

Format for ANSWERING REVIEWERS



June 5, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17999-review.doc).

Title: Platelet count with MRI-liver and spleen volume identifying cirrhosis and esophageal varices.

Research report

Author: Xiao-li Chen, Tian-wu Chen, Xiao-ming Zhang, Zhen-lin Li, Nan-lin Zeng, Ping Zhou, Hang Li, Jing Ren, Guo-hui Xu, Jiani Hu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 17999

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

3 Responses to Reviewer 1:

Comment: The table on the characteristic of patients should include more variables such as

the percentage of patients with additional etiologies for chronic liver disease (alcohol, HDV infection, obesity/metabolic syndrome) and the endoscopic signs of portal hypertension including the diameter of varices, the presence or not of red color signs at endoscopy, the presence of portal hypertensive gastropathy and gastro-esophageal varices according to Sarin's classification. Varices should also be classified as varices at risk of bleeding/rebleeding or not.

Response: This manuscript only studied the patients with hepatitis B related liver cirrhosis and esophageal varices (EV). Therefore, we did not include the patients with additional etiologies for chronic liver disease (alcohol, HDV infection, obesity/metabolic syndrome) in the table 1. Because the modified Child-Pugh classification system (CPS) is an important prognostic factor for cirrhotic patients and is extensively used and reported system in assessment the severity of cirrhosis. The esophageal varices were confirmed by esophageal varices and abdominal contrast enhanced CT or MRI. In the first step, we performed this study to determine how the combination of platelet count (PLT) with spleen volume and right liver volume (RV) at MRI are associated with Child-Pugh class of liver cirrhosis and the presence of esophageal varices (EV) in patients with hepatitis B. In the future, we will perform the study to determine whether these parameters were associated with gastro-esophageal varices according to Sarin's classification. In addition, the patients with varices bleeding were excluded in this study.

Comment: Authors state that the combination of parameters explored in this study is able to discriminate the presence of cirrhosis. The design of the study does not allow to pursue this aim since, as authors state in the discussion, they did not include patients with non cirrhotic chronic

hepatitis.

Response: We give the much thanks to the reviewer's good question. We have noticed that this study only include the patients with cirrhotic chronic hepatitis. However, this study also provided some positive suggestion that the combined parameters including SV/PLT, SI/PLT and RVPS could be used to identify the occurrence of cirrhosis and to differentiate the CPS classes, and to identify the presence of EV. We also stated in the section of limitation. In the future, our further studies will include patients with hepatitis B.

Comment: The aim of hepatologists is not only detecting the presence of varices but also understanding the risk of bleeding/rebleeding in patients with varices in order to decide the best prophylactic treatment for bleeding/rebleeding. Therefore, in accordance with the aim of the study, a sub-analysis should be done to test the applicability of the combined parameters explored in this study to detect varices at risk, in other words, varices that require a prophylactic treatment for bleeding/rebleeding. This should be done in each Child-Pugh class in order to remark the real number of number of endoscopies that could be potentially avoided in each Child-Pugh class.

Response: We give much thanks to the reviewer's suggestion. Although we didn't test the applicability of the combined parameters explored in this study to detect varices at risk, We found that SV/PLT and SI/PLT increased with the progress of Child-Pugh class, PLT and RVPS decreased with the progress of Child-Pugh class; RVPS can be an optimized marker to identify the occurrence of cirrhosis and differentiate the CPS class; and SV/PLT could be recommended for identifying the presence of EV. Results of our study could be helpful to determine the appropriate treatment approach. In our future study, we will test the

applicability of the combined parameters explored in our study to detect varices at risk in each Child-Pugh class.

Comment: Some concerns could be raised in terms of costs. The avoidance of upper gastro intestinal endoscopies has to be challenged with the costs related with a routinely use of magnetic resonance in all patients with cirrhosis. This is an important aspect that could be discussed.

Response: I agree with the reviewer's suggestion. Although MRI examination was more expensive than upper gastro intestinal endoscopies, most of patients, especially for these patients who can't endure invasive upper gastro intestinal endoscopies examination, would like to receive non-invasive such as MRI other than upper gastro intestinal endoscopies. As suggested, we added this in the limitation in the section of discussion.

Comment: overall good study but grammatical errors in discussion need to be corrected

Response: As required, we corrected some of the grammatical errors in discussion.

Response to Reviewer 2:

Comment: The diagnosis of liver cirrhosis was made according to AASLD guidelines. By this diagnosis criteria, the prevalence of varices was quite low, only 45% or 59% in child B or C respectively. According to the literature, the prevalence should be around 80% in Child B or C. Some of the cases could be over diagnosis because of recent acute exacerbation. Please add data of albumin, AST, ALT, PT-INR, total bilirubin, alfa-fetoprotein and ascites into table 1.

Response: There were only 45% or 59% patients having varices because patients with previous

or active gastrointestinal bleeding were excluded from this study. In addition, Child-Pugh score of liver cirrhosis were classified according to albumin, PT-INR, total bilirubin, and ascites. Therefore, we didn't added data of these indicators in into table 1.

Comment: Body weight and BMI may be removed.

Response: As required, we have removed Body weight and BMI in Table 1.

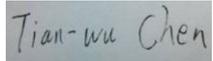
Comment: There is no doubt that combination of RV, SV and PLT will improved the diagnosis of liver cirrhosis by MRI. The diagnosis for advance liver cirrhosis is actually easy. We may use AASLD guidelines to diagnose liver cirrhosis. The main problem is how to make diagnosis between chronic hepatitis B and liver cirrhosis. In this series, the different between Child A liver cirrhosis and normal liver was quite small. This finding decrease the significant of this manuscript.

Response: We found that there were significant differences for combination of RV, SV and PLT between CPS Class A of liver cirrhosis and normal liver. This difference can be found in Table 1. We didn't make diagnosis between chronic hepatitis B and liver cirrhosis because the patients with chronic hepatitis B related liver cirrhosis and normal liver were admitted into this study and the patients with chronic hepatitis B alone were excluded from this study. We added this into the limitation, and in our future study, we will perform a study to differentiate patients with chronic hepatitis B from liver cirrhosis.

3 References and typesetting were corrected

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

Sincerely yours,

A rectangular box containing a handwritten signature in cursive script that reads "Tian-wu Chen".

Tian-wu Chen, M.D.,

Sichuan Key Laboratory of Medical Imaging, and Department of Radiology, Affiliated Hospital of North Sichuan Medical College, 63# Wenhua Road, Shunqing District, Nanchong, Sichuan 637000, China.

E-mail: chentw@aliyun.com.

Tel: 86-817-2262236.