

Dear Editors:

Thank you for your letter concerning our manuscript entitled "Short- and long-term outcomes of laparoscopic versus open surgery for T2 gallbladder cancer: a systematic review and meta-analysis" (NO: 80375). Those reviewers' 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 yellow in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Editor comments

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A). Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

--Respond:

At the request of the magazine, the manuscript was further polished by a professional English language editing company and a Certificate Of English Editing was attached to the supplementary file.

Reviewer #1:

The manuscript by Zhang et al. provided new systematic review on outcomes of laparoscopic versus open surgery for T2 gallbladder cancer. The review is conducted very well based on PRISMA guidelines. However, there are some minor issues before publication.

1. In abstract, the effectiveness of each operational method should be mention based on 1-RR. This method is very understandable for the readers.

--Respond: Thank you to the reviewers for this suggestion. For binary data, it is customary to use relative risk (RR) to assess the difference between two groups, even though 1-RR provides a visual representation of the difference between the two groups. RR is the ratio of the probability of an event occurring in the experimental group to that of the control group. 1-RR is the difference in the ratio of the probability of an event occurring in the experimental group to that of the control group. If 1-RR is positive, it means that the experimental group has decreased the probability of an event; if 1-RR is negative, it means that the experimental group has increased the probability of an event. In fact, both statistics are often used in statistics, but we use RR more often. We use RR and its 95% confidence intervals in both the abstract and the full text. If 1-RR were used, its 95% confidence interval would be more complex.

2. In search strategy I could not find supplementary material showing the full search strategy in each data-base.

--Respond: In accordance with the reviewers' comments, we have attached a search strategy for each database to *Supplementary file 1* to enable readers to replicate the search process.

3. For quality assessment the authors used NOS and Cochrane tools which were the best way for this concern. However, the reference citation for this part is missed. Please cite the following references for this

part: <https://doi.org/10.1002/jcsm.13043>, <https://doi.org/10.1093/ptj/pzab144>, <https://doi.org/10.1016/j.physio.2021.04.005>.

--Respond: Considering the reviewer's suggestion, we have revised and cited the literature mentioned.

4. The number of included studies is too small for this meta-analysis, which should be mentioned at least in the limitation.

--Respond: Considering the reviewer's suggestion, we have added a 4th limitation to the Limitations section, which was mentioned by the reviewer. The revised part of the article is marked in yellow.

5. In statistical analysis, it is mentioned 'Heterogeneity was assessed using the chi-square test, with the significance level set at $P = 0.05$.' please cite the following citation for this part: <https://doi.org/10.1002/jmv.27996>

--Respond: We have revised it in accordance with the reviewers' comments. The revised part of the article is marked in yellow.

Reviewer #2:

Specific Comments to Authors: The authors systematically reviewed the short-term and long-term outcomes of laparoscopic surgery (LS) versus open surgery (OS) for T2 gallbladder cancer (GBC). A meta-analysis based on the two groups found that the long-term outcomes of LS for T2 GBC are similar to those of OS, but LS is superior to OS in terms of operative time, intraoperative bleeding, and postoperative hospital stay. The article had specific clinical research value. However, the article's content was insufficient, and many substantive problems need to be solved.

My detailed comments are as follows:

Abstract Methods: It is suggested to supplement the selection of relevant outcome indicators and the risk of the bias assessment method.

--Respond: Considering the reviewer's suggestion, we refer to the study

outcome indicators in the results section of the abstract, the 9 points of the Inclusion criteria in the main text and the results in the main text. The outcome indicators are classified as dichotomous variables and continuous type variables. We have supplemented the methods used to assess both types of outcome indicators in the Methods section of the abstract, as well as the methods used to assess publication bias for each of the outcome indicators.

Results: It is suggested to add a statistical symbol to indicate the statistical difference between the two groups and the corresponding confidence interval.

--Respond: It has been revised in accordance with the reviewers' comments. Revised ones are marked in yellow.

Materials and Methods If the article is registered on PROSPERO in advance as required, please provide the CRD number, or according to the protocol implementation, the article will be explained accordingly.

--Respond: Considering the reviewer's suggestion, we have added a CRD number (CRD42022367334) to the article.

Search Strategy: It is suggested to supplement the start date of literature retrieval and retrieval strategy.

--Respond: Considering the reviewer's suggestion, we placed the search strategy into a new *Supplementary File 1*. The *supplementary Files* was reordered.

Inclusion criteria: "(ii) Intervention:" should introduce the intervention method, and the type of study should be presented separately. "(vi) Outcomes:" should be divided into primary outcome measures and secondary outcome measures

--Respond: We have revised it in line with the reviewers' comments. Revised

sections are marked in yellow.

Results "Figure 1 Flow Diagram": The exclusion process should be kept on the same side. "1. Search results and study selection": Some statements in the text are inconsistent with the content. It is recommended that the author check the relevant content for errata. Following: "These 5 publications involved 5 studies from Japan and 4 studies from South Korea." "The clinical characteristics of the two groups in the included studies are presented in Table 2."

--Respond: Considering the reviewer's suggestion, errors in the text have been revised accordingly. Revised sections are marked in yellow.

"3. Sensitivity analysis and publication bias" The number of studies is 5, whether the funnel plot is applicable.

--Respond: The funnel plot was weak in assessing publication bias for the five studies, and we further used Begg's test and Egger's test for quantitative assessment.

Discussion It is suggested to point out the existing bias and analyze the existing bias

--Respond: Considering the reviewer's suggestion, we added potential existing biases in the Limitations section of the text, including selection bias due to non-random controlled studies and confounding bias due to heterogeneity between studies. Revisions are marked in yellow. Publication bias was not detected.

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. And here we did not list the changes but marked in revised paper. We appreciate for Editors' warm work earnestly, and hope that the

correction will meet with approval. Once again, we would like to express our great appreciation to you. Looking forward to hearing from you.

Yours

Sincerely

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