Dear Editors and Reviewers,

Thank you for your letter and we were pleased to know that our manuscript (Manuscript NO.: 79137, Retrospective Study) was rated as potentially acceptable for publication in *World Journal of Gastroenterology*, subject to adequate revision. We thank the reviewers for the time and effort that they have put into reviewing the previous version of the manuscript. Their suggestions are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The modified part is marked in red on the paper (a marked version of the revised manuscript is provided in the supplementary material). The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responses to the Reviewer comments:

To the reviewer #1 comments:

1: In this well written manuscript, the authors investigated survivals following liver resection in patients affected by multinodular BCLC-B stage HCC. Study patients were stratified according to the sum of HCC number (N) and maximum size (S, in cm) into two subgroups (N+S>10 VS <=10), which showed significantly different survivals, mainly related to a different timing and pattern of postoperative recurrence. In particular, patients with a (N+S<=10) had survivals similar to those of patients within BCLC-A stage Group.

Authors response: Thank you very much for your positive comments on our work and your summary of the manuscript.

2: Few previous reports have suggested that the sum of N+S may help to stratify prognosis of patients undergoing liver resection for HCC. However, N and S have been previously combined in different ways to improve survival stratification of HCC patients. My comment: did the authors try to evaluate the prognostic performance of tumor burden score and total tumor volume in their study population? I believe that comparing N+S with above mentioned pre-existing scores may increase the clinical validity of the N+S and clarify the real advantage of such novel stratification over the pre-existing ones.

Authors response: Thanks for your suggestion. Your proposal is extremely meaningful and we have collected and calculated tumor burden score (TBS) and total tumor volume (TTV) for each Barcelona Clinic Liver Cancer (BCLC) intermediate-stage hepatocellular carcinoma (HCC) patient according to your suggestion. TBS was defined as the distance from the origin of a Cartesian plane and comprised two variables: maximum tumor size (x-axis) and number of tumors (y-axis) so that TBS^2 = (maximum tumor diameter)^2 + (number of tumors)^2[1]. Measurement of the tumor volume was calculated using this calculation: 4/3 × 3.14 × (maximum radius of the tumor nodule in cm)^3[2]. By receiver operating characteristic (ROC) analysis, we compared the predictive accuracy of N+S with those of TBS and TTV in predicting OS in BCLC-B patients. The results showed that the AUCs of N+S at 3 and 5 years were both greater than those of TBS (3-year AUC, 0.650 vs 0.646, *P* = 0.552; 5-year AUC, 0.646 vs 0.643, *P* = 0.762) and TTV (3-year AUC, 0.650 vs 0.628, *P* = 0.171; 5-year AUC, 0.646 vs 0.636, *P* = 0.535) (Figure 1). Although the results of this study showed that the prediction accuracy of N+S was not better than those of TBS and TTV, the calculation of N+S is simpler and more applicable to clinical practice.

To the reviewer #2 comments:

1. This study investigated the outcomes and recurrence patterns of BCLC-B hepatocellular carcinoma after liver resection by evaluating the sum of tumor size and number.

Authors response: Thank you for your summary.

2. Do the exclusion criteria include pre-treated with other therapies?

Authors response: Thanks for your question. The patients included in this study had not received any anticancer treatment other than transarterial chemoembolization (TACE) prior to liver resection. Considering that there was no statistically significant difference in the proportion of patients who received preoperative TACE among BCLC-A, BCLC-B1, and BCLC-B2 patients, we did not exclude patients who received preoperative TACE. And we have added “no preoperative anticancer treatment other than TACE” to the inclusion criteria in the revised manuscript.

3. Amplify Figure 1 to make the letters in the figure clear. Figure 2 is too dim, increase the size same as Figure 3, in two rows. Similarly, supplementary Figures 1 and 2 should be increased in size to increase the resolution.

Authors response: Thanks for your suggestion. We have adjusted all figures.

Responses to the Editorial Corrections:

To company editor-in-chief:

1. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Authors response: Thanks for your kind suggestion. We have adjusted all figures and figure legends to a unified format that meets the journal’s publication requirements. In addition, we also provide decomposable figures (where all components are movable and editable) and organize them into a single PowerPoint file.

2. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Authors response: Thanks for your suggestion. we have revised and adjusted all tables according to your suggestions and requirements.

Q3. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is ‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

Authors response: Thanks for your suggestion. The pictures provided in this study are original, so we have signed the pictures in the PowerPoint (PPT) according to your

requirements.

1 Tsilimigras DI, Moris D, Hyer JM, Bagante F, Sahara K, Moro A, Paredes AZ, Mehta R, Ratti F, Marques HP, Silva S, Soubrane O, Lam V, Poultsides GA, Popescu I, Alexandrescu S, Martel G, Workneh A, Guglielmi A, Hugh T, Aldrighetti L, Endo I, Sasaki K, Rodarte AI, Aucejo FN, Pawlik TM. Hepatocellular carcinoma tumour burden score to stratify prognosis after resection. *The British journal of surgery* 2020; **107**(7): 854-864 [PMID: 32057105 DOI: 10.1002/bjs.11464]

2 Zakaria HM, Macshut M, Gaballa NK, Sherif AE, Abdel-Samea ME, Abdel-Samiee M, Marwan I, Yassein T. Total tumor volume as a prognostic value for survival following liver resection in patients with hepatocellular carcinoma. Retrospective cohort study. *Annals of medicine and surgery (2012)* 2020; **54**: 47-53 [PMID: 32368340 PMCID: PMC7184266 DOI: 10.1016/j.amsu.2020.04.001]