

Peer Review File

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Reviewer A:

Comment 1: In the submitted manuscript by Zhang et al., the authors explore the available literature on the ALPPS method in HCC in the form of a systematic review focusing on safety, feasibility, and efficacy.

Reply 1: Thanks for the reviewer's opinion.

Changes in the text: There is no change in the article.

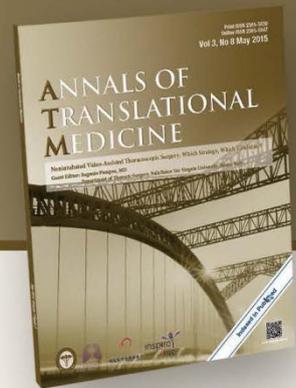
Comment 2: This systematic review is in an interesting area with potentially interesting findings, but according to the PRISMA guidelines for systematic reviews, I do not see any reference to the pre-registration or ex-ante publication of the study protocol. Systematic review and meta-analysis are forms of observational research, and so are particularly prone to bias which arises if the study is not pre-registered (doing multiple studies, publish the ones which are interesting) or where there is not an ex-ante protocol (define scope as the review process goes along, analysis driven by data and so on). This is not in any way a suggestion that the authors have done these, but others might, and the reader cannot distinguish between these possibilities. Therefore, the referee considers the lack of these methodical details as a major flaw of this report. I also do not see any reference to the PRISMA guidelines as an internationally recognized standard in performing systematic reviews.

Reply 2: We appreciate very much for this reviewer's opinion on our study. We followed the ex-ante protocol strictly. We referred the PRISMA guidelines in our manuscript.

Changes in the text: We have modified our text as advised (see Page 6 line 14-15)

Reviewer B:

Comment: I read with interest the systematic review on ALPPS for HCC. Authors have focused the right point and certainly open some potential consideration for other studies. The main point is the single experience of all included papers. However, due to the very rare indication of eligible patients multicentric or RC studies are extremely difficult to be performed.



Reply: We appreciate very much for this reviewer's opinion on our study, and it is very difficult to perform the RC studies for HCC of ALPPS.

Changes in the text: There is no change in the article.

Reviewer C:

Comment 1: 1. This is a very interesting topic that attracts the attention of many surgeons who are interested in ALPPS. The overall study is organized and well structured. The manuscript is well written in a concise manner and the message is straightforward.

Reply 1: We appreciate very much for this reviewer's interest on our study.

Changes in the text: There is no change in the article.

Comment 2: 2. 'Discussion' paragraph 1st line, full form of ALPPS is already described in 'Introduction' and doesn't need to repeat again.

Reply 2: Thanks very much for this reviewer's opinion on our study, and we change the form of ALPPS in our study.

Changes in the text: We have modified our text as advised (see Page 10 line 19)

Comment 3: 3. Page 8 second to the last paragraph; 'In terms of the timing of... when considering the timing of the second stage surgery.' Yes, this could be true, however, this is not something author can conclude from this manuscript and does not appear to be relevant.

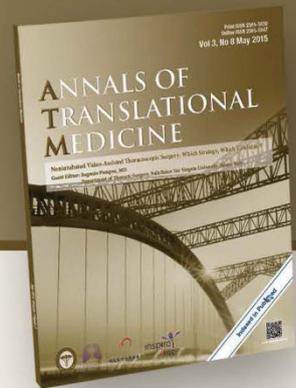
Reply 3: We appreciate very much for this reviewer's opinion on our study, and deleted the part of 'In terms of the timing of... when considering the timing of the second stage surgery.' in our study. This part was learned from our center experience in performing ALPPS but not from this study, so we deleted them.

Changes in the text: We have modified our text as advised (see Page 13 line 15-16)

Comment 4: 4. Page 8 last paragraph; 'Notably, the anterior approach ALPPS on HCC patients has been well investigated, which...' Please provide the reference article.

Reply 4: We appreciate the reviewer's opinion. We found "anterior approach ALPPS" was used to reduce the adhesion but not the bile leakage complication. We have corrected it and added the references in the manuscript.

Changes in the text: We have modified our text as advised (see Page 13 line 18-20)



Comment 5: 5. Page 8, Third to the last line, ‘slow and restricted’ > ‘slow and restricted’

Reply 5: We appreciate the reviewer’s opinion, and we have corrected the ‘slow and restricted’.

Changes in the text: We have modified our text as advised (see Page 14 line 1)

Comment 6:6. Page 9, ‘Conclusions’; This paragraph sounds to include too many authors’ opinions, e.g. first 10 lines. The conclusion should be a summary of the findings, as the conclusion in the abstract of this manuscript. The above part can be moved to the discussion part.

Reply 6: We appreciate the reviewer’s opinion, and we have moved the above part of conclusion to the discussion part.

Changes in the text: We have modified our text as advised (see Page15 line 1-10)

Comment 7: I read this manuscript with a strong interest. A similar systematic review of ALPPS for colorectal cancer liver metastases has been reported, however, this is the first systematic review of ALPPS for HCC, which is a more controversial indication due to theoretical concern for the regenerative capability of liver parenchyma with background chronic hepatitis. The study design, selection process appears to be legitimate and manuscript is well structured and organized. Unfortunately, the meta-analysis was not performed due to lack of granular data, which makes the impact of this manuscript relatively low, but as commented above, the study itself is well designed, structured, and concise. As far as above mentioned points are revised, I feel this manuscript has enough impact to be considered for publication even without meta-analysis, however, I think ultimately it is up to editorial office whether the impact of this manuscript is sufficient to be published on this level of the journal.

Reply 7: We appreciate very much for this reviewer’s interest and approval about our study, and we have carefully revised our manuscript according to the reviewer’s suggestions.

Changes in the text: There is no change in the article.