Dear Dr. Gong,

Thank you for your letter and the advice concerning our manuscript entitled "Early prediction of survival in hepatocellular carcinoma with transarterial chemoembolization plus sorafenib" (Manuscript No: 36495). Those comments are all valuable and very helpful for revising and improving our paper. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in the revised manuscript. Point by point responses to the reviewers' comments are listed below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in ***World Journal of Gastroenterology.***

We look forward to hearing from you soon.

Best wishes,

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We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Reviewer #1: The authors demonstrated that prognosis of HCC patients who showed early disease-controll-response after TACE-S (TACE plus sorafenib) was better, especially in the case of non-PVTT or non-TACE history. This information is very important, since sorafenib is very expensive and many HCC patients give up sorafenib because of its adverse effect. Therefore, such selection is beneficial. However, I doubt that all HCC patients can be evaluated by mRECIST. Some kinds of HCC do not show hypervascularity. How did the authors evaluate TACE-S response

in such cases? Also, why did the authors include HCC patients having extrahepatic metastases? I think that the authors should address the above-mentioned issue. If they can respond well, this paper will be suitable for publication in World Journal of Gastroenterology.

Comment 1: The authors should describe the methods of tumor measurement in mRECIST. In original paper by Lencioni et al., they measure the well-enhanced tumor part after TACE. However, in this paper, there was no such description.

Answer: We agree your comment. Therefore, we have added the description in paragraph 5 of MATERIALS AND METHODS section as follows: “Tumor response was assessed according to the overall mRECIST (Ref. 25-27), which included a combined assessment of target lesions, nontarget lesions and new lesions. At baseline, measurable lesions with diameters 1 cm or greater, suitability for repeat measurement and intratumoral arterial enhancement on contrast-enhanced CT or MR imaging were qualified as target lesions. The longest diameter of the viable tumor (defined as the enhanced area during the arterial phase) was measured on contrast-enhanced CT or MR imaging. Non-enhancing atypical lesions and extrahepatic lesions were assessed using RECIST criteria. The presence or absence of nontarget lesions and the appearance of new lesions were assessed during follow-up. Overall responses were classified into the following four categories: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD).” The above added contents about the overall mRECIST evaluation are based on the original paper by Lencioni et al. (Ref. 25).

Comment 2: Why did the authors perform TACE for HCC patients with main PV PVTT? Basically, TACE in such case would cause hepatic infarction because of both artery/PV blood flow loss. Was PV flow patent in such case? The authors should describe the PVTT situation.

Answer: We agree your comment. In order to more accurately describe the PVTT situation, we had revised the original expression of exclusion criteria (a) into “had

complete main portal vein obstruction without collateral circulation around the portal trunk" in paragraph 1 of MATERIALS AND METHODS section.

Comment 3: Why did the authors include HCC patients having extrahepatic metastases? What is the purpose of TACE in such cases? (maybe, the life-limiting factor would be the intrahepatic foci.) Also, in such cases, how did the authors evaluate response via mRECIST?

Answer: To answer these questions, we have added one paragraph in DISCUSSION section: "Considering that the cause of death of HCC patients with extrahepatic metastases is mainly intrahepatic HCC or hepatic failure, rather than extrahepatic metastasis (Ref. 33&34), a local treatment modality such as TACE is often performed at some centers (Ref. 14&33). Our result showed that extrahepatic metastases was not an independent prognostic factor for worse survival. This implied that the combination of delaying intrahepatic tumor progression with TACE and targeting extrahepatic metastasis with sorafenib might be benefit for survival, although further trials are required." As described in the answer to Comment 1, response of extrahepatic lesion was assessed using RECIST criteria.

Reviewer #2: Minor language polishing is required.

Answer: We have thoroughly reviewed the manuscript and corrected the grammar and word usage errors.