

Review Comments-reviewer A

Comment 1: First of all, my major concern regarding this study is the unclear focus of this study, hepatic hemodynamics, the prognostic factors of DEB-ACE patients, or the prognostic role of CSPH. Please make this clear according to the research work in the main text and indicate the clinical research design in the title, i.e., a retrospective cohort study.

Reply 1: The current study mainly focused on the changes of hepatic hemodynamics for HCC patients receiving DEB-TACE, which had never been investigated and reported previously. Considering that hepatic hemodynamics (especially for CSPH) were correlated with the severity of liver cirrhosis, the prognostic factors including CSPH were also explored in such group of patients. Therefore, in the present study we aimed to investigate the effects of DEB-TACE on hepatic hemodynamics measured by HVPG, as well as its prognostic factors including CSPH in patients with unresectable HCC. It was made clear in the main text. In addition, study design was indicated in the title according to your suggestion.

Changes in the text: We have modified our text as advised. (See Page 1, Line 4-5; Page 4, Line 18-20)

Comment 2: Second, the abstract needs some revisions. The background needs to indicate the clinical importance of hepatic hemodynamics. The methods need to describe the inclusion of subjects, the assessment of hepatic hemodynamics, baseline clinical factors, follow up, and prognosis outcomes. The results need to summarize the clinical characteristics of the study sample and quantify the findings on the hepatic hemodynamics by using detailed figures and P values. The conclusion needs to be consistent with the research focus, and have comments on the clinical implications of the findings.

Reply 2: Thank you very much for the comments and suggestions.

Changes in the text: We have modified our text as advised. (See Page 2, Line 6-19; Page 3, Line 1-14)

Comment 3: Third, the introduction of the main text needs to explain the clinical importance of hepatic hemodynamics. Please also review the known prognostic factors and prognosis of HCC if the authors decided to focus on them.

Reply 3: Primary objective of current study was investigating the changes of hepatic hemodynamics after DEB-TACE therapy; by the way, we explored its prognostic factors which was also focused on the hepatic hemodynamics, namely CSPH based on the measurement of HVP. Different from other types of solid malignancies, the prognosis of HCC patients is influenced not only by tumor itself but also by the underlying liver diseases; therefore, prognostic factors including tumor burden, liver function and performance status were closely correlated with the survival of HCC patients. Hepatic hemodynamics of patients with cirrhosis were usually characterized of portal hypertension, which was both relevant with the decompensated events and patient prognosis. Particularly, clinically significant portal hypertension (CSPH) is highly correlated with the long-term survival of HCC patients.

Changes in the text: We have added these points in text as advised. (See Page 4, Line 6-13)

Comment 4: Fourth, in the methodology of the main text, please describe the sample size estimation, assessment of baseline clinical factors, follow up details, and measurements of prognosis outcomes. The statistical analysis must be consistent with the research focus, so please describe the analysis of hepatic hemodynamics. Please also describe the details of multiple Cox regression analysis.

Reply 4: Laboratory examinations including routine blood test, liver and kidney function, and tumor markers were performed before 1-2 days of treatment; imaging assessments were judged by two different investigators, and the final decision was rendered based on discussions when disagreements arose. During follow-up, laboratory examination and imaging assessment were performed 4–6 weeks after each procedure. For patients with preserved liver function, repeated TACE sessions were implemented upon confirmation of viable tumor or local and/or distant intrahepatic recurrences. During the study period, none participant was lost to follow up. Overall survival (OS) was defined as the time from DEB-TACE treatment until death or last follow-up. Due to the design of retrospective cohort study, we included all the patients eligible for current study protocol in our center during the period.

Changes in the text: We have added these points in text as advised. (See Page 5, line

4-7, Line 14-19; Page 6, Line 5-15)

Great thanks for reviewers again for the valuable comments and suggestions.

Review Comments-reviewer B

Comment 1. STROBE checklist:

- a. Item 13(c): There's no such flow diagram in your paper, please check.
- b. Please fill "N/A" in Line 2-3 of Item 15 in the checklist.

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page4/Line25-33	Methods/Paragraph1
		(b) Give reasons for non- participation [at each stage	Page4/Line30-33	Methods/Paragraph1
		(c) Consider use of a flow diagram	Page4/Line25-33	Methods/Paragraph1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page5/Line20-33	Results/Paragraph1
		(b) Indicate number of participants with missing data for each variable of interest	Table1	Table1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Page7/Line7-8	Results/Paragraph2
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Page7/Line7-8	Results/Paragraph2
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure		
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures		

Response:

- a. Considering that we have clearly demonstrated the inclusion/exclusion criteria and the patient enrollment flow in Methods section, there is no need for using a flow diagram in such section. Therefore, we fill "N/A" in this item.
- b. We have fill "N/A" in Line 2-3 of Item 15 in the checklist.

Comment 2: Please structure your Main Text as: Introduction, Methods, Results, Discussion, Conclusion. Please add "Conclusion" section for your manuscript.

Response: We have revised it as your comments. (See Page 10, Line 7)