List of Responses

Subject: Revision and Response to Reviewer's Comments for the Manuscript "Establishment and evaluation of a prognostic model for patients with unresectable gastric cancer liver metastases" (No.: 92656)

Dear Editors and Reviewers:

We appreciate the time and effort that you and the reviewers have dedicated to providing your invaluable and professional feedback on our manuscript. Your comments have been instrumental in refining our work and have significantly contributed to the improvement of our research. After thorough consideration of each comment, we have diligently incorporated the suggested revisions, which are highlighted the revised/added contents with yellow color within the manuscript.

Responds to comments:

Reviewer #1:

This study identifies pivotal prognostic factors and introduces a nomogram model for predicting individualized prognosis in GCML. The authors found five independent risk factors including albumin levels, primary tumor size, presence of extrahepatic metastases, surgical treatment status, and chemotherapy administration. This retrospective study is well organized, however, some major issues were raised.

1-Comment: The AUC of 0.7-0.8, 0.8-0.9, and 0.9-1.0 indicate fair, good, and excellent predictive accuracies, respectively. The AUC for OSs from 1 to 3 years is fair, so please change the article including the Abstract accordingly.

Reply: Thank you for your feedback regarding the AUC values and their corresponding predictive accuracies. We appreciate your insight into the classification of AUC ranges. We have duly noted your suggestion to update the article, specifically in the Abstract section, to reflect that the AUC for OSs from 1 to 3 years is fair. We have make the necessary adjustments in the revised manuscript to accurately convey this information.

In response to your concern about the AUC values for 1 to 3 years being considered "fair," I would emphasize that while the AUC values for those time points may fall within the fair range (0.753-0.859), they still demonstrate a reasonable level of predictive accuracy according to

established criteria. Moreover, the AUC values for the nomogram model at these time points exceed the acceptable threshold of 0.7, indicating a meaningful predictive capacity.I could elaborate by noting that although the AUC values for 1 to 3 years may not reach the higher levels of predictive accuracy (good or excellent), they are still indicative of a useful predictive tool.

2-Comment: It is unclear which variables were enrolled into the multivariate analysis. Please describe the method in the Statistical analysis. Age and gender should be included in multivariate analysis. There was a significant difference in BMI in univariate analysis, but was it enrolled into multivariate analysis?

Reply: Thanks for your feedback regarding the variables included in the multivariate analysis, we have addressed this concern in our revised manuscript. We have clarified in the Statistical Analysis section that all variables showing statistical significance ($P < 0.05$) in the univariate analysis (as presented in Table 2) were included in the multivariate analysis. Specifically, we stated, "Prognostic variables with P-value < 0.05 in the univariate Cox regression analysis were further included in the multivariate Cox regression analysis." Regarding age and gender, although they did not show statistical significance in the univariate analysis ($P > 0.05$), we have explicitly mentioned in our methodology that BMI was included in the multivariate analysis. However, as the final results indicated a P-value > 0.05 for BMI, it was subsequently not retained in the final model. Furthermore, we have updated the relevant content in Table 2 to reflect these adjustments accurately. These modifications ensure transparency and clarity in our analysis approach and variable selection process. Thank you for bringing this to our attention, and we believe these revisions enhance the robustness and integrity of our study findings.

3-Comment: Since gastric cancer and H. pylori infection status have a clinically important relationship, they should be included in the analysis. Did you assess this relationship?

Reply: Thank you for your inquiry regarding the assessment of the relationship between gastric cancer and H. pylori infection status in our analysis. In our study, we focused on evaluating patients with unresectable advanced gastric cancer with liver metastasis. Given this specific patient population under investigation, we did not include the variable of H. pylori infection status in our model. While we acknowledge the clinical significance of the association between H. pylori

infection and gastric cancer development, our research was aimed to address the outcomes and characteristics of patients with advanced stages of gastric cancer and liver metastasis where the focus was on different variables pertinent to their condition.

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Responds to comments:

Reviewer #1:

1-Comment: Age and sex are clinically significant factors for this study. The variables that are enrolled into multivariate analysis must be clinically significant rather than statistically relevant. Therefore, even if age and sex are not significantly associated in univariate analysis, they should be included in multivariate analysis.

Reply: Age and sex are important clinical factors for this study. Although they did not show statistical significance in the univariate Cox regression, we still included them in the multivariate COX regression for analysis. Finally, 8 clinical factors were included in multivariate COX regression analysis. We have added this point in the results section and Table 2 of the revised manuscript.

2-Comment: Although the section on Statistical analysis has been revised, the method for selecting explanatory variables used in multivariate analysis is still not clear.

Reply: The 20 clinical facors underwent univariate Cox regression analysis to evaluate their individual associations with the outcome. Subsequently, significant prognostic variables ($P < 0.05$) related to GCLM were incorporated into multivariate Cox regression to identify independent risk factors for predicting patient prognosis. We have added this point in the methods and results

section of the revised manuscript.

3-Comment: Regarding the relationship with H. pylori, please explain in the limitations why this was not included in the analysis, given that most cases of gastric cancer are infected with H. pylori.

Reply: H. pylori infection is prevalent in most cases of gastric cancer, but our analysis concentrated on factors directly impacting the prognosis of patients with gastric cancer liver metastases, aiming to provide a targeted and detailed investigation in this specific context. Therefore, the relationship with H. pylori was not included in our study. We have explained this point in the limitations section of the revised manuscript.