RESPONSE TO LETTER

Gamma-Glutamyl Transpeptidase to Neutrophil Ratio: Prognostic Indicator for Hepatocellular **Carcinoma Patients Post-Curative Resection** [Response to Letter]

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Dear editor

We have thoroughly reviewed the letter to the editor regarding our article titled "Gamma-Glutamyl Transpeptidase to Neutrophil Ratio as Prognostic Indicator for Hepatocellular Carcinoma Patients Post-Curative Resection" written by Yu Hao.^{1,2} It is an insightful letter that addresses several inquiries of our interest. In response, we have prepared a detailed response to each of the raised concerns.

1. First, although the utility of the Cox regression model is widely recognized, it may inadvertently lead to an overestimation of risk in the presence of potentially competing risks. Therefore, for the assessment of prognostically relevant independent factors explored in this article, especially when other competing outcome events occur, the use of competing risk model seems more appropriate. While traditional survival analysis techniques may not adequately account for the impact of secondary events on the primary study outcome, contributing to assessment bias, competing risk model provides a more comprehensive analytical perspective.

Response 1: Thank you for your valuable suggestion. We agree with your point that in cases where other competing outcome events occur, a competing risk model can provide more accurate results for the outcome events. In our current study, for recurrence-free survival (RFS), we reanalyzed using a multivariable competing risk model, which showed that a high GNR level was associated with poor RFS (HR: 2.28; 95% CI: 1.24–4.20; P < 0.01). This is consistent with the previous multivariable Cox analysis results (HR: 2.37; 95% CI: 1.38-4.08; P < 0.01).

2. Second, the authors are to be commended for incorporating important information such as demographic characteristics and laboratory tests to adjust for potential covariates. However, we recommend further expansion of the covariates. The study showed a higher incidence of postoperative complications of HCC in patients with low and high body mass index (BMI) compared with patients with normal BMI, and it can be inferred that BMI may be an important covariate affecting clinical prognosis.4 Moreover, in order to assess the stability and reliability of the results more comprehensively, lifestyle such as smoking and alcohol consumption should also be considered.

Response 2: Thank you very much for your insightful suggestion. Due to limitations in the retrospective nature of the study, there are a significant number of missing values for patients' BMI and lifestyle factors (such as smoking and alcohol consumption). Therefore, we did not include these variables in the current analysis. We agree with your point that

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BMI and lifestyle are related to the prognosis of HCC patients, and we are currently working on collecting more patient data and expanding the sample size for further analysis. Once again, thank you for your suggestion.

3. In addition, this article focuses on the relationship between GNR and postoperative HCC in the general population. Given previous studies on type II diabetes mellitus and HCC, subgroup analyses based on blood glucose levels may enhance the applicability and generalizability of the results of study.

Response 3: Thank you very much for your careful suggestion. Investigating the history and treatment of type II diabetes mellitus is not included in the current dataset. Therefore, relying solely on a subgroup analysis based on blood glucose levels may have certain limitations in interpreting the results. Your suggestion has provided us with a new research perspective. We hope to further collect more data in future studies to analyze the impact of type II diabetes mellitus on the prognosis of HCC patients.

Disclosure

The authors report no conflicts of interest in this communication.

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 Shen X, Niu X. Gamma-glutamyl transpeptidase to neutrophil ratio as prognostic indicator for hepatocellular carcinoma patients post-curative resection. J Hepatocell Carcinoma. 2024;11:2077–2085. doi:10.2147/JHC.S478186

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^{1.} Hao Y. Gamma-glutamyl transpeptidase to neutrophil ratio: prognostic indicator for hepatocellular carcinoma patients post-curative resection [Letter]. J Hepatocell Carcinoma. 2024;11:2391–2392. doi:10.2147/JHC.S508062