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Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 18522
Title: Non-alcoholic fatty liver disease: disparate predictive ability for cardiometabolic risk and all-cause mortality
Reviewer's code: 02861137
Reviewer's country: France
Science editor: Ya-Juan Ma
Date sent for review: 2015-04-24 10:08
Date reviewed: 2015-06-18 07:05

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Onat et al reported an interesting prospective study that aimed to describe the prognostic value of a non-invasive method for diagnosis of fatty liver for incidence of diabetes, coronary heart disease (CHD) and overall mortality. This is an interesting study. However, there are multiple issues that need to be addressed/clarified to ensure that the data fully support the statements and conclusions made. This is a relatively large study which is a positive feature for diabetes / CHD and negative for mortality. Major points 1. The diagnosis of NAFLD is broader than presence of liