ANSWERING REVIEWERS

March 31, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9175-review.doc).

Title: A scoring model based on γ-glutamyltransferase and alanine aminotransferase to predict outcomes of hepatocellular carcinoma

Author: Xinsen Xu, Yong Wan, Sidong Song, Wei Chen, Runchen Miao, Yanyan Zhou, Lingqiang Zhang, Kai Qu, Sinan Liu, Yuelang Zhang, Yafeng Dong, Chang Liu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9175

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) In these patients the Child classification is available for every patient. I would be happy to see a correlation/regression analysis combining GGT, ALP and AFP with Child scoring.

Answer: Thanks for your kindly suggestion. We have made the correlation analysis combining GGT, ALP and AFP with Child scoring. Unfortunately, there's no significant correlation between these tumor markers with the Child scoring, so we didn't provide the data in the manuscript.

With this respect, we added this part in the discussion as follows:

Although we demonstrated the prognostic roles of GGT and ALP in predicting the prognosis of HCC, however, there's no significant correlation with respect to the Child scoring, when we explored the potential mechanisms of GGT and ALP in cancer prognosis. We speculated that it was the tumor characteristics resembling by GGT and ALP, rather than the traditional values of GGT and ALP in liver function reserve, that affect the overall survival of HCC patients.

(2) The patients involved in this study underwent a variety of surgical procedures. The extent of resection (and consequent parenchymal changes) would be expected to influence aspects that the authors are studying. This needs to be taken into account more clearly and should be discussed in details.

Answer: Thanks for your kindly suggestion. The extent of resection indeed might influence the prognosis of HCC patients. In our department, the mainly surgical procedures performed were liver segmental resection or subsegmental resection. However, there are no effective ways to evaluate the resection volume of the liver, and the surgical procedures were very different from patient to patient, that we weren't able to unify them consistently. On the other hand, the extent of resection was mainly depended on the tumor characteristics such as tumor size, and liver functional reserve, which was represented by the Child-Pugh classification. So we thought the parameters we included in this manuscript might to some extent represent the surgical procedures. Thanks for your kindly suggestion again.

(3) The discussion could benefit by having an extra sentence or two discussing the different ratios of viral etiologies (HBV- or HBC-related cirrhosis, respectively) in China and the rest of the world.

Answer: Thanks for your kindly suggestion. We have added this part in the discussion as follows:

With respect to hepatitis virus, as one of the most common etiology of HCC, the estimated risk of HCC is 15-20 fold higher in persons infected with hepatitis virus than in uninfected persons. As HBV domains in the Orient and HCV in the Occident, both carriers have substantial risk of HCC-related death. However, in our manuscript, we failed to demonstrate the HBV or HCV as the independent risk factor, probably due to the development of anti-virus therapy in recent years, or because of the small number of patients in our cohort.

(4) Abbreviations in the title should be avoided.

Answer: Thanks for your kindly suggestion. According to the style of Brief Article in WJG and the words limit, we avoided the abbreviations and deleleted some words in the title. The new revised title is:

A scoring model based on γ-glutamyltransferase and alanine aminotransferase to predict outcomes of hepatocellular carcinoma

Reviewer 2:

(1) The authors should more elaborate how many patients had advanced liver cirrhosis and at what stage. How many patients had chronic active hepatitis? The authors should at least discuss these issues in more detail.

Answer: Thanks for your kindly suggestion. As there's no obvious boundaries between the compensated and decompensated cirrhosis, we used the most commonly used criteria for advanced liver cirrhosis, which is the Child-Pugh Classification, as follows:

We were able to determine Child-Pugh classification from the available clinical records in all the enrolled patients, based on which, 160 cases were classified as class A, 12 cases as class B. None class C patients were enrolled in this study, as class C patients were contraindications for hepatic resection in our department.

As to how many patients had chronic active hepatitis, we are very sorry that our patients didn't routinely get the HBV DNA tests.

(2) Were any of studied patients treated with sorafenib?

Answer: Thanks for your kindly suggestion. We excluded the patients treated with sorafenib, because in our department, the data of the patients treated with sorafenib were seperately collected together, distinguished from our patient series in our manuscript.

(3) style and language:

a) the title and a running title is grammatically incorrect and require revisions:

"A Scoring Model Based on GGT and ALP to Predict outcomes of Hepatocellular Carcinoma underwent Liver Resection" should be changed to: A Scoring Model Based on GGT and ALP to Predict outcomes of patients with Hepatocellular Carcinoma who underwent Liver Resection or .....following liver resection

Running title: "GGT and ALP to predict HCC prognosis" should be changed to: GGT and ALP predict HCC prognosis

b) abstract - conclusion "were risk predictors of HCC patients underwent liver resection" should be rephrased and "who" should be inserted after patients. All abbreviations in the abstract, e.g. ROC, OS, TSF should be clearly explained.

Answer: Thanks for your kindly suggestion. According to the style of Brief Article in WJG and the words limit, we avoided the abbreviations and deleleted some words in the title.

The new revised title is:

A scoring model based on γ-glutamyltransferase and alanine aminotransferase to predict outcomes

of hepatocellular carcinoma.

The revised running title:

GGT and ALP predict HCC prognosis.

The revised abstract:

receiver operating characteristic (ROC), overall survival (OS), tumor-free survival (TFS)

Reviewer 3:

(1) About the study on the prognostic factors of HCC after liver resection, it is very difficult to have in-depth results if the study is just a cross-sectional survey which can only get some superficial views. Therefore, in this study, if there is a data accumulation from a long-time follow-up cohort, it is easy to obtain better results.

Answer: Thanks for your kindly suggeston. We will accumulate the data and do some long-time follow-up in future.

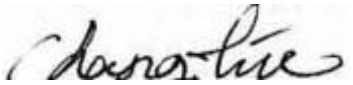
(2) For viral hepatitis-related HCC, there is a significant correlation between the viral load and HCC prognosis. Therefore, anti-viral therapy is an important prognostic factor for HCC after liver resection. However, this study did not pay close attention to the problems above mentioned.

Answer: Thanks for your kindly suggestion. In our department, we mainly focused on the hepatobiliary surgery, and with respect to the anti-viral therapy, it was managed by the department of infectious diseases. So the patients who underwent surgeries in our department got the anti-virus therapy in other departments. Furthermore, the specific treatment procedure wasn't consistent from patient to patient, and we could't get the very detailed information. So we weren't able to systemically analyze the anti-viral therapy here. We 're very sorry for our defect here..

3 References and typesetting were corrected

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

Sincerely yours,



Chang Liu, MD, PhD
Dept. of Hepatobiliary Surgery
The First Affiliated Hospital of Medical College
Xi'an Jiaotong University
Xi'an 710061, China
Fax: +86-29-82654746
E-mail: liuchangdoctor@163.com