

Dear editor and reviewers,

Thank you for your letter and for the comments concerning our manuscript entitled “Laparoscopic versus open radical resection in the management of gallbladder carcinoma: A systematic review and meta-analysis” (Manuscript ID: 85714). It is of very good experience for us to submit our manuscript to **World Journal of Clinical Cases**, and we are very grateful for the opinions from the reviewers, which are of high value to improve the quality of our study. We made several amendments to this paper based on reviewers’ suggestions, and the important modifications were summarized as follows:

**Reviewer #1:**

**Comments (Brief comments):** *“Gallbladder carcinoma The Abstract summarizes the contents of the study. The Introduction is correct. However, I have the suggestion of adding the pathological classification of gallbladder carcinoma, albeit in a very concise form. In the Materials and methods section, the subsections Search strategy and study selection, Study selection, Data extraction and outcome measures, Statistical analysis, Subgroup analysis, Risk of Bias are presented in detail. All subsections clearly set out the programme, objectives and related calculations. The results of the meta-analysis are presented in great detail for all identified subsections and are shown to be credible. The Discussion illustrates the results of this meta-analysis. However, it presents an interesting observation on the correctness of including studies in previous meta-analyses which would not have put the results of the comparison in terms of radical resection in the right light. The observations on previous studies are appreciable. The conclusions fully correspond with the objectives and results of the present meta-analysis. References are appropriate and up to date. The Figures and Tables are clear and useful for understanding the results.”.*

**Response:** We thanked the reviewer for his/her suggestion.

We briefly introduced the pathological classification of gallbladder cancer. We added the sentence as “The most common pathological type of GBC is adenocarcinoma, which accounts for more than 80% of all GBCs.<sup>3, 4</sup> Others include adenosquamous carcinoma, squamous carcinoma and neuroendocrine carcinoma, etc.” in “*Introduction*” section in page 5 for this question.

**Reviewer #2:**

**Comments (Brief comments):** *“Dear Editor, thank you so much for inviting me to revise this manuscript about gallbladder cancer. This study addresses a current topic. The manuscript is quite well written and organized. English should be improved. Figures and tables are comprehensive and clear. The introduction explains in a clear and coherent manner the background of this study. We suggest the following modifications:”.*

**1. Comments (Q1):** *“Introduction section: although the authors correctly included important papers in this setting, we the systemic treatment scenario for gallbladder cancer and biliary tract tumors should be briefly discussed and some recently published papers added within the introduction (PMID: 32806956 ; PMID: 32994319; PMID: 33592561; PMID: 36633661), only for a matter of consistency. We think it might be useful to introduce the topic of this interesting study.”.*

**Response:** We fully agree with this suggestion. We have discussed the systemic treatment for gallbladder and biliary tract tumors, and we added the sentence as “Systemic therapy has always been an important part of the treatment of GBC and biliary tract cancer (BTC), considering the low resection rate at the diagnosis. Cisplatin combined with gemcitabine (CisGem) has been used as the main chemotherapy regimen for advanced gallbladder cancer to this day.<sup>7</sup> In the past decade, immune checkpoint inhibitors (ICIs) have made major breakthroughs in the field of cancer treatment, and have changed the treatment pattern of several malignant tumors, especially for malignancies with dMMR, high TMB or MSI-high.<sup>8-10</sup> However, the role of ICIs in BTC needs to be further studied and clarified, and its combination with other anti-cancer drugs (such as chemotherapy, targeted agents, etc.) may be a more promising direction.<sup>10-15</sup> Some scholars are also exploring the relationship between ICIs and other therapeutic targets, such as BRCA 1/2 mutations (BRCAm), in order to provide patients with more personalized and precise treatment.<sup>16”</sup> in “Introduction” section in page 5 for this question.

**2. Comment (Q2):** *•“Methods and Statistical Analysis: nothing to add. Discussion section: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers. However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic , the methods sound good and their discussion is well balanced. One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion. We believe this article is suitable for publication in the journal although some revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations. We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points.”.*

**Response:** We thanked the reviewer for these suggestions. We expanded the Discussion section, and we added the sentence as “The treatment of GBC will be a comprehensive pattern based on surgery and combined with chemotherapy, immunotherapy and targeted therapy. And it is developing towards the trend of minimally invasive, precise and individualized. In this study,

LRR not only provided satisfactory survival, but also showed the characteristics of minimally invasive and enhanced postoperative recovery. It will inevitably play a more important role in the treatment of GBC. In addition, the rapid development of targeted and immunotherapy may provide more treatment options for GBC.” in “*Discussion*” section for these questions.

We also discussed the limitations again. We added the sentence as “Sixth, most of the included studies did not report detailed adjuvant therapy data, so it is difficult to judge the impact of adjuvant therapy on long-term prognosis. ” in the last part of the “*Discussion*”.

Thank you again for the suggestions from the reviewers, and the help from the editorial office of World Journal of Clinical Cases. I am looking forward to hearing from you.

Sincerely,

Shilin He, MD. (21118171@zju.edu.cn)

Xiao Liang, MD., PhD. (srrshlx@zju.edu.cn),

Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, 310016, Zhejiang Province, China