

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 34669

Title: Intrahepatic vascular changes in NAFLD: potential role of insulin-resistance and endothelial dysfunction

Reviewer's code: 02447189

Reviewer's country: Germany

Science editor: Ya-Juan Ma

Date sent for review: 2017-05-19

Date reviewed: 2017-05-20

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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" 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 current review addresses an important and timely topic. I therefore found this article interesting and relevant. 1.The authors summarize very nicely the pathogenic concept of endothelial dysfunction in NAFLD. Many pathways are being described. What is currently lacking is a paragraph about biomarkers related to ED – and the potential dysregulation in NAFLD (or, chronic liver diseases in general). I am thinking about tissue factor, thrombomodulin, ADMA, SDMA, CT-proET1, circulating selectins etc. – The authors only mention HVPG measurement, but this would not allow to detect more subtle changes in early diseases. Possibly, a table summarizing the value of potential biomarkers, could be stimulating for the field and increase the outreach of the review article. 2.Along this line, the therapeutic consequences remain vague. There is a lot of speculation (partially grounded on original data and meta-analyses) on the value of statins for NAFLD, but many other cardiovascular drugs as well as investigational

NAFLD drugs (elafibranor, selonsertib etc.) might have an impact on ED. This topic would justify a bit more detailed exploration, possibly also with a figure or table, linking pathogenic observations to current or future therapeutic options. 3. It is well described that fibrosis by itself is associated with aberrant vascularization. There are indications of monocyte-derived macrophages promoting angiogenesis in experimental fibrosis. To which extent are fibrosis and ED linked – or should they be viewed as separate pathogenic events? How will IR affect ED in the context of ongoing fibrogenesis? – I found these processes not clearly delineated in the current review (the impact of fibrosis is more or less neglected, but is probably relevant in this context).



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https:// www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 34669

Title: Intrahepatic vascular changes in NAFLD: potential role of insulin-resistance and endothelial dysfunction

Reviewer's code: 00722239

Reviewer's country: Japan

Science editor: Ya-Juan Ma

Date sent for review: 2017-06-04

Date reviewed: 2017-06-12

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

This is a good review of insulin-resistance and vascular changes per NAFLD. The quality of the paper and English worth publishing. I have no specific comment.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 34669

Title: Intrahepatic vascular changes in NAFLD: potential role of insulin-resistance and endothelial dysfunction

Reviewer's code: 02860653

Reviewer's country: Ukraine

Science editor: Ya-Juan Ma

Date sent for review: 2017-06-04

Date reviewed: 2017-06-20

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 checked="" 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
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		<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 'Intrahepatic vascular changes in NAFLD: potential role of insulin-resistance and endothelial dysfunction' by Pasarin M. et al. is an interesting study which poses an intriguing hypothesis of association vascular dysfunction with liver disease development. This provide new insights on metabolic syndrome. MS is well written and elaborated, its clinical relevance is obvious. I would give rather minor recommendations to Authors (optional) that might improve manuscript - to consider important condition as Fatty liver syndrome on the NAFLD development, complexity of vascular abnormalities that might develop in liver including portal hypertension, issues like thrombogenesis, vascular malformations, hypoxia-related mechanisms leading to fibrosis, etc. Some illustrations / scheme would be helpful.