Peer Review File

Article information: https://dx.doi.org/10.21037/jgo-23-69

Review comments-Reviewer A

1) First of all, the clinical question or the focus of this study was not clearly indicated. The authors did not different stratified analysis and subgroup analysis, however, these are all univariate analyses. There is a need for an overall model to analyze the relationships between the up-to-7 criteria, two treatments, and other clinical factors. The title is also difficult to understand, which should be whether the prognostic role of the up-to-7 criteria differs between patients underwent hepatectomy and TACE. The title also needs to indicate the clinical research design of this study, i.e., a retrospective cohort study.

Reply 1: This study is based on two factors (tumor size and diameter) of up-to-seven standard to explore whether the standard is suitable for the choice of treatment scheme for patients with stage B HCC, and to extend the two dimensions (tumor size and diameter) of the standard to explore the influence of tumor size and diameter on the prognosis of patients with stage B HCC surgery. In the next step, we will also establish an overall model to predict the prognosis of patients undergoing stage B surgery. As for the suggestion of the title, our research is not only aimed at comparing the prognosis of surgery and TACE that meet the up-to-seven standard, but also expanded on the basis of this standard, so we think the meaning expressed by the title is reasonable. We supplemented the title and explained the clinical research design of this study (see page 1, line2-4).

Changes in the text: Evaluation of the up-to-7 criteria for determining the treatment of hepatocellular carcinoma in Barcelona Clinic Liver Cancer stage B： A Single-Center Retrospective Cohort Study

2) Second, the abstract needs some revisions. The background did not describe the clinical needs for this research focus and its knowledge gap. The methods need to describe the inclusion of subjects, the assessment of baseline clinical factors including the up-to-7 criteria, demographics, tumor number and diameter, and other clinical factors, follow up procedures, and measurements of prognosis outcomes. The results need to summarize the clinical characteristics of the study sample and quantify the findings by reporting HR and accurate P values. The conclusion needs comments for the clinical implications of the findings.

Reply 2: We have modified our text as advised (see page 2-3, line37-65).

Changes in the text: Background: At present, there are still disputes on the treatment options of surgery for patients with stage B HCC. This study sought to investigate whether the up-to-7 criteria could be used to decide the treatment for HCC in BCLC-B. Methods: We analyzed 340 patients with HCC in BCLC-B who treated with hepatectomy or TACE. Of the 285 HCC

patients who underwent hepatectomy, 108 met the up-to-7 criteria and 177 exceeded the up-to-7 criteria. All 55 patients in the TACE group met the up-to-7 criteria. We obtained the tumor progression and survival status of the patients through inpatient medical records, outpatient electronic medical records, and telephone follow-up of the hospital. We compared OS and PFS were compared between patients who met the up-to-7 criteria and who underwent either hepatectomy or TACE. OS and recurrence time were also compared between the patients who were treated with hepatectomy and who either met or exceeded the up-to-7 criteria. Across all patients, we compared the OS of BCLC-B HCC patients after surgical treatment between subgroups stratified by tumor number and diameter. Results: Patients who met the up-to-7 criteria had significantly higher OS rates after hepatectomy than TACE (P=0.000). However, the 2 groups did not differ significantly in terms of PFS (P=0.758). Among the patients treated by hepatectomy, the OS rates were significantly higher in patients who met the up-to-7 criteria than in those who exceeded it (P=0.001). The recurrence rates did not differ significantly between patients who met or exceeded the criteria (P=0.662). OS was significantly higher in patients with ≤3 tumors than those with > 3 tumors(P=0.001). When we stratified patients with ≤3 tumors based in whether they met or exceeded the up-to-8 to up-to-15 criteria, OS was significantly better among those who met the criteria in all cases. Conclusions: Hepatectomy appears to be associated with better survival than TACE in patients with BCLC-B HCC who meet the up-to-7 criteria, but this criteria is not a strict indication for deciding whether to treat patients with BCLC-B surgically. Tumor number, but not tumor size, strongly affects the prognosis of BCLC-B patients after hepatectomy.

