

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 86430

Title: Impact of guideline adherence on the prognosis of Barcelona clinic liver cancer stage B hepatocellular carcinoma

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02731847

Position: Editorial Board

Academic degree: MD, MSc

Professional title: Associate Professor, Staff Physician

Reviewer's Country/Territory: Brazil

Author's Country/Territory: South Korea

Manuscript submission date: 2023-08-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-08-28 23:54

Reviewer performed review: 2023-09-03 14:12

Review time: 5 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is nice a study that analyzes the adherence to BCLC HCC guidelines for stage B patients in Korea. It is weel designed, and concludes that over time, the adherence rate has not improved. Curative treatments such as liver resection, transplantation, and radiofrequency ablation have shown significantly better 5-year survival rates than trans-arterial chemoembolization (TACE), especially in patients aged under 70 with specific platelet count and serum albumin levels. These treatments also yielded improved survival outcomes in both the B1 and B2 groups classified by the Kinki criteria. However, caution is advised in selecting liver resection for B2 patients due to their considerable heterogeneity. Some suggestions: Abstract: Clearly define the research's objective in the Aim section; provide a concise summary of the methodology used; mention the key findings regarding guideline adherence rates, treatment effectiveness, and factors impacting survival outcomes; conclude with a succinct statement summarizing the study's main outcome and its potential implications for HCC treatment.

Introduction: Specify the significance of studying stage B HCC, emphasizing its heterogeneity; mention the global impact of HCC and its ranking among cancer-related



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deaths; highlight the multiple existing international guidelines for HCC treatment; emphasize the challenges in predicting prognosis for stage B patients due to tumor and patient heterogeneity; stress the importance of efforts to improve prognosis for stage B HCC patients, even if it means diverging from guidelines; clarify the role and scope of the Korea Central Cancer Registry (KCCR); state the study's objectives: assessing changes in guideline adherence rates and investigating the impact of non-adherence on survival outcomes; convey the potential contribution of the study to refining HCC guidelines for real-world stage B HCC management. Methods: provide a brief rationale for the retrospective multicenter cohort study; clarify the criteria used for patient selection and inclusion; define stage B (intermediate stage) HCC according to the BCLC staging system; describe the criteria used to classify patients into guideline-adherent, upward, and downward treatment groups; explain the primary and secondary endpoints clearly; simplify and rephrase the definition of guideline adherence for each guideline; mention the statistical software used for analysis; describe the presentation of continuous variables with normal distribution; explain the purpose and methodology of Kaplan-Meier analysis; simplify the explanation of the modified Bolondi or Kinki criteria for classifying patients with stage B HCC. Results: clarify the significance of specific percentages and statistics in the results section; simplify the presentation of baseline characteristics; highlight the most significant differences and trends within the baseline characteristics; present the changes in guideline adherence rates over time more concisely; summarize key findings regarding factors affecting HCC-related mortality for each guideline; provide a more concise and straightforward explanation of the impact of guideline adherence on PFS; simplify and clarify the results of subgroup analysis according to BCLC subclassification, focusing on the most relevant findings; avoid excessive repetition of statistical information; ensure that all relevant information and variables are explained clearly for each analysis. Discussion: provide a more concise and



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clear introduction to the discussion; summarize the main findings of the study in a more straightforward manner; clarify the reasons behind the lack of significant increase in guideline adherence rates; discuss the implications of these findings in the context of real-world clinical practice; highlight the importance of multidisciplinary opinions in treatment decisions for stage B HCC; address the limitations of the study more explicitly and discuss their potential impact on the results; consider discussing the potential clinical implications and recommendations based on the findings; ensure that the discussion is well-organized and flows logically from one point to the next; p Provide a clear and concise conclusion summarizing the key takeaways from the study.

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Reviewer's code: 04668435

Position: Executive Associate Editor-in-Chief

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Author's Country/Territory: South Korea

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript assessed the changes in the rate of adherence to hepatocellular carcinoma (HCC) guidelines over time in Korea and investigated the impact of guideline non-adherence on the survival of patients with stage B HCC. In addition, it was a longitudinal, large-scale retrospective study using real-world data of patients in Korea for 8 years, which showed that the guideline adherence rate in patients with stage B HCC has not increased over time in Korea, curative treatments accounted for most of the treatment strategies adopted by physicians in real-world clinical practice in Korea that deviated from the guideline recommendations. However, data inconsistency is the major flaw of the study, MINOR revision has to be done before this manuscript could be accepted for publication in the World Journal of Hepatology. Question 1: In the background of the abstract, "...non-adherent treatments to HCC guidelines, other than trans arterial chemoembolization (TACE) have...", with regards to "trans arterial", do the authors mean "transarterial" or "trans-arterial"? Question 2: The data of the manuscript could be checked through in the section (Baseline characteristics and distribution of treatment strategies according to each HCC guideline). Authors stated the average age (57.6 years) and proportion of patients with diabetes mellitus (13.7%) were lower in the upward treatment group, however, the data are inconsistent with the data in Table 1. Same as above, "42 (23.2%) of 181 patients with HCC between 2008 and 2010 received upward treatment and had higher total bilirubin levels, CPS, and MELD scores, and lower numbers of tumors" does not match the data in Table 2. Further checking by the author is required. Question3: "Compared with guideline adherence, upward treatment (HR 0.500, 95% CI 0.347–0.719) and a higher platelet count ($>10^5$ / μ L; HR



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0.670, 95% CI 0.507–0.890) ...” and “Upward treatment (HR 0.673, 95% CI, 0.437–1.036) did not meaningfully improve ...” in the section “Factors affecting HCC-related mortality according to guideline adherence” were not consistent with Table 4. The author needs to make further verifications. Question4: In the discussion, the connection between this sentence “In patients with stage B HCC, the adherence rate to each HCC guidelines did not significantly increase...” and the following does not flow logically.