Peer Review File

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Reviewer A

First of all, the current conclusion is misleading because the authors did not have an independent sample to validate the predictive value of GLR and the AUC of 0.698 was also poor. The current data were not feasible to answer the question of prognosis prediction accuracy. Please focus on the prognostic value of GLR.

Second, the title did not indicate the clinical research design of this study, i.e., a retrospective cohort study.

Third, the abstract needs further revisions. The background did not indicate the clinical needs for this research focus and why the GLR is a potential predictor in HCC. The methods need to describe the inclusion of subjects, the assessment of baseline factors and GLR, follow up procedures, and measurements of prognosis outcomes. The results need to briefly summarize the baseline clinical characteristics of the sample and report the HR and P values of the identified factors. The conclusion needs to be revised according to my above comments.

Fourth, in the introduction of the main text, the authors need to review what has been known on the prognostic factors and biomarkers in HCC, explain how GLR was developed, indicate why GLR is a potentially important prognostic factor, and why the GLR is better than globulin alone and LDL-C alone, as a prognostic factor.

Fifth, the methodology of the main text needs to describe the clinical research design and sample size estimation. In statistics, the focus should be to investigate the independent prognostic role of GLR, not to identify all significant prognostic factors. Please specify these details and ensure $P<0.05$ is two-sided.
Reviewer A Thank you very much for your advices, as per your requests I have revised our article and the following is the response to each of your suggestions:

Reply 1: We greatly appreciate your suggestions and we have revised our conclusions (see Page 16, line 327-329).
Reply 2: Following your recommendation, we have modified our title as advised (see Page 1, line 2).
Reply 3: We are very grateful for your valuable comments on our abstract, and as you suggested, I have made a complete revision of my abstract section (see Page 2-4, line 24-81).
Reply 4: Thank you for your recommendation, we have added the relevant content in the introduction (see Page 6, line 109-117).

Reply 5: We thank you for your proposal, we have added experimental design content (see Page 6, line 123). Since this study was a retrospective study, no sample size calculation was performed. we have added the relevant content in the material method (see Page 9, line 174-184).

Reviewer B

Low-density lipoprotein and globulin have been found to be predictors for some malignant tumors, but their predictive value in hepatocellular carcinoma (HCC) has hardly been elucidated. In the manuscript "Prognostic significance of globulin/low-density lipoprotein ratio in patients with hepatocellular carcinoma after local ablative therapy", authors assessed the prognostic significance of globulin to low-density lipoprotein ratio (GLR) in HCC patients before ablation.
Couple questions are required to be answered before it will be accepted.
(1) The serum low-density lipoprotein was the crucial topic in the study. What were the roles of low-density lipoprotein in the process of HCC? Please state in the introduction.
(2) It was advised to add reference (DOI: 10.21037/apm-20-451) about low-density lipoprotein in the introduction.
(3) Globulin could be an independent risk factor for the incidence of colorectal and stomach cancers. How about the globulin for HCC?
(4) In the text, "Students t-test" should be revised to "Student's t-test".
(5) In the study, the GLR data were collected before ablation. How about the GLR data after ablation? Whether it also could be used as prognostic biomarkers? Please state in the discussion.
(6) In the study, the patients were undergone local ablative therapy. Whether the patients were treated by surgical resection, the GLR could be used as prognostic biomarker for patients? Please state in the discussion.
(7) Compared to other prognostic biomarkers for HCC, what were the advantages of GLR? Please state in the discussion.
Many thanks for your suggestions, I have revised our article and the following is a response to each of your recommendations:
Reply 1: Thank you for your advice, we have added relevant content (see Page 5, line 97-100).
Reply 2: We appreciate your suggestion and have added relevant content (see Page 5, line 98).
Reply 3: According to previous literature, high preoperative serum globulin in hepatocellular carcinoma is a risk factor for poor survival. We have added the relevant content (see Page 6, line107-108).
Reply 4: Thank you for your reminder, we have revised the relevant content (see Page9, line 117).
Reply 5: This is a retrospective study to predict HCC patient prognosis by collecting baseline data. Ultimately, baseline GLR was found to be a marker to predict outcome in HCC patients after ablation. Due to the lack of complete post-ablation data for all

patients in this study, research on the predictive value of GLR after ablation was not performed. Related content has been reflected in our revised article (see Page 15, line 320-323).

Reply 6: For early-stage HCC patients, ablative therapy and surgery are equally effective and are recommended as first-line treatment by guidelines. In this study, all patients received ablative therapy and did not receive surgical treatment. Since the two treatment modalities may affect GLR differently, whether GLR is predictive of surgical patients will need to be demonstrated in further surgical cohorts in the future. We have added the contents above to the discussion (see Page 15, line 312-316).

Reply 7: In contrast to other predictive markers, GLR is a ratio of common and easy-to-obtain indicators in clinical practice. Also, the calculation of the ratio of the two variables is relatively straightforward, facilitating clinical utilization. We have added the relevant content in the discussion (see Page 14, line 298-301).