there any data on that? Did AKI etiology actually influence the prognosis? (AKI-HRS vs. prerenal AKI). 3. The nomogram is included, but I am not sure how to use it in practice, could authors describe more in detail, how to calculate it in practice - mathematical formula is usually included. 4. Were any patients of these patients liver transplanted ? If so, how many, and how were they handled statistically?

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Title: Development and validation of a nomogram for predicting overall survival in cirrhotic patients with acute kidney injury

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Reviewer's code: 05934449
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

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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 [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

Wan et al. established a nomogram to predict the overall survival rate of cirrhotic patients with AKI through risk factor assessment. The manuscript has the following deficiencies. 1. On "Short title", the main body of the article is “cirrhosis”, so it should not be ignored, but should be included in the Short title. 2. 250 eligible patients were randomly divided into training cohort (n = 173) and validation cohort (n = 77). The difference in the number of cases between the two groups was more than twice. What method is used here? It should be clear. 3. In Figure 1, the total number of cirrhotic patients with AKI is 382, compared with 305 in the text (page 5). Why? Please clarify. 4. The logarithm based on constant e is a natural logarithm and should be recorded as lnN instead of logeN. The latter is not concise enough and should be modified.. 5. In “Calculations of the CTP, ……” section, there are four times signs (×) symbol is in Chinese format, please change it to the Western format. 6. This is a retrospective research, the cases were selected from January 2015 to December 2016, but the ICA consensus, one of the diagnostic criteria cited by the author, was published in April 2015 (according to Ref. 1). Its publication time later than the starting point of the study. How to deal with the previous cases? The author should make an explanation. Similarly, it has been more than 6 years since 2015. Why does the author limit the time to 2016 instead of now? If the research time is up to now, the number of cases can be greatly increased. Please clarify. 7. Throughout the full text, all percentages expressed as (n = 190, 76.0%) or 69.6% (n = 174) should be modified to (190/250, 76.0%) or 69.6% (174/250). All confidence limits expressed as “95% CI 1.081 – 1.787” should be modified to “95% CI, 1.081 – 1.787”, or “95% CI = 1.081 – 1.787”, or “95% CI: 1.081 – 1.787”. Choose any one and keep the full text

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consistent. 8. With regard to patient selection, cirrhosis should be the first, followed by AKI. Therefore, the order of inclusion criteria (1) and (2) should be adjusted to each other. 9. It is equally a quantitative observation indicator. Why only the heart rate and peak SCr given the cut-off values, while other indicators do not? What is the basis for the selection of their cut-off values? Please clarify. In Figure 3, the unit of peak SCR should not be “mg/ml”, but the “times baseline”. 10. It may be more reasonable to change the “independent predictors” into “potential risk factors” in this paper.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75460

Title: Development and validation of a nomogram for predicting overall survival in cirrhotic patients with acute kidney injury

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03555502
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

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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
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Author and colleagues set out to determine the risk factors for mortality in patients with cirrhosis and complicated with AKI. The workload of this study is relatively sufficient and the study process is logical. Apart from these achievements, new biomarkers and innovative predictive methods are expecting in the future study.

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Reviewer's code: 02567669
Position: Editorial Board
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Professional title: Emeritus Professor
Reviewer's Country/Territory: Germany
Author's Country/Territory: China

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Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript is now suitable for publication.

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Reviewer's code: 06151472
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: Italy
Author's Country/Territory: China

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] 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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

the Authors fairly answered my previous comments. No further remarks.