

## Responses to the reviewer's comments

Dear Editor,

Many thanks for your kind consideration of our manuscript for revision. Our evidence synthesis group are very grateful to you and the Reviewers for the valid comments which undoubtedly will enhance the quality of our manuscript. Please find below our responses to the Reviewer's comments.

Reviewer #1:

I have reviewed the paper entitled "General anesthesia versus regional anesthesia for laparoscopic cholecystectomy: A systematic review, meta-analysis, and trial sequential analysis of randomized controlled trials". The paper is an interesting and well-conducted meta-analysis on the topic of regional anaesthesia for cholecystectomy. The presentation of the meta-analysis and the conclusion respects the principles for this type of paper. The conclusion also corresponds to the analysis. There is no significant change to make to the analysis.

**Our response: we are very grateful to Reviewer 1 for the detailed evaluation of our manuscript and kind positive comments.**

The main criticism of this paper relates to the value and the level of the publications considered to realise this meta-analysis. In fact, they are of real poor value with a very low impact factor. We can take as an example the study in reference n°14, Kalaivani et al., in which patients are excluded of the study in case of failure of the regional anaesthetic. This study does not follow the principle of 'intent to treat' and consequently the results give significant potential additional value to regional anaesthesia considering this bias. Furthermore, in this study, the mean OP time is at least 80-97 mins to perform laparoscopic cholecystectomy... Overall, this represents the main weakness of the paper, and the issue should be addressed in the discussion and in the conclusion.

**Our response: we absolutely agree with the comment. Following Reviewer 1's valid recommendation, we added the following statements to:**

**Discussion → Last paragraph (limitations)**

*" Moreover, some the included studies excluded patients who had failure of RA which is not consistent with intention to treat concept. This might have significantly affected the results in favor of RA and subsequently introduced bias to our findings. Finally, all the risk of performance and detection bias was high among the included studies due to lack of blinding. With regards to the performance bias, the blinding of participants and surgeons would have been impossible; however, blinding of outcome assessor would have been possible to reduce the risk of detection bias.. "*

**Conclusions**

*" ..... Moreover, lack of knowledge on the impact of RA on specific procedure related outcomes may discourage surgeons from selecting RA as the first choice of anesthesia for laparoscopic cholecystectomy. Most importantly, intention to treat principle has been breached in some of the included studies by excluding failed RA attempts. Considering our findings and the limitations of the available evidence, we do not hesitate to highlight that available evidence does not justify using RA as the first line anesthetic choice for laparoscopic cholecystectomy although it may be an option in patients who are not fit for GA . Future research should focus on procedure related outcomes of RA and GA in laparoscopic cholecystectomy with respect to intention to treat concept.. "*

Science Editor; Peer Reviewer; Company Editor-in-Chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Endoscopy, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

**Our response: we are grateful to the Science Editor; Peer Reviewer; and Company Editor-in-Chief for the kind positive comments. We have amended the title as per recommendation**

Science Editor:

1 Scientific quality: The manuscript describes a meta-analysis of the general anesthesia versus regional anesthesia for laparoscopic cholecystectomy. The topic is within the scope of the WJGE. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The paper is an interesting and well-conducted meta-analysis on the topic of regional anaesthesia for cholecystectomy. The presentation of the meta-analysis and the conclusion respects the principles for this type of paper. The conclusion also corresponds to the analysis. The questions raised by the reviewers should be answered; and (3) Format: There are 3 tables and 4 figures. A total of 31 references are cited, including 7 references published in the last 3 years. There is 1 self-citation (Ref. 24). The topic of the self-citations is related to this study. 2 Language evaluation: Classification: Grade A. The authors are native English speakers. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJGE

**Our response: We are very grateful to the science editor for the accurate and detailed evaluation of our manuscript and the valid comments.**

(1) The "Author Contributions" section is missing. Please provide the author contributions

**Our response: we totally agree with comments and author contributions has been provided**

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

**Our response: Following the valid recommendation, we have provided the pictures in both word document manuscript and Power Point for Figures 2, 3, and 4 in which there are pictures which are software generated.**

(3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout

**Our response: We totally agree with this valid comment. We have amended the reference list in line with recommendations**

(4) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text;

Our response: We totally agree with this valid comment. "Article Highlights" section has been provided as per recommendation.

(5) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study.

Our response: we totally agree with the comment. We have removed once reference which was not completely irrelevant but the content was covered by another reference

6 Recommendation: Conditional acceptance

Our response: We are very grateful to the science editor for the kind recommendation

Looking forward to your favourable consideration

Yours sincerely

Corresponding author