3) Third, in the introduction of the main text, the authors need to have a brief review on known prognostic factors in HCC and explain why the prognostic role of the up-to-7 criteria would be differ between TACE and hepatectomy. There is no need to emphasize the prognostic roles of tumor number and diameter, because the two factors, together with other clinical factors, should be adjusted when analyzing the relationships between prognosis, treatment, and the up-to-7 criteria.

Reply 3: We have reviewed the known prognostic factors in HCC and explained why the prognostic role of the up-to-7 criteria would be differ between TACE and hepatectomy. (see page 3-4, line82-87).

Changes in the text: At present, it is considered that the factors influence survival in the surgical treatment of HCC are: tumor size, tumor number, tumor site, tumor capsule integrity, microvascular invasion (MVI)(7-12). Up-to-seven standard is established based on the number of tumors and tumor diameter. Patients who meet the up-to-seven criterion have small numbers and diameters of tumors and are relatively early in clinical staging, so it is speculated that surgical treatment in these patients may be more effective than TACE.

4) Fourth, the methodology of the main text needs to indicate the clinical research design and sample size estimation. In statistics, the proposed stratified analysis and univariate analysis cannot answer the clinical question, the prognostic role of the up-to-7 criteria differs between patients underwent hepatectomy and TACE. I suggest the authors to establish a multiple Cox regression analysis that focused on the interactive effect of the up-to-7 criteria*treatment, adjusting for the confounding effect of other clinical covariates including tumor number and diameter.

Reply 4: We have indicated the clinical research design and sample size estimation in the methodology of the main text. (see page 4, line109-113). We have performed COX regression analysis in the original text. Albumin, prothrombin time and tumor site are the independent risk factors affecting the prognosis of patients who met the up-to-7 criterion, those who underwent hepatectomy or TACE. AST, number of tumors, and MVI were the independent risk factors for postoperative survival in the surgical group of the BCLC-B patients who met or exceeded the up-to-7 criterion (see Table2 and Table4).

Changes in the text: The clinical records of 340 patients with HCC in BCLC-B who treated with hepatectomy or TACE at the Department of Hepatobiliary, Pancreatic and Splenic Surgery at Guangxi Medical University Cancer Hospital between November 2013 –October 2019 were retrospectively collected, and the number of patients determined the sample size.

5) Finally, please consider to cite the below related papers: 1. Deng M, Li S, Wei W, Guo R. What clinicopathological factors affect the recurrence of hepatocellular carcinoma after surgery? Ann Transl Med 2022;10(21):1185. doi: 10.21037/atm-22-3473. 2. Gao R. Hypoxia features as potential indicators in prognosis, immunotherapy and drug screening in hepatocellular carcinoma patients. Transl Cancer Res 2022;11(11):3932-3934. doi: 10.21037/tcr-22-2173. 3. Dai Y, Chen G, Chen Y, Shi Z, Pan J, Fan X, Lin H. Usefulness of the estimation of physiologic ability and surgical stress (E-PASS) system for prediction of complication and prognosis in hepatocellular carcinoma patients after hepatectomy. Transl Cancer Res 2022;11(8):2700-2712. doi: 10.21037/tcr-22-352.

Reply 5: We have quoted the literature provided in the peer review comments (see page 12, line361-363; page 13, line389-396).

Changes in the text: 3. Gao R. Hypoxia features as potential indicators in prognosis, immunotherapy and drug screening in hepatocellular carcinoma patients. TRANSL CANCER RES. [Comment; Editorial]. 2022 2022-11-01;11(11):3932-4; 10. Dai Y, Chen G, Chen Y, Shi Z, Pan J, Fan X, et al. Usefulness of the estimation of physiologic ability and surgical stress (E-PASS) system for prediction of complication and prognosis in hepatocellular carcinoma patients after hepatectomy. TRANSL CANCER RES. [Journal Article]. 2022 2022-08-01;11(8):2700-12; 11. Deng M, Li S, Wei W, Guo R. What clinicopathological factors affect the recurrence of hepatocellular carcinoma after surgery? Ann Transl Med. [Comment; Journal Article]. 2022 2022-11-01;10(21):1185.

