Peer Review File

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Reviewer A

1) First of all, my major concern regarding this paper is whether the current data are appropriate to examine the predictive accuracy of SII index because of its low sensitivity and poor specificity. The authors also analyzed the diagnostic accuracy of other biomarkers but did not consider to combine them together with SII index to improve the diagnostic accuracy. Because this is a failed diagnostic test, I suggest the authors to focus on the independent prognostic role of SII index, not to test its predictive accuracy.

Reply1: We have revised the title and the conclusion accordingly. Thanks. See page 1, line 2; and page 7, line 226-228.

2) Second, accordingly, the title needs to indicate the focus of the prognostic role of SII index and the clinical research design, i.e., a retrospective cohort study.

Reply 2: We have revised the title accordingly. See page 1, line 2-4.

3) Third, the abstract is not standardized and needs further revisions. The background did not explain why SII index is potentially associated with the prognosis of PLC and what the knowledge gap is. The methods did not describe the assessment of baseline clinical factors, follow up details, and diagnoses of recurrence or metastasis, as well as the statistical methods for ascertaining the independent prognostic role of SII. The results need to briefly summarize the clinical characteristics of the study sample, and the independent prognostic role of SII by using OR and P values. P=0.000 should be expressed as P<0.001. The conclusion should be made strictly based on the findings of this study.

Reply 3: Thanks for your advise. We have tried our best to revised the abstract. However, due to the limitations of the words (not more than 350 words. Now it was 349 words), we failed to add some content in the abstract. See page 2-3, line 36-67.

4) Fourth, the introduction needs to review known prognostic factors in PLC, have comments on the limitations and knowledge gaps of prior studies, review on the incidence rates of recurrence or metastasis in PLC after interventional therapy, and clearly clarify the clinical significance of the focus on the prognostic role of SII in PLC.

Reply 4: We have revised the introduction accordingly. See page 3-4, line 84-102.

5) Fifth, the methodology of the main text needs to correctly describe the clinical research design, sample size estimation, and follow up details of this study. In statistics, please delete the ROC analysis, and describe the details of multiple Cox regression analysis for the independent prognostic role of SII index.

Reply 5: We have added the Multivariate regression analysis, see table 4.

6) Finally, please consider to cite the below papers to enrich the background and discussion of this paper: 1. Yu Y, Fu J, Xia P, Chu C. A systematic review and meta-analysis on the

efficacy and safety of transcatheter arterial chemoembolization combined with radiofrequency ablation in the treatment of primary liver cancer. Transl Cancer Res 2022;11(5):1297-1308. doi: 10.21037/tcr-22-816. 2. Wang T, Dong J, Zhang Y, Ren Z, Liu Y, Yang X, Sun D, Wang Y. Efficacy and safety of hepatic artery infusion chemotherapy with mFOLFOX in primary liver cancer patients with hyperbilirubinemia and ineffective drainage: a retrospective cohort study. Ann Transl Med 2022;10(7):411. doi: 10.21037/atm-22-978. 3. Han R, Tian Z, Jiang Y, Guan G, Sun X, Yu Y, Zhang L, Zhou J, Jing X. Prognostic significance of systemic immune-inflammation index and platelet-albumin-bilirubin grade in patients with pancreatic cancer undergoing radical surgery. Gland Surg 2022;11(3):576-587. doi: 10.21037/gs-22-117. 4. Wang J, Yin S, Chen K. Predictive value of the systemic immune-inflammation index for the efficacy of neoadjuvant chemotherapy and prognosis in patients with stage III ovarian cancer—a retrospective cohort study. Gland Surg 2022;11(10):1639-1646. doi: 10.21037/gs-22-459.

Reply 5: We have added in the content. See refs 5, 32 and 33.

Reviewer B

Abstract

1. Page 2 line 50-51: The result (19.64% vs. 8.12%, 51 P=0.005) is confusing please rewrite as per group.

Reply: Thanks for your comment. We have revised in the revised manuscript.

Changes in the text: Compared with the control group (8.12%), the proportion of patients with ≥2 lesions in the recurrence or metastasis group (19.64%) was significantly increased (P=0.005). See page 2-3, line 51-53.

2. Results mentioned in the abstract should be concise and mature. Please mention ±SD/SE for all the results provided in numerical form.

Reply: We added the results in the abstract.

Changes in the text: Systemic immune inflammation index was valuable in predicting recurrence or metastasis, and the area under the curve was 0.795 [95% confidence interval: 0.742–0.848, P<0.001]. See page 3, line 61-64.

3. Study is based on the relevance of "immune inflammation index" the required information is missing in abstract which give different impact after reading the abstract. Author should rewrite the abstract in such a way that indicates the association of immune inflammation index with liver cancer recurrence and metastasis.

Reply: It was provided in the background.

Changes in the text: This study aimed to investigate the association between the systemic immune inflammation index and recurrence or metastasis after interventional therapy in patients with PLC. See page 2, line 38-40.

Introduction

4. Page 3-4 line 74-94: The introduction part misinterprets the relevance of the present study. It should be given TACE and AFP should be mentioned in 2-3 lines with their limitations. The

entire intro part should be focused on “immune inflammation index” and its relevance as a predictor recurrence and metastasis in other cancer.

Reply: We have revised the introduction accordingly and deleted some contents.

Changes in the text: Please see page 2-3, line 81-98.

Methodology

5. Major concern in this section is sample size calculation which I am not able to see. Author should provide the formula and statistical analysis on which ground the sample size has been considered as this has potential effect on study claim, output, reproducibility and authenticity of the results.

Reply: We have added in the method.

Changes in the text: See page 4, line 106-109.

6. Other important concern of the study is the absence of proper demography of the study individual. Moreover, there no mentioning of exclusion and inclusion criteria for the individuals involved in the study.

Reply: We have added accordingly.

Changes in the text: See page 4, line 112-120 and page 6, line 162 and page 15, figure 1.

7. Pathological evidence and other parameters for metastasis is missing in methodology section.

Reply: We have added related content in the methodology.

Changes in the text: Recurrence rate or metastasis: At least once a year after surgery, liver magnetic resonance imaging, abdominal computed tomography, head computed tomography, and chest computed tomography examinations should be performed. If imaging suggests recurrence or metastasis, lesion biopsy should be performed to confirm the presence of recurrence or metastasis. See page 5, line 148-152.

8. There is no reference in the methodology section. Author should mention that on what basis and parameters the metastasis and immune inflammation index have been selected.

Reply: We have added in the methodology section.

Changes in the text: ⑴ Recurrence rate or metastasis: At least once a year after surgery, liver magnetic resonance imaging, abdominal computed tomography, head computed tomography, and chest computed tomography examinations should be performed. If imaging suggests recurrence or metastasis, lesion biopsy should be performed to confirm the presence of recurrence or metastasis. ⑵ Systemic immune inflammation index: Platelet count x Neutrophil count/Lymphocyte count (15). See page 5, line 148-153.

Results and discussion

9. The discussion is done in a qualitative manner. It should be quantitative in nature as the study deals with the “prediction value”.

Reply: We have revised the manuscript. Page 8, line 228-232.

Changes in the text: A study in patients with hepatocellular carcinoma has also shown that elevated systemic immune inflammation index is a risk factor for poor prognosis in liver transplant patients, and systemic immune inflammation index was valuable in predicting the survival, the area under the ROC curve was 0.632 (27).