

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6892

Title: Relationship between non-alcoholic fatty liver disease and obesity: biochemical, metabolic and clinical presentation.

Reviewer code: 00000456

Science editor: Qi, Yuan

Date sent for review: 2013-10-31 18:20

Date reviewed: 2013-11-13 00:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

GENERAL COMMENT This submission covers a topic of outstanding interest and therefore it is worth full consideration for publication. Major flaws of the study design need to be amended. HCC should be discussed as well as the pros and cons of bariatric surgery. Repetitions need to be carefully avoided. The choice of references is open to major criticism. **SPECIFIC COMMENTS** Introduction – 1. The section on NAFLD is too long. Clearly the presentation of this liver condition spans asymptomatic patients through cryptogenic cirrhosis with or without hepatocellular carcinoma. This easy concept should be presented in a direct manner, avoiding long and unnecessary sentences (147 words in present version). 2. The authors allude to endocrine DYSfunction/derangement (rather than MALfunction); however ref. 11 is inappropriate to support such a statement and needs to be replaced (e.g. Loria P, Nat Rev Gastroenterol Hepatol. 2009;6:236-47.). Moreover, allusion is made to the role of age, gender and ethnicity which has best been reviewed in detail elsewhere (e.g. Vernon G, Aliment Pharmacol Ther. 2011;34:274-85.). 3. As far as the concept of NAFLD as “the hepatic manifestation of MS” I think this to be outdated and NAFLD should better be envisaged as an essential component of MS (e.g. Vanni E, Dig Liver Dis 2010; 42: 320–330; Anstee QM, Nat Rev Gastroenterol Hepatol. 2013;10:330-44.) 4. The natural history of hepatic and extrahepatic complications is poorly defined. In particular the risk of hepatic and extrahepatic cancers and cardiovascular risk are poorly outlined (Targher G, Curr Pharm Des. 2013;19:5177-92. Anstee QM, Nat Rev Gastroenterol Hepatol. 2013;10:330-44.) 5. The spectrum of cancer types associated with obesity needs to be mentioned here. Emphasize the risk of HCC in those NAFLD obese individuals (Canbay A. J Hepatol. 2012 ;56:952-64.) 6. Ref 25. Please make sure to read and discuss: Stefan N, Diabetes. 2011;60:2011-7. ; Stefan N, Arch

Intern Med. 2008;168:1609-16. Biochemical presentation – 7. The comment that the fatty hepatocyte resembles adipocyte has been reported earlier and this needs to be acknowledged (Caldwell SH Expert Review of Endocrinology & Metabolism 2010; 5:403-23). Metabolical presentation – 8. Authors may be willing to acknowledge the interactions between lipidome and insulin signalling (Quehenberger O, N Engl J Med. 2011;365:1812-23.). 9. Is there an increase risk of developing type 2 diabetes in those obese with NAFLD ? This is of importance given that diabetes worsens NAFLD course and predisposes to HCC (Anania F, Hepatol Res. 2013 ;43:51-64). 10. Again, discuss the role of metabolic derangements in the development of hepatic cancerogenesis (Canbay A. J Hepatol. 2012 ;56:952-64.) Clinical Presentation - 11. Do not repeat that NAFLD is associated with MS: this has already been pointed out elsewhere in the manuscript. 12. Authors should be aware that not all studies agree that NAFLD is more prevalent in women and more severe in men (e.g. Loria J Hepatol. 2006;44:1196-207.) 13. The contention that ultrasonography detects only steatosis > 33% conflicts with modern views (Dasarathy S, J Hepatol. 2009 ;51:1061-7.). 14. Shortly discuss whether bariatric surgery reverses NAFLD histology and reduces diabetes risk Conclusions - 15. Please provide some clinical indications as to how these obese NAFLD patients should be followed in clinical practice, with specific reference to diabetes risk and surveillance for HCC. Are there any practical methods to identify those NAFLD obese who are at particularly increased HCC risk ?

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Title: Relationship between non-alcoholic fatty liver disease and obesity: biochemical, metabolic and clinical presentation.

Reviewer code: 02541600

Science editor: Qi, Yuan

Date sent for review: 2013-10-31 18:20

Date reviewed: 2013-11-27 15:19

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The review article of Milic et al., summarizing biochemical, metabolic and clinical links between obesity and non-alcoholic fatty liver disease, covers a topic of substantial importance considering the high and increasing prevalence of both diseases. However, the authors should highlight more clearly the novelty of their current submission. Major comment: Although the importance of visceral adipose tissue-lipolysis for hepatic FFA-delivery is generally recognized, the authors should also mention that it is not solely visceral fat that contributes to FFAs in the circulation, but that subcutaneous fat is a major source of systemic FFA-release in the fasting state (e.g. Koutsari and Jensen 2006, J Lipid Res). Thus, the statement that “FFAs are derived from [...] stored lipids that are being released from VAT into the portal system, dietary sources, and de novo lipogenesis...” (page 8, lines 6-8) should be changed accordingly. Minor comments: Question: Regarding the role of leptin in NAFLD-development (Page 6), are there any studies specifically demonstrating hepatic leptin resistance in NAFLD-patients? Please correct references on page 3, line 14. Page 8, line 9: Please correct to “lipolysis”.