Review comments-Reviewer B

I read with interest the retrospective study comparing survival outcomes of BCLC-B patients treated by hepatic resection and comparing them with patients treated with TACE, Authors have sub-grouped the patients based on the qualification of up to 7 criteria. While this study is of interest, there are many issues that need refinement in the introduction and discussion segment of the manuscript. I also find grammar errors in sentence formation in the abstract and introduction and I shall not comment on language and leave it to the authors to tidy this up.

1. I kind of disagree with the introduction segment that Milan criteria are used to determine hepatic resection eligibility. It is done and dusted that (a) Milan criteria were originally proposed for transplant and not universally they are of historic interest and almost all transplant units have expanded indications (b) Hepatic resection eligibility is largely determined by local experience and local resources rather than BCLC as everyone has reported that BCLC is too restrictive, especially from East (China, Singapore, Japan, Thailand, Taiwan, etc). Thus, I suggest that you omit the Milan from resection. That was not the job of Milan and neither widely acknowledged as a job of Milan.

Reply 1: Milan criteria are proposed based on liver transplantation for patients with end-stage cirrhosis. Patients with liver cancer who meet the Milan criteria have better survival after surgery, and both the Milan criteria and the up-to-seven criteria of our article are based on the size and number of tumors, so we propose the Milan criteria in the introduction section.

2. In section on "treatment" please refine the terminology. For example - lobectomy. May be use segmentectomy or sectionectomy or something more standard. Also tell if these were anatomical or non anatomical or a mix of both etc.

Reply 2: In patients with hepatocellular carcinoma often combined with cirrhosis, many patients cannot be completely operated by radical hepatic segmentectomy, and available data confirm that radical resection can be achieved if a sufficiently wide margin is available. In this study, the patients enrolled for hepatocellular carcinoma surgery were all BCLC-B stage, and many patients' tumor lesions were not located in the same liver segment, and many patients could not tolerate the surgery if they all underwent anatomical hepatectomy, and if patients could achieve the conditions of anatomical hepatectomy all underwent anatomical hepatectomy. Therefore, we formulated the appropriate surgical plan according to the tumor size and location, and all the surgical patients underwent radical hepatectomy. Whenever feasible, anatomic resections were preferred. We have made additional explanation in the text (see Page 5, line 129-130).

Changes in the text: The surgical patients underwent radical hepatectomy, depending on the

tumor size and location. Whenever feasible, anatomic resections were preferred.

3. We need authors to state how did they diagnose HCC. What is the unit protocol of imaging. Did you not do Hepatitis C virus testing at all?

Reply 3: We enrolled patients who were diagnosed with HCC by histology or by imaging techniques [magnetic resonance imaging and/or triphasic computed tomography (CT)] according to the available European Association for the Study of the Liver (EASL) guidelines version. We have modified our text as advised (see Page 4-5, line 115-118). The incidence of viral hepatitis C is low in China, but we all tested our patients during hospitalization, because the hepatitis C virus test was negative so it was not presented in the article.

Changes in the text: if their HCC was diagnosed histologically or by imaging techniques [magnetic resonance imaging and/or triphasic computed tomography (CT)] according to the available European Association for the Study of the Liver (EASL) guidelines version.

4. Generally waiver of consent is granted when there is no contact with the patient or family. Did your ethics team know that the investigators will contact patient / family - and with this knowledge they granted the waiver? To me, this is quite a surprise. Please comment and clarify. I am also unclear as to what information was solicited from patient and / or family?

Reply 4: At the time of treatment, the patients consented to the analysis and publication of their anonymized medical data for research purposes and signed relevant documents. We have modified our text (see Page5, line 123-125).

