

November 4th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript 14387-Review.doc).

Title: Prognostic roles of preoperative α -fetoprotein and des- γ -carboxy prothrombin in hepatocellular carcinoma patients

Author: Makoto Meguro, Toru Mizuguchi, Toshihiko Nishidate, Kenji Okita, Masayuki Ishii, Shigenori Ota, Tomomi Ueki, Emi Akizuki, Koichi Hirata

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 14387

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

To Reviewer (00069105):

- (1) Dear authors: nice paper, well written, interesting topic.
→Thank you very much for your comments.
- (2) Major problems: statistical analysis is nice but in my opinion you need taking into account every factor that could change survival analysis (regression) because if you only study HBV/HCV infection and tumoral markers could perform a severe bias. Perhaps patients with high tumoral markers had big tumors or vascular invasion and these data are crucial for survival. I am MD not mathematic and in discussion you said that analysis of factors did not show differences but I think a regression model is needed.
→In our revised version, we performed also an univariate and multivariate analysis for tumor recurrence and poor overall survival using a Cox forward stepwise logistic regression model. We have added those things (red color words) in the Materials and Methods, Results (Table 2 and 3) (Table 5 and 6), and Discussion.
- (3) Minor problems; legends of the figures are too long. Table 1 and 2 could be joined in one table. First column would be the total group. Table 3 and 4 could be joined in one table.
→In our revised version, we have made figure legends shortening. We have joined Table 1 and 2, and then the Table is Table 1. Furthermore, we have also joined Table 3 and 4, and then the Table is Table 4.
- (4) References are OK but a little bit older. Few references are written in five last years.
→Our references are a little bit older as you pointed, so we have changed ref. 2, 3, 11, 14, 23, 27, 32, and 33 to those of five last years.

To Reviewer (00058381):

- (1) For the convenience of the readers, please make your manuscript more concise.
→Thank you very much for your important comment. We made our manuscript more concise. We put Table associated with characteristics of patients in one.
- (2) What are the clinical implications of these observations? Is there an impact on treatment strategies that you propose?
→Thank you very much for your important comment. We added our clinical suggestion and ref. 19 in INTRODUCTION.
【The prognostic findings associated with these tumor marker levels might be useful for making

new selection criteria of living donor liver transplantation candidates with HCC, especially beyond the Milan criteria^{[19].}】

(3) Who wrote the section "peer review" in this manuscript?

→I had a misunderstanding, and this peer review was written by myself, so I removed it.

(4) Linguistic problems

a) (e.g., "Results", paragraph 4: "Table 4 depicts the characteristics of patients the LL group (n = 34), HL group (n = 39), and HH group (n = 27) when these cutoff levels were used as the reference levels"

→In our revised version, " Table 4 summarizes the characteristics of HCC patients with HCV infection in the LL group (n = 34), HL group (n = 39), and HH group (n = 27), with these cutoff levels as baseline levels"

b) "Among preoperative liver function parameters, there were significant differences in preoperative ALB levels (P = 0.006), but no significant difference was observed for other parameter";

→In our revised version, " There were significant differences in preoperative ALB levels (P = 0.006); however, no significant difference was observed for other laboratory variables"

c) "Discussion", paragraph 3: "The difference between the cutoff levels for the diagnosis of cancer those to predict prognosis is almost double that for diagnosis"

→In our revised version, " The cutoff levels to predict cancer prognosis were almost twice of those used for cancer diagnosis"

To Reviewer (01429599):

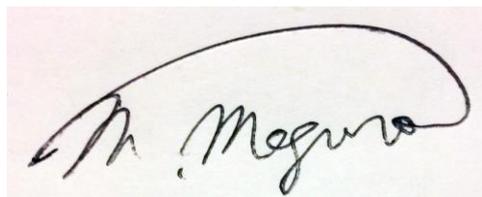
(1) The study was well done and the results clinically useful

→Thank you very much.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink on a light-colored background. The signature is written in a cursive style and reads "M. Meguro".

Makoto Meguro, MD, PhD

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