

**Dear Editors and Reviewers:**

Thank you for your letter and for those comments concerning our manuscript entitled “Prognostic Factors and Predictors of PA-TACE Benefit in Patients with Resected Hepatocellular Carcinoma” (ID:52687). Those comments are valuable and helpful for revising and improving our paper, as well as the important guiding significance to our researches. According to your advices, we revised the relevant parts in this manuscript. Some revised portions are marked in red. The main corrections in the paper and the responses to the Editors’ and Reviews’ comments are as follows:

**Special comments from the editor:** 1. Upload Funding Agency Copy of any Approval Document; 2. image using PPT.

**Response:** Thank you very much for your kind comments. Now we have provided the two fundings (No.2018KFJJ09 and 81827804) Agency Copy of any Approval Document. Beside, we have uploaded our image using PPT. Thanks.

**Reviewer #1:** Reviewer’s Code 00225294

**Comments:** *The authors evaluate prognostic factors and predictor indicators of the benefits of postoperative adjuvant trans-catheter arterial chemoembolization (PA-TACE) in patients with resected HCC. They incorporate this study under the umbrella of two gold-standards in the field: the BCLC and the FHR scores. Overall, the idea is of practical interest and has been applied to a cohort of HCC patients sufficiently representative and with application of equivalent criteria. The size group is relatively high and, perhaps a better statistical revision of the data for future developments of the project will enhance the value of the conclusions obtained from this study. In fact, this study offers the possibility of clinicians in the HCC surgery field to introduce rationale criteria to better decide introduction of a PA-TACE strategy. Regarding specific aspects, the title is correct in the description of the working hypothesis, the ethics is adequate for this type of studies and is relevant for transferring to the clinical practice in HCC surgery. The statistics perhaps deserves additional implementation as far as the cohort size is increased. The organization of the manuscript is perfect and the conclusions are supported by the data obtained.*

**Response:** Thank you very much for your kind comments. We agree with your comments that the statistics perhaps deserves addition implementation as far as the cohort size is increased. Therefore, we will perform exploratory analysis in the future study. However, based on our current sample size from multiple medical centers, our results are reliable and suitable in this study.

**Reviewer #2:** Reviewer's Code 00053888

**Comments:** *This is an interesting retrospective analysis of patients who have either undergone surgery alone or surgery and the post-operative adjuvant TACE. These patients have been retrospectively recruited over a four year period from three centres and do not appear to have had a standard regimen of treatment. They are definitely not randomised. The authors begin their long (too long) discussion by suggesting that the improvement in survival that they have seen with post-operative TACE suggests that this should be standard treatment. By the end of the discussion and conclusion they have realised that their data does not support this statement. The study is really a safety and tolerability (Stage 2) trial rather than a stage 3 outcome trial. The authors should acknowledge this more clearly. The only reason for comparing the two groups is to show that adjuvant TACE does not increase the risk over surgery alone. The discussion is too long but the manuscript is well written.*

**Response:** Thank you very much for your remarks. We have modified our manuscripts based on your suggestions. We believe that the quality of our manuscript has been significantly improved by your comments.

**Q1.** *The patients have been retrospectively recruited over a four-year period from three centers and do not appear to have had a standard regimen of treatment and they are definitely not randomized.*

**Answer to Q1:** Thank you very much for your comment. Your remarks regarding the standard regiment of treatment across three medical centers and the randomized study sample have already been noted in the limitation section of our discussion. For example, *“The major limitation of this study is the retrospective nature of the data we acquired. Even if a propensity score matching analysis was performed, potential bias could not be*

*eliminated completely. Moreover, several clinical variables in the data could not be measured, for example, PA-TACE drugs and dosages can vary across the three different centers.” ( Page 12) . Thereby, we hope to be able to perform a prospective study in the future to confirm PA-TACE treatment efficacy and its impact on overall survival.*

**Q2.** *The authors begin their too long discussion by suggesting that the improvement in survival that they have seen with post-operative TACE suggests that this should be standard treatment. By the end of the discussion and conclusion they have realized that their data does not support this statement.*

**Answer to Q2:** Thank you very much for your suggestions. We have followed your suggestion and revised our manuscript with a concise discussion. The discussion and conclusion were revised so that it supports the statement that we indicated. Beside, Multiple sections in the discussion were removed to shorten the discussion and avoid repetition. We believe that the revision has made the discussion much more comprehensible for the readers. We believe that this revision had made our manuscript much more coherent and comprehensible.

**Reviewer #3:** Reviewer’s Code 02992848

**Comments:** *When was PA-TACE done after surgery, weeks or months? Hope authors can elaborate more on this issue.*

**Response:** Thank you very much for pointing out this issue. We apologize for the lack of description for PA-TACE surgery time. PA-TACE were performed on patients within a month period. We have revised our manuscript and elaborated on this issue as your comment suggested. For example, *“It is recommended that patients should undergo PA-TACE when the liver function had recovered at 1-3 months after the initial operation.<sup>[1]</sup>”* ( Page 5) and *“According to our medical center regulations, after the selection of suitable patients for PA-TACE, all patients were suggested to undergo PA-TACE when the patient had recovered liver function at 1 month after the initial operation. The patients were followed up once every 3 months. At each follow-up visits, tumor markers, abdominal*

*ultrasounds, and liver function assessments were performed. Every 6 months or when recurrence was suspected, enhanced CT scans or MRI imaging were performed.” (Page 6-7)*

1. Wang H, Du PC, Wu MC, Cong WM. Postoperative adjuvant transarterial chemoembolization for multinodular hepatocellular carcinoma within the Barcelona Clinic Liver Cancer early stage and microvascular invasion. *Hepatobiliary surgery and nutrition* 2018; 7(6): 418-428 [PMID: 30652086 PMID: PMC6295398 DOI: 10.21037/hbsn.2018.09.05]

In a word, the comments given by the reviewers were studied carefully and revised our manuscript accordingly. I am certain that these revisions have significantly improved the quality of our manuscript. Looking forward to receiving your feedback soon. Thank you.

Best Regards,

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