Changes in the text: The study was approved by board of Ethics Committee of Guangxi Medical University Cancer Hospital (No. LW2022030) and informed consent was taken from all the patients.

5. Line 204-211 confusing in results. Simplify.

Reply 5: We have modified our text as advised (see Page 7, line 189-199)

Changes in the text: The study was followed up until October 2022, the median OS time of the TACE group was 31.0 months, and the median OS time of the hepatectomy group was prolonged compared to that of the TACE group, the median OS was approximately 95.0 months until the last follow-up. The OS rates were significantly higher in the hepatectomy group than the TACE group at 1 year (92.6% vs. 75.2%), 2 years (82.0% vs. 61.6%), and 3 years (73.8% vs. 42.8%) ($P < 0.05$) (Figure 1). The median PFS time of the TACE group was 45.0 months and that of the hepatectomy group was 50.0 months, but the difference between the 2 groups was not significant. Similarly, the PFS rates tended to be higher in the hepatectomy group than the TACE group at 1 year (80.1% vs. 85.7%), 2 years (71.8% vs. 68.4%), and 3 years (62.7% vs. 50.3%), but the differences were not significant($P > 0.05$) (Figure 2).

6. I understand that your aim is to compare BCLC B cases with upto7 and beyond 7. But any

report on HCC and resection should mention 30 and 90-day mortality. Please add this.
Reply 6: None of the cases we enrolled had perioperative deaths, so they were not shown in this study.

7. So how is the study result going to change your practice? I did not see this in discussion. I read about general discussions on size and number and MVI and other commonly known issues in HCC - but i do not see specific discussion of your results. What does author propose to do for patients outside upto 7, technically resectable? Neoadjuvant or resect and adjuvant? Within the upto 7 if resected and histo comes as MVI - what do authors propose?
Reply 7: We have modified our text as advised (see Page 10, line 296-307).
Changes in the text: From our existing data, all patients who met up-to-seven criteria in BCLC-B underwent hepatectomy was superior to TACE. From the point of view of exceeding the up-to-seven criteria, the recurrence rate was higher than that of met up-to-seven criteria group, which suggests that the risk of recurrence was relatively high. If the tumor was not located in the same liver lobe, the recurrence rate was relatively high. Based on the progress of targeted therapy and immunotherapy, for the patients who exceeded up-to-seven criteria, we tend to perform neoadjuvant TACE, targeted therapy, or immunotherapy first, and then perform surgical resection after the tumor is appropriately reduced, which may improve the prognosis of the patient. Because it is very difficult to judge MVI before surgery, it can only be detected by postoperative pathology. If patients who meet the up-to-seven criteria confirm the existence of MVI after surgery, we recommend adjuvant TACE treatment after surgery.

8. About 5% of HCC will have combined cholangio with HCC. I don't read any such thing.
Reply 8: The incidence of intrahepatic cholangiocarcinoma is low within malignant tumor of liver, and all of the patients included in our study had postoperative pathology of hepatocellular carcinoma. We did not mention in the text that "About 5% of HCC will have combined cholangio with HCC".

9. I do know that you did not want to compare other criteria like HKLC - this was not your aim - but any reference from East has to include this too as we all know that BCLC is simply too restrictive.
Reply 9: This study is a preliminary exploration of the up-to-seven criteria in the application of BCLC-stage B. Our next step will be to compare with the Chinese CNLC criteria and HKLC criteria to investigate the differences in their prognosis.

10. You have done upto 8, upto 10, upto 12 etc., but never introduced this in method section and not told the dentition of these criteria and especially tell that these are your hypothetical constructs and novel criteria that is widely validated.
Reply 10: We have modified our text as advised (see Page 5, line 142-147)

Changes in the text: To evaluate whether the up-to-seven criteria can be used as an indication for choosing surgery in patients with stage BCLC-B HCC, we extended the range of the sum of the number of tumors and the maximum diameter of the tumor, i.e., up-to-8, up-to-9, up-to-10, up-to-12, etc., to investigate the survival prognosis of patients with stage BCLC-B HCC who underwent surgery within the range of our hypothesized criteria.

