

ANSWERING REVIEWERS

August 14, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 4671-review.doc).

Title: Up-to-seven criteria for hepatocellular carcinoma liver transplantation: a single center analysis

Author: Lei Jianyong, Wang Wentao, Yan Lunan

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4671

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

Reviewer #1:

1. Response to comment: (I want to summarize this topic. Hepatocellular carcinoma is a major health problem worldwide. This disease is especially problematic for Asian countries, which have a high prevalence of HBV and HCV infection. Effective management of early Hepatocellular carcinoma includes resection, radiofrequency ablation and liver transplantation. Liver transplantation remains the best treatment for small Hepatocellular carcinoma resulting from end stage liver disease. However, post-operative recurrence is still a major problem related to Hepatocellular carcinoma after Liver transplantation. Stringent inclusion criteria have been adopted to ensure tumor free survival after Liver transplantation. The Milan criteria have been used as the standard selection criteria for Hepatocellular carcinoma Liver transplantation all over the world. Several groups argued the Milan criteria were too strict and excluded some Hepatocellular carcinoma patients from Liver transplantation, despite the possibility of benefit, and that the criteria should be expanded. Therefore, the Milan group attempted to expand the Milan criteria and create a new set called the up-to-seven criteria (new Milan criteria) Object of that study is the lack of data on this topic in China. Except the number of living donor transplant study groups similar characteristics between the two groups. Characteristics of the tumor size and the number of group 1 and 2 no significant difference. However, there are significant differences between the other groups. As a result, No significant difference in AFP. As expected, lower than the observed survival time and increased tumor recurrence. Although the up-to-seven criteria have been analyzed all over the world, they have not been as widely accepted as the Milan criteria, even 4 years after their conception. Meanwhile, there is still no research on these criteria in China, where most HBC infections .Therefore, this study is important)

Response: Thanks for your full affirmation

Reviewer #2:

1. Response to comment: This paper describes the utility of Up-to-seven criteria for HCC Liver transplantation. Although the paper is well written and interesting, it includes a problem as described below. 1) In this paper, the patients are divided into 3 groups. However, Group 1 is included in Group 2. It may be not adequate to compare Group 1 with Group 2. Group 2 should include patients who are beyond Milan criteria and within Up-to-seven criteria (n=32). This

comparison will make the importance of the paper more clear

Response: It is really true as Reviewer stated that Group 1 is included in Group 2, Group 1 included the 58 patients whose HCC met the Milan criteria, Group 2 included 90 patients whose HCC met the Up-to-Seven criteria. The Up-to-Seven criteria include the Milan criteria. These two criterias were the two independent inclusion criterias, so we directly compared these two groups. Most importantly, our results suggested that patients in the up-to-seven criteria group exhibited a much lower survival rate compared with the Milan criteria group ($P < 0.05$), so even we compared the 32 patients whose HCC were within Up-to-Seven but beyond Milan criteria, the result must be that the survival rate in the 32 patients was much lower than that in the Milan criteria group, so comparison between the Milan group and the 32 patients was unnecessary in our present study.

Reviewer #3:

1. Response to comment: This is an interesting study comparing liver transplant outcomes in 3 groups of patients with different stage of HCC. The study as the authors suggests, suffers from being retrospective and also comparing a radiological system of selection with a histological evaluation of the explanted liver. However the study will add to the published literature, it would be unusual anywhere else to have a cohort of patients with such advanced HCC undergoing transplantation.

Response: It is really true as Reviewer suggested that a cohort of patients with advanced HCC underwent transplantation in our center: Firstly, most of these advanced cases who accepted LT were in the early period; Secondly, in China, the inclusion criteria was expanded and used extensively, such as the Hangzhou criteria, Chengdu Criteria, Shanghai Criteria. So some of the patients in these criterias were the advanced HCCs. In recent years, we tried to unify the Chinese inclusion criteria for HCC LT, this criteria will include more HCC patients but be with comparable outcomes.

3 References and typesetting were corrected

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

Sincerely yours,

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