

Dear Editors and Reviewers:

Thanks very much for your letter and for the reviewers' comments concerning our manuscript entitled "Change of tumor-infiltrating lymphocyte in the perioperative period of associating liver partition and portal vein ligation for staged hepatectomy for massive hepatocellular carcinoma" (75201). These comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to this research. We have studied comments carefully and have made some corrections. The responds to the reviewer's comments are below:

Dear Reviewer #1:

1.Biostatistics. The authors did not provide a formal biostatistical certificate.

Response: The statistical methods of this study were reviewed by a biostatistician of Department of Hepatobiliary Surgery, The First Affiliated Hospital of Guangxi Medical University. At the same time, he provides a formal biostatistical certificate.

2.Moreover, several issues regarding their statistical analysis plan should be clarified, such as: -normality test results should be provided as supplementary data.

Response: We added normality test results in supplementary file format.

3.PSM module approach should be further clarified.

Response: As suggested by the reviewer, we have added PSM modeling to the methods section of the manuscript.

4.References. The references adhere to the journal principles

Response: We have reformatted the references in accordance with the standard principles of this journal.

5.The overall quality of the manuscript is low; The manuscript needs an extensive review by an English native speaker.

Response: The manuscript has been polished by a professional English language center.

6.The manuscript does not report adherence to specific reporting guidelines

Response: Based on the reviewers' comments, we present the process and reporting guidelines of this study in the form of a STROBE Statement, which gives the reviewers a clearer understanding of the content and structure of our study.

7.14 Ethics statements. The informed consent template was not provided by the authors.

Response: We have added the informed consent technique for this study to the revision system. All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

8.Please provide data regarding perioperative KI therapy

Response: Our article focuses on evaluating the feasibility of ALPPS as an innovative surgical approach for massive hepatocellular carcinoma from an immunological perspective, while also confirming that CD8⁺ T cell infiltration is associated with increased tumor necrosis. For perioperative KI treatment in patients with hepatocellular carcinoma, we will study this in more depth in the future.

Dear Reviewer #2:

1. Table 3 was suggested to integrate into Figure 2 legend, at least, Figure 2 legend should be mentioned the different color shown in Table 3.

Response: According to the suggestion of the reviewer, we integrate Table 3

with the legend of Figure 2, which makes the article more concise and convenient for readers.

2. In Figure 1, some letters were covered by the border line; In addition, some other minors: Correct 3% H₂O₂ to 3% H₂O₂ (Subscript); and (3) FLR/SLV > and (3) FLR/SLV; expressed as quantity (%). > expressed as quantity (%); 36.9% (21.6% ~ 45.4%) > 36.9% (21.6% -45.4%), as well as ~ in all the Tables. Abbreviations such as alpha-fetoprotein (AFP) showed twice in the manuscript.

Response: We are grateful to the reviewers for their careful comments and we have reworked these irregularities and improved the manuscript.

Using journal style for the words and references in the manuscript.

Response: We have improved the words and references in the article to make the article more in line with the standards of this journal.

Dear Science editor:

This manuscript explored the role of tumor-infiltrating lymphocyte (TIL) subsets in the tumor microenvironment and assesses the feasibility of liver zoning and portal junction in the treatment of massive hepatocellular carcinoma (HCC) by staged liver resection (ALPPS).

1.Please provide data on perioperative KI treatment;

Response: Our article focuses on evaluating the feasibility of ALPPS as an innovative surgical approach for massive hepatocellular carcinoma from an immunological perspective, while also confirming that CD8⁺ T cell infiltration is associated with increased tumor necrosis. For perioperative KI treatment in

patients with hepatocellular carcinoma, we will study this in more depth in the future.

2.in Figure 1, some letters are covered by border lines, please revise; it is suggested to integrate Table 3 into the figure 2 legend;

Response: We are grateful to the Science editor for their careful comments. The parts of this study manuscript that have shortcomings have been carefully checked and revised, and the perfected manuscript has been submitted to the revision system.

3.please revise the language further.

Response: This study manuscript was polished by a professional language editing center and the language editing certificate was made available in the revision system.

4.Please verify all ethical documents again. The title in the Institutional Review Board Approval Form or Document is inconsistent with this manuscript, and the Signed Informed Consent Form(s) or Document(s) are not provided; etc.

Response: We verified all ethical documents again and filled in all the missing information.

Once again, thanks very much for your comments and suggestions.

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Thank you and best regards!