

Format for ANSWERING REVIEWERS

13th Oct 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13572_revise.docx).

Title: Role of surgical resection for hepatocellular carcinoma based on Japanese clinical guidelines for hepatocellular carcinoma

Author: Hisashi Nakayama, Tadatoshi Takayama

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 13572

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

1) Reviewed by 00919239

Thank you for the adequate and kind suggestions.

1. Title was corrected according to your suggestion.
2. Based on your suggestion "It would be interesting if more detailed description on the various staging system.", details of other guidelines were added on Table 1.
3. The pros and cons in BCLC system and Japanese guideline were described on Table 2.

2) Reviewed by 00002055

Thank you for the detailed comments, and the accurate instructions.

1. Page 3, line 23. The phrase of "many years ago" is a vague description.: I corrected.
2. Page 4, line 23. The abbreviation of "MELD" should be spelled out because it is expressed firstly.: I corrected.
3. Page 5, line 10. It is unnecessary of the symbol of ".": It was deleted.
4. Page 5, line 13. The phrase of " ≤ 3 lesions and a diameter ≤ 3 cm" is more appropriate compared to "<3 lesions and a diameter <3 cm.": I corrected.
5. Page 5, line 15. The authors described "transarterial chemoembolization (TACE) for a lesion of diameter >3 cm." This is not accurate description because, in the BCLC algorism, it is not always that the TACE is performed to the lesion of diameter >3 cm.: It was deleted.
6. Page 5, line 16. The phrase of " ≤ 3 lesions" is more appropriate compared to "<3 lesions.": It was corrected.
7. Page 6, line 4-6. The authors argued that early HCC should be observed without aggressive treatment. It is better to be mentioned that this strategy is accepted according to the HCC treatment algorism based on the consensus in the Japan Society of Hepatology.: The paper was added in ref. #26 and mentioned.
8. Page 6, line 18-20. The authors described "Patients who still have ascites after diuretic administration or those with a serum bilirubin level that is consistently >2.0 mg/dl are not

indicated for surgery. For eligible patients with serum bilirubin in the normal range of ≤ 1.0 mg/dl, ~.” However, the authors did not refer to the patients of $1 < T. bil \leq 2.0$ mg/dl.: I corrected. Those patients are indicated for limited resection of liver.

9. Page 6, line 24. The phrase of “If $ICGR_{15}$ is $\geq 30\%$, limited resection or enucleation should be applied.” is more appropriate compared to “If $ICGR_{15}$ is $> 30\%$, segmentectomy or enucleation should be applied.”: I corrected.
10. Page 7, line 8. The expression of “serum albumin < 4.0 g/dl” is more common compared to the phrase of “serum albumin < 40 g/l.”: I corrected.
11. Page 7, line 9. The abbreviation of “pTNM” should be spelled out for “pathological TNM” because it is expressed firstly.: I corrected.
12. Page 7, line 12. The phrase of “good indicator” seems to be inappropriate. The phrase of “poor indicator” is appropriate. : I corrected.
13. Page 7, line 15, 16. The phrase of “after anatomical resection compared to that after nonanatomical resection” is more appropriate compared to “after subsegmentectomy compared to that after segmentectomy.”: I corrected.
14. Page 7, line 19. The authors described that “In general, it is desirable to preserve the TLV or 20-40% of the standard liver volume (SLV).” However, there is no concrete number about what percentage of the TLV should be preserved. : I corrected. “20-40% of the TLV or the SLV” is right.
15. Page 7, line 20-23. The authors described that “The MD Anderson group proposed that the smallest acceptable liver remnant volume is $\geq 20\%$ of the SLV in cases without chronic underlying liver disease³³, with the validity of this proposal supported by an analysis of 301 consecutive patients after extended right lobectomy⁴⁰.” On the other hand, the authors should mention that there was a mortality rate on postoperative day 60 of 4.7% in this literature cited.: I mentioned it.
16. Page 8, line 4. The phrase of “ $ICGR_{15} \geq 10\% - < 20\%$ ” is more appropriate compared to “ $ICGR_{15} \leq 10\% - < 20\%$.”: I corrected.
17. Page 8, line 8. The description of “Hepatic resection with hepatectomy” is inappropriate.: I corrected.
18. Page 11, line 3. The phrase of “post-hepatectomy liver failure” is more appropriate compared to “post-hepatic failure.”: I corrected.
19. Page 11, line 9. The phrase of “indicating that PHLF” is more appropriate compared to “indicating that PHFL.”: I corrected.
20. Page 11, line 6-10. The authors described that “Compared with MELD, which is currently the most commonly used prognostic factor¹⁵ and 50-50 criteria⁸³, the odds ratio of MELD and PHLF for the incidence of post-hepatectomy complications are 2.06 and 5.61, respectively, and the odds ratio of the 50-50 criteria and PHLF for post-hepatectomy mortality are 16.45 and 13.80, respectively, indicating that PHFL is an adequate prognostic factor⁸⁴.” These descriptions were hard to understand. The authors should describe that PHLF seems to be the more efficient indicator comprehensively compared to 50-50 criteria and MELD score because it is significantly associated with both of the incidence of post-hepatectomy complications and the post-hepatectomy mortality. As for 50-50 criteria, it was not significantly related to the incidence of post-hepatectomy complications. As for MELD score, it revealed less strong association of the odds ratio (2.86) to the post-hepatectomy mortality.: I corrected.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

A handwritten signature in black ink that reads "Hisashi Nakayama". The script is cursive and fluid, with the first name "Hisashi" and last name "Nakayama" clearly distinguishable.

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