

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 03646639

Reviewer's country: Japan

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-08

Review time: 8 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 type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The paper by et al entitled 'Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent alcoholic liver disease (ALD) is an interesting study on collagen proportionate area in alcoholic cirrhotic patients. The authors found that a positive correlation between high fibrosis density and the hepatic venous pressure gradient (HVPG) was observed only in active alcohol drinkers. The active drinkers showed a higher HVPG value than the abstinent alcoholic patients at 12-month of follow-up, while collagen proportionate area values were not significant different between two groups. They concluded that quantification of hepatic fibrosis on transjugular liver biopsy in advanced ALD correlated to HVPG in the active drinkers. Alcohol consumption play a pivotal role to regulate portal hypertension. However, I have following concerns. 1) The average child pugh score of the patients in this study is more than 9. It would be of more interest if authors should focus more on non-invasive evaluation of hepatic fibrosis and

portal pressure. 2) The authors should show what composite clinical outcome is. 3) I would encourage the authors to exclude the healthy candidates who underwent transjugular liver biopsy in this study. There may be some ethical concerns raised from liver biopsy on healthy cases.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 02945170

Reviewer's country: China

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-11

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 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 checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript reports explore the relationship between collagen proportionate area (CPA) and portal hypertension-related clinical manifestations in alcoholic liver disease (ALD). The authors have compared the CPA in 41 patients with active drinkers and 20 abstinent patients. They found there was no difference between these two groups. Moreover, they found CPA cannot predict the clinical events. The results was interested. There are several points to be addressed. 1) why were the sections stained with picrosirius red ? The CPA were seemed too low in cirrhosis patients, what were the reasons? 2) The information about the septal width , number of nodules and nodules size in biopsy slides and the relationship with HVGP should be discussion.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 03647931

Reviewer's country: Egypt

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-12

Review time: 12 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"/> [Y] 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> [Y] No	<input type="checkbox"/> [] Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> [] Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

This study is well designed, conducted on a fair number of patients. However, I have one question to the authors, what is the medical indication of transjugular liver biopsy in healthy donors who normally undergo a percutaneous liver biopsy? This very good study is a retrospective study, which is another limitation, which necessitates future validation in prospective studies.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 03665102

Reviewer's country: Italy

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-13

Review time: 13 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input 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 checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The retrospective study by Restellini et al. explored the relationship between fibrosis density, assessed by collagen proportionate area (CPA) in liver biopsy, hepatic venous pressure gradient (HVPG) and development/worsening of clinical manifestations of portal hypertension in alcoholic cirrhotic patients (active drinkers or abstinent). The authors observed a positive correlation between fibrosis density and HVPG only in active drinkers. However, only HVPG was able to predict clinical events in this group of cirrhotic patients. This is an interesting study, conducted on 61 cirrhotic patients, who underwent hemodynamic study e transjugular liver biopsy: the two groups of patients (active drinkers and abstinent) were homogeneous and well characterized. The results are intriguing: CPA positively correlated with HVPG only in active drinkers, although the two groups were homogeneous. Only HVPG, as extensively demonstrated, was a predictor of further liver complications. However, in my modest opinion, the



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physiopathological significance and the clinical impact of this study are not very clear: the discussion should be improved in order to clarify these aspects. Furthermore, there are several methodological flaws in this study: the percentage of patients with decompensated liver cirrhosis and especially with clinical manifestations of portal hypertension was very high; a control group with compensated cirrhosis, without complications of portal hypertension, or with chronic hepatitis with moderate to severe liver fibrosis, but without cirrhosis, was not included; determination of liver stiffness was available only in few patients and, for this reason, it was useless; the history and the amount of alcohol consumption, the length of the withdrawal period were not indicated. Minor points: page 10: 4/41 in active drinkers and 3/20 in abstinent patients died as expected, the prevalence of clinical manifestations of portal hypertension was higher in patients with higher fibrosis density, although the difference was not statistically significant (Table 3). The authors could subcategorize their patients not only according to fibrosis density, but also according to their drinking habits.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 03563089

Reviewer's country: Kuwait

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-14

Review time: 14 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Lack of some histological images to go hand-in-hand with the rest of the outstanding results. If added, would enhance the quality of the paper even better.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 00053433

Reviewer's country: Brazil

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-15

Review time: 14 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This was an interesting retrospective study with 61 patients with ALD submitted to transjugular liver biopsy and hepatic hemodynamic evaluation. A positive correlation between high fibrosis density (measured by collagen proportionate area, CPA) and the hepatic venous pressure gradient (HVPG) was only observed in active drinkers. In addition, HVPG, but not CPA predicted clinical events. The manuscript is well written and has scientific value, but authors are kindly asked to consider the following comments and suggestions. 1. For the sake of clarity, authors should provide details about the duration of abstinence in abstinent patients. 2. In a multivariate model including active and inactive alcohol users, only HVPG was independently associated with fibrosis density. This finding is relevant and should be stressed in the discussion section. 3. It should be clarified how many abstinent subjects resumed alcohol consumption during follow-up. If all of those patients resumed alcohol abuse, this could



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severely compromise associations with clinical outcomes. 4. In the group of patients abstinent from alcohol, neither HVPg nor CPA was associated with the development of a composite clinical outcome. However, the exact number of cases with hepatic decompensation within this group has not been mentioned, and one could speculate that it would be just a few. In addition, if all abstinent subjects resumed alcohol consumption during follow-up, both facts could have precluded the identification of association between HVPg/CPA and clinical outcomes. This possibility should be briefly discussed. 5. The number of patients with clinical complications due to PHT should be indicated in each subgroup of Figure 2.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36238

Title: Collagen proportionate area is correlated to HVPG in cirrhotic non-abstinent ALD.

Reviewer's code: 00006459

Reviewer's country: Australia

Science editor: Yuan Qi

Date sent for review: 2017-09-30

Date reviewed: 2017-10-16

Review time: 16 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input 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 type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This small-medium size study is adequate to support the conclusions made. Please add clarity to the description of the liver biopsy method on page 8, regarding how the liver tissue was obtained. There is detail on how blood pressure was measured. In the abstract, why is there no mention of the fibroscan data?