11. How many lap vs open. Conversion rate? Do you do Pringle? Selective or routine? Length of stay? Pleuropulmonary complications? Bile leak? Some data is necessary.

Reply 11: In this study, the surgical methods of our patients with HCC were open, and we basically used the Pringle method for porta hepatis occlusion during the resection process. This study explored whether the up-to-seven criteria could be used as the criteria for surgical treatment of BCLC-B HCC, using the number and size of tumors as the evaluation criteria, and explored the effects of different treatment options on the long-term prognosis and survival of patients with BCLC-B HCC. Therefore, surgical techniques, hospital stay, and postoperative complications were not included in the analysis, but this is a good suggestion, and we may conduct research in these areas in the future.

Review comments-Reviewer C

The authors have completed a very important retrospective study, exploring the effects of up-to-7 criteria in selecting patients for hepatectomy. They also describe the outcomes of the patients with intermediate stage B Barcelona stage HCC over 2 treatment arms: hepatectomy and TACE.

However, the authors have made several comments and inferences which are not based on the study findings. They should present the data with more transparency and reserve inferences in the discussion and conclusions section. The authors should provide clarifications for the following:

1) In Line 73 - mention what are late and intermediate Barcelona stages.

Reply 1: The intermediate Barcelona stages means BCLC-B patients, and the late Barcelona stages means BCLC-C patients.

2) In Line 80, I think the authors are referring to factors that influence survival in the surgical treatment of HCC. This should be changed.

Reply 2: We have modified our text as advised (see Page 3-4, line 82-83)

Changes in the text: At present, it is considered that the factors that influence survival in the surgical treatment of HCC.

3) Lines 110 - 113 are repeated in lines 179-181. This should likely be listed in the results

section only.

Reply 3: We have deleted the contents of lines 110-113

4) Include p-values for comparisons in line 180 to 182.

Reply 4: We have modified our text as advised (see Page7, line192-199)

Changes in the text: The OS rates were significantly higher in the hepatectomy group than the TACE group at 1 year (92.6% vs. 75.2%), 2 years (82.0% vs. 61.6%), and 3 years (73.8% vs. 42.8%) ($P < 0.05$) (Figure 1). The median PFS time of the TACE group was 45.0 months and that of the hepatectomy group was 50.0 months, but the difference between the 2 groups was not significant. Similarly, the PFS rates tended to be higher in the hepatectomy group than the TACE group at 1 year (80.1% vs. 85.7%), 2 years (71.8% vs. 68.4%), and 3 years (62.7% vs. 50.3%), but the differences were not significant($P > 0.05$)

5) Why did patients who exceeded upto - 7 criteria not get TACE? This should be clarified.

Reply 5: The up-to-seven criteria can be used as a choice of whether to treat surgically in Japanese patients with BCLC-B HCC. The starting point of this study was to investigate whether the up-to-seven criteria can be used as criteria for treatment selection in Chinese patients with BCLC-B HCC. Japan is dominated by hepatitis C-associated HCC, while China is dominated by hepatitis B-associated HCC, and there are differences in biological behavior and liver cirrhosis background between them. And our aim was to investigate whether the up-to-seven criteria can be used as criteria for surgical treatment of HCC in BCLC-B, so we did not collect HCC patients who received TACE treatment in exceeded up-to-seven criteria. We can know from the data analysis that the comments made by the reviewers are very good suggestions, and we are also collecting the data of such patients for further analysis.

7) The number of cox regression analysis should be limited to 1 or 2. Running so many regressions increase chances that some are due to chance. (increases alpha error).

Reply 7: We accepted the reviewer's comments and revised the article, and have now limited the number of Univariate and multivariate COX regression analyses in the article. (See table 2 and table 4).

8) Inferences such as line 229 and line 235 should be moved to discussion and not presented in the results section.

Reply 8: We have deleted the contents of line 229 and line 235.

