

October 19, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13574-edited.doc).

Title: Surgical management of hepatocellular carcinoma

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Name of Journal: *World Journal of Hepatology*

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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

(i) Reviewer 1:

- a. The author should emphasize about the high recurrence rate after hepatic resection. In the patients with multiple HCCs and good liver function, the tumors can resectable and cure for a while, however the recurrent rate is very high and it related to poor prognosis. Then resection is discussing with comparison to less invasive treatments such as radiofrequency ablation (RFA) or transarterial chemoembolization (TACE) or these combination therapy in such cases.
 - i. *A paragraph emphasizing the high recurrence rate after hepatic resection was added to the end of the Surgical Resection section (page 8)*
- b. The author should be discussed about issues related “surveillance for HCC in chronic hepatitis C virus or hepatitis B virus infection.” Because the almost of the symptomatic patients with HCC are already in advanced stage, they can’t treat with surgical resection or transplantation. Also HCC is one of cancers in which we can set high risk groups.
 - i. *On page 5 in the first paragraph of the Surgical Resection section, I have added a brief discussion on HCC screening. This was kept brief as the major topic of this paper is “Surgical management of HCC”.*
- c. There may be not only selection bias but publication bias or others for systematic review related the topic “laparoscopic liver resection.”
- d. The authors should discuss about disadvantage of laparoscopic resection because they seem to emphasize the advantage.
 - i. *Response to c and d above: A paragraph was added to the end of the section (page 9) to caution the readers on the potential biases and generalizability of the systematic review findings.*
- e. As ablative therapy, RFA is favored more than percutaneous ethanol injection (PEI). The authors should find systematic reviews comparing RFA with surgical resection.
 - i. *Reference 42 is a meta-analysis of randomised and nonrandomised controlled trials published in 2014 on RFA vs resection. This represents the latest available systematic review on the subject.*

f. The authors should be discussed about ethical issues when they mention about randomized controlled trial comparing resection with transplantation.

i. *I do not see that there are necessarily any ethical issues related to RCT comparing resection with transplantation. Given the comparable intention-to-treat results suggested on systematic review, there is adequate equipoise on this subject to perform ethical trials.*

g. In core-tip, the authors mention about local expertise but they little discuss about it.

i. *When I meant local expertise, this included the availability of laparoscopic surgeons, transplant surgeons, skilled radiologist, etc. That is, local resources which may alter the exact patient management plan.*

Minor

h. In introduction, the authors used “standard potentially curative treatments.” The authors should explain “standard” and also the definition of curative treatment because radiofrequency ablation is also included in the category of curative treatment in some cases.

i. It would be difficult to explain “standard” and “potentially curative” in the introduction. These concepts are subsequently discussed in the discussion. Therefore, I have simply added the phrase “..., although radiofrequency ablation is considered curative therapy in some cases” to suggest to the reader that RFA is sometimes considered potentially curative.

i. In page 4 line 13, “in the west” should be “in the western countries.”

i. *This has been corrected as suggested.*

j. In page 4 line 14, “late” should be “advanced.”

i. *This has been corrected as suggested.*

k. The meaning of “Also, whilst tumor size and number are factors associated with poorer survival, these are neither the only nor the most important factors influencing survival” is difficult to understand.

i. *This has been simplified to “Tumour size and number are not the most important factors influencing survival”*

l. In page 5 line 6, “Child Pugh” should be “Child-Pugh.”

i. *This has been corrected as suggested.*

m. The authors should be clearly described “hepatic vein pressure gradient” is reflects “portal vein pressure.”

i. I have added the following sentence to clarify this point: “This is a measure of the pressure difference between the wedged hepatic venous pressure (an estimation of portal venous pressure) and the free hepatic venous pressure (inferior vena caval pressure).”

n. “If inadequate future liver remnant is not achievable” should be “If inadequate future liver remnant is achievable” or “If adequate future liver remnant is not achievable.”

i. *This has been changed to “If adequate future liver remnant is not achievable”*

o. The authors should add references after the sentence “There have been several systematic reviews on this topic.”

i. *The reviews are described subsequently and referenced appropriately. In order to reduce confusion, I have added “with meta-analyses” to this sentence to clearly indicate the following meta-analyses described pertain to this current sentence.*

p. In page 9 line 6, “patients operated on for non-cancer indications” should be “those of patients operated on for non-cancer indications.”

i. *The words “those of” have been added as suggested.*

q. 10. In page 9 line 11, “Those outside criteria” means outside of Milan criteria or outside of UCSF criteria”?

i. Because the outcomes appeared similar for Milan and UCSF criteria, “outside criteria” actually meant both criteria. Whilst technically, this essentially means outside UCSF criteria, however, I have changed this to “outside Milan or UCSF criteria” as the previous sentence refers to both.

(ii) Reviewer 2: No comments

i. *We thank the reviewer for his/her lack of comments for revision.*

3 References and typesetting were corrected

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

Sincerely yours,

Dr Tony Pang
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