

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34083

Title: Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis

Reviewer's code: 00061674

Reviewer's country: Egypt

Science editor: Jin-Xin Kong

Date sent for review: 2017-05-23

Date reviewed: 2017-05-26

Review time: 2 Days

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> No | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | BPG Search: | <input checked="" type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

The authors conducted this study to provide a simple surrogate marker predictive of liver cirrhosis. The authors used parameters associated with hepatic functional reserve in 302 patients who underwent liver resection for hepatocellular carcinoma divided into two groups, with or without liver cirrhosis and performed logistic regression analysis to identify factors independently predictive of LC. Of all the parameters that were found to be significant in the regression analysis output, the highest odds ratio was that of the ratio of mean platelet volume to platelet count (MPV/PLT). Also MPV/PLT ROC curve analysis was the highest (=0.78). The authors correctly stated in the title, in the abstract objective, and in the conclusion of the discussion that this is a potentially simple surrogate marker of liver cirrhosis and needs further validation. As they mentioned in the limitation of the study section, the work suffers from the small sample size, its



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retrospective nature, and from the fact that it is restricted to patient who underwent liver resection of hepatocellular carcinoma. Comments: 1. In the Methods section, the authors did not comment on whether any of the patients included in the study had one of the conditions that may be associated with increased mean platelet volume such as inflammatory bowel disease, immune thrombocytopenic purpura, myeloproliferative diseases or Bernard-Soulier syndrome as this may introduce high platelet volume that may not be associated with liver cirrhosis. 2. The authors should explain in the discussion section why they failed to compare this potential non-invasive marker of liver cirrhosis with other non-invasive tests such as Fibrotest, aspartate aminotransferase platelet index (APRI), and Fibroscan. 3. The authors are required to support their citation of the new Inuyama Classification with an appropriate reference. 4. In describing the new Inuyama classification, the authors need to define the histopathologic features of F4 liver cirrhosis that distinguishes it from F3 liver fibrosis.

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34083

Title: Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis

Reviewer's code: 02939199

Reviewer's country: China

Science editor: Jin-Xin Kong

Date sent for review: 2017-05-23

Date reviewed: 2017-06-03

Review time: 11 Days

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--------------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> No | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | BPG Search: | <input checked="" type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

Review comments for the manuscript WJH 34083: MPV/PLT ratio had been reported as an useful marker for assessing the liver fibrosis and liver cirrhosis, such as HBV or HCV infection, nonalcoholic fatty liver disease, etc. In this manuscript, Iida et al. has demonstrated that MPV/PLT ratio can predicts the degree of liver fibrosis and liver cirrhosis in patients with HCC underwent surgical resection with favorable sensitivity and specificity at a cut-off value of 0.8. This article is certainly true and includes some useful results, especially its present a simple, noninvasive and economical method to the severity of liver fibrosis, as well as LC. I think this manuscript can be accepted with a revision. Major comments: 1. All of the patients with HCC in the study, whether samples can represent non-HCC populations. At least, authors need to add "the results should not be generalized to patients without HCC before verification", when describe



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the limits of the study. 2. Author need to present the etiology of liver disease, such as HBV, HCV, NASH, AIH, PBC, etc. Since MPV and/or MPV/PLT ratio to predict the severity of liver fibrosis and LC for NASH remains controversial, and as describe by author "LC arising from NASH was recently shown to be a worldwide problem". 3. Of 302 patients with HCC in the study, only 100 patients presented LC. Although HCC can appear in no-LC patients, but most patient present HCC in the setting of liver cirrhosis, especially for HCV infection. Since HCV infection is the main etiology of liver disease in Japan, again author need to present the etiology of the populations in their study. And then, their clarify about why more than 2/3 patients without LC is need. Minor comments 1. The reference is inadequate, for example, "Moreover, MPV is higher whenand Bernard-Soulier syndrome.[references?] MPV may also befrom transient hypoplasia[references?].",..... 2. References format have not referred to the journal guidelines. 3. The unit of PLTs is need in the section of Results: "Their average PLTs were 11.6 ± 4.6 and 18.9 ± 8.1 [unit]" 4. grammar and language needs further working.

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34083

Title: Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis

Reviewer's code: 03260503

Reviewer's country: Romania

Science editor: Jin-Xin Kong

Date sent for review: 2017-05-23

Date reviewed: 2017-06-07

Review time: 15 Days

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
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COMMENTS TO AUTHORS

The ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis – review The authors of the manuscript researched the predicting value of the ratio of mean platelet volume to platelet count in liver cirrhosis. The article is very interesting, because this issue was never explored in liver cirrhosis, the patient database is quite large, but there are some major issues to be clarified: 1. More than 90% of hepatocellular carcinoma appear in patients with liver cirrhosis, but in this study most of the cases are in patients without cirrhosis. What is the explanation for this situation? What is the cause of liver disease in the 2 groups? 2. The ratio of mean platelet volume to platelet count was studied until now in various diseases (non small cell lung cancer, myocardial infarction, sepsis, SIRS), so the reason why it is increased in liver cirrhosis might be actually the chronic inflammatory state. The statistical analysis



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must also explore the correlation between the inflammation in the liver and the ratio of mean platelet volume to platelet count 3. In the introduction section it should have been: “ to determine whether liver fibrosis and LC are associated with MPV/PLT ratio or not”. 4. In the results section there is no distribution regarding gender or age, which may have been important for the purpose of the study. Moreover, the groups involved might have other co-morbidities or none, but the authors did not clarify that issue. I feel that the groups involved in the study have not been appropriately characterized for the study. 5. In the discussion section, 5th paragraph, it should have been said: “MPV has been reported to strongly correlate with...”. 6. Table 1 needs to be completed with the cause of liver disease in the two groups, and this issue must be commented because it might be a bias induced by the etiology. 7. In the results section from the abstract it says that “The AUC value of MPV/PLT was 0.78, with a 0.71 cut off value having a sensitivity of 72% and a specificity of 70%” whereas in the results section from the article it says that “the MPV/PLT ratio had the highest AUC, 0.78. A cut-off value of 0.8 had a sensitivity of 65% and a specificity of 78% in predicting LC”. I would like to know which is the real cut-off value. 8. I suggest that the author should explain the grading of hepatocarcinoma (Edmonson Steiner) for the two groups in the table 1 9. Were independent variables from the logistic regression (Table 2) dichotomized, and if yes, with which cut-off? I am asking this because it is hard to believe that quantitative scale variables might have such high odds ratios (see especially AST, ALT, MCV/PLT, PT). Moreover, it is unusual that both AST and ALT, highly correlated, remained in the model (if so, there is a multicollinearity problem).