9) Line 260 to 261: the authors have provided data that the number of lesions affects prognosis more than.

Reply 9: We have modified our text as advised (see Page9, line 264-265).

Changes in the text: the 5-year survival rate of BCLC-B patients with 2 or 3 tumors is 52.3%,

while the 5-year postoperative survival rate is only 29.0% in patients with more than 4 tumors.

10) In line 266, the authors should just state their observations rather than make recommendations. This is the first retrospective study and not enough to make recommendations on treatment.

Reply 10: Thanks to the reviewers for their suggestions, we have deleted the contents of lines 266.

11) Tumor site has not been studied by the authors even though it is a prognostic factor per line 267. Why was this not studied. IT has not been mentioned in the introduction section as a predictive factor also.

Reply 11: In the discussion part, we have analyzed the influence of tumor site on the prognosis of patients. (see Page9, line 272-275)

Changes in the text: As the growth site of the tumor varies, the recurrence rate is relatively high if the tumor is not in the same liver lobe, the choice of surgery (e.g., hemi-hepatectomy, hepatic segmentectomy, and local resection of tumor) varies, and the choice of surgery will have a different effect on the prognosis of patients.

12) Line 290 - the authors have found that tumor size plays a larger influence in upto7 criteria. Their conclusion that this is not a decisive factor is not supported by their findings.

Reply 12: In this study, our findings support that tumor number is the main factor affecting prognostic survival in patients undergoing surgery for BCLC-B, while tumor size is not a criterion for surgical treatment. (see Page10, line 317-318)

13) The authors should explain why selection by upto7 criteria led to improvement in OS but not PFS.

Reply 13: We have modified our text as advised (see Page 10, line 287-295)

Changes in the text: Initial treatment has a great impact on the long-term survival of patients with liver cancer. This paper mainly compares and evaluates the efficacy of BCLC-B patients with up-to-seven criteria from the perspective of surgery and TACE, so we use OS as the main evaluation standard. However, due to the high recurrence rate of BCLC-B patients after surgical resection, the reason of recurrence is related to the theory of intrahepatic diffusion or multicenter recurrence of the tumor, and there are various options for the treatment of HCC recurrence, which will affect the survival of patients, so we believe that OS should be used as an important criterion for the efficacy evaluation of cancer patients.

14) English needs to be refined as well.

Reply 14: We will further improve our English level, and this article has been polished by English institutions before. The article touch-up certificate will be sent with the attachment.

Review comments-Reviewer D

1. Abstract

a) Please defined HCC, OS, TACE, PFS, and BCLC-B in the abstract.

b) Please make sure that the abstract within 200-350 words.

Reply: a) We have defined HCC, OS, TACE, PFS, and BCLC-B in the abstract. (see Page 2, line 36-47). b) We ensure that the abstract is within 200-350 words. (see Page 2-3, line 36-64)

Changes in the text: Background: At present, there are still disputes on the treatment of surgery for patients with stage B hepatocellular carcinoma (HCC). This study sought to investigate whether the up-to-7 criterion could be used to decide the treatment for HCC in Barcelona Clinic Liver Cancer stage B (BCLC-B). **Methods:** We analyzed 340 patients with HCC in BCLC-B who treated with hepatectomy or transcatheter arterial chemoembolization (TACE). Of the 285 HCC patients who underwent hepatectomy, 108 met the up-to-7 criterion and 177 exceeded it. All 55 patients in the TACE group met the up-to-7 criterion. We obtained the tumor status of the patients through inpatient medical records, outpatient medical records, and telephone follow-up of the hospital. We compared overall survival (OS) and progression-free survival (PFS) were compared between patients who met the up-to-7 criterion and who underwent either hepatectomy or TACE. OS and recurrence time were also compared between the patients who were treated with hepatectomy and who either met or exceeded the up-to-7 criterion. Across BCLC-B patients, we compared the OS of patients after surgical treatment between subgroups stratified by tumor number and diameter. **Results:** Patients who met the up-to-7 criterion had significantly higher OS rates after hepatectomy than TACE (P=0.000). However, the 2 groups did not differ in terms of PFS (P=0.758). Among the patients treated by hepatectomy, the OS rates were significantly higher in patients who met the up-to-7 criterion than in those who exceeded it (P=0.001). The recurrence rates did not differ between patients who met or exceeded the criterion (P=0.662). OS was significantly higher in patients with ≤3 tumors than those with > 3 tumors(P=0.001). When we stratified patients with ≤3 tumors based in whether they met or exceeded the up-to-8 to up-to-15 criterion, OS was significantly better among those who met the criterion in all cases. **Conclusions:** Hepatectomy appears to be associated with better survival than TACE in patients with BCLC-B HCC who meet the up-to-7 criterion, but this criterion is not a strict indication for deciding whether to treat patients with BCLC-B surgically. Tumor number strongly affects the prognosis of BCLC-B patients after hepatectomy.

