

Round 1

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "*Impact of perioperative blood transfusion on oncological outcomes in ampullary carcinoma patients underwent pancreaticoduodenectomy*" (ID: 83592).

Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: **(the language writing requires major improvements)**

Response: Thanks for your suggestion. We tried our best to improve the manuscript and made some changes to the manuscript. These changes will not influence the content and framework of the paper. In addition, we used language editing services provided by the biomedical editing companies to help polish our article as suggested by the editor. And we hope the revised manuscript could be acceptable for you. Special thanks to you for your good comments.

Reviewer #2:

1. Response to comment: **(Only the comparison between blood transfusion group and non-transfusion group in blood loss patients who need blood transfusion during surgery can give the correct prognostic value of PBT on survival, the reasonable use of transfusion provides no useful information for doctors, because doctors have no method to decide PBT before surgery)**

Response: We sincerely thank the reviewer for careful reading. Transfusion could restore hemodynamic stability for blood loss patients who need blood transfusion during surgery, and then we want to compare patients who received PBT with who did not underwent pancreaticoduodenectomy. Because previous studies showed transfusion related with immune modulation, however its influence on immune competence in the recipient and its effects on cancer recurrence after a curative resection remains controversial. An association between perioperative transfusion of allogeneic blood products and risk for recurrence has been shown in colorectal cancer in randomized trials; whether the same is true for ampullary carcinoma remains to be determined. We apologized for not explaining the purpose of this study clearly, causing inconvenience and misunderstanding, and we added relevant background in the “introduction” part marked with red text.

We fully agree with the reviewer that doctors have no method to decide PBT before surgery and PBT may be life-saving in some circumstance, but there has been growing evidence that transfusions are associated with adverse postoperative outcomes. There were still unreasonable transfusion during surgery. We think increasing frequency of monitoring of hemoglobin, reasonable and restrictive perioperative transfusion practices are a possible strategy to reduce sepsis rates and improve survival after colon cancer surgery.

2. Response to comment: **(what is the "short-term" survival, a month? 3 months?)**

Response: We were really sorry for our careless mistakes, we added the definition “Short-term was defined as the index hospitalization and Long-term was defined as discharge during the follow-up period” in the “MATERIAL AND METHODS” part marked with red text.

3. Response to comment: **(Abstract part: The effect of perioperative blood transfusion on the prognosis of "digestive system tumors" is still debated. should be "ampullary carcinoma")**

Response: We have revised it to “ampullary carcinoma” according to the reviewer’s suggestion and marked with red text.

Reviewer #3:

1. Response to comment: **(they must highlight what their manuscript adds to the medical literature)**

Response: We added the “**ARTICLE HIGHLIGHTS**” section at the end of the article and marked with red text.

2. Response to comment: **(Please add more recent references)**

Response: We sincerely appreciate the valuable comments. We used RCA as recommended, and enter the keywords and to find the latest highlight articles. We have checked the literature carefully and updated most of the references. However, we have to cite an old literature since there are few studies on the relationship between ampullary carcinoma and blood transfusion.

3. Response to comment: **(The style, language and grammar require minor revision)**

Response: Thanks for your suggestion. We tried our best to improve the manuscript and made some changes to the manuscript. In addition, we used language editing services provided by the biomedical editing companies to help polish our article as suggested by the editor. And we hope the revised manuscript could be acceptable for you. Special thanks to you for your good comments.

4. Response to comment: **(The figure legends should not contain abbreviations)**

Response: We deleted the abbreviations in the the figure legends according to the basic rules on abbreviations.

5. Response to comment: **(The authors used reliable research methods. The accompanying data and methods are authentic. The use of statistics is appropriate but must be verified by professionals)**

Response: Our use of statistics was verified by professionals.

Company editor-in-chief #4:

Response to comment: **(the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of**

the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA))

Response: We sincerely appreciate the valuable comments. We used RCA as recommended, and enter the keywords and to find the latest highlight articles. We have checked the literature carefully and updated most of the references. However, we have to cite an old literature since there are few studies on the relationship between ampullary carcinoma and blood transfusion.

Other revision: **P values** which did not reach the threshold of statistical significance were deleted in “Abstract-results” part.

The manuscript was automatically generated and we have no idea about the figure and table, so we put **the revised manuscript** on the “**supplementary Material**” part, we were sorry for the inconvenience.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.

Round 2

Responds to the reviewer’s comments:

1. Response to comment: **(in the main text there are some sentences without citations. The style, language and grammar require minor revision)**

Response:

- 1) We sincerely thank the reviewers for carefully reading. We have checked the literature carefully and added the citation [15] in the end of **Discussion paragraph 3**; citation [28] in the **Discussion paragraph 4**, and marked with red color.
- 2) We changed the “**pancreaticoduodenectomy**” in the **Discussion paragraph 2** into “**PD**”, we also changed “**of**” to “**in**”, and marked with red color.

3) We changed “**may have impacted**” to “**might impact**” in the **Discussion paragraph 2**, and marked with red color.

4) We deleted “**and**” in the first sentence of **Discussion paragraph 5**.

2. Response to comment: **(Please offer the audio core tip)**

Response: We deleted the mp3 file named “**audio core tip**” in the zip.

3. Response to comment: **(the institutional review board (IRB) name, stated explicitly on the title page)**

Response: We add the name “**Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College**” on the title page.

4. Response to comment: **(Please fill out the "STROBE-Statement" with page numbers.)**

Response: We add **a new STROBE-Statement** with page number.

5. Response to comment: **(Please provide high-resolution figures (300 dpi).)**

Response: We submit the high-resolution figures (300 dpi) in a folder named “**Figure**”.

6. Response to comment: **(Please complete all the revisions based on the version of "2175-83592_Auto_Edited-v1", and upload above mentioned files in a ".zip" file.)**

Response: We completed all the revisions and upload the files.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.