2. Reporting Checklist

Here should be filled with “Table1 and Table 4”, please revise.

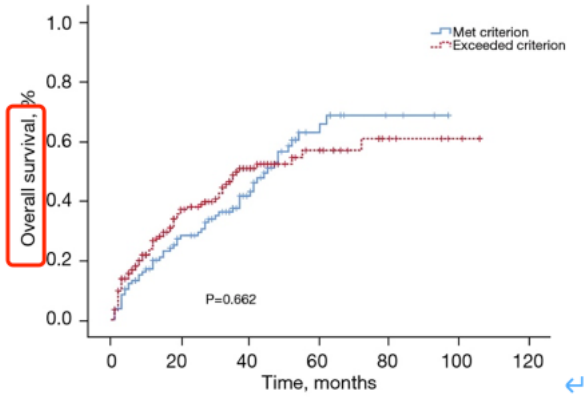
16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A	N/A
	(b) Report category boundaries when continuous variables were categorized	Table1 、Table4	Table1 、Table4
	(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page7/line196-199 Page8/line221-225	Results/ Paragraph4 Results/ Paragraph8

Reply: We have modified the Reporting Checklist as advised and sent it back to editor (see Reporting Checklist).

3. Figure 4

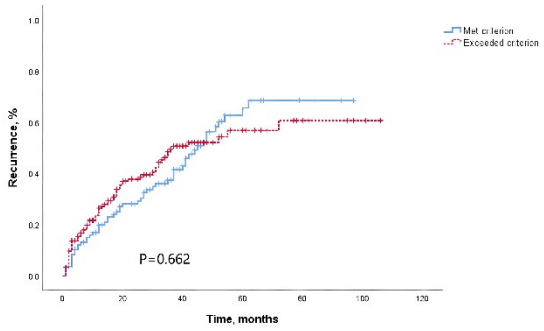
Please check if the figure matches with the legend.

Figure 4 Comparison of the recurrence rates between patients who underwent hepatectomy and who either met or exceeded the up-to-7 criteria.



Reply: We have replaced the new figure in the main manuscript. (see Page21, Figure 4)

Changes in the text:



4. Table 1

Please explain TACE in the table footnote.

Reply: We have explained TACE in the table footnote. (see Page 16, line 448)

Changes in the text: TACE, transcatheter arterial chemoembolization.

5. Table 2-6

Please explain HR and CI in the table footnote.

Reply: We have explained CI and HR in the table footnote. (see Page 16, line 454; Page 16, line 458; Page 19, line 469; Page 17, line 473)

Changes in the text: CI, confidence interval; HR, hazard ratio.

6. References/Citations

Please double-check if more studies should be cited as you mentioned “studies”. OR use “study” rather than “studies”.

127 or radical resection. European and American studies (13) have recommended TACE for

Reply: We have modified our text as advised. (see Page 4, line 88)

Changes in the text: European study (13) have recommended TACE for patients with BCLC-B HCC who met the up-to-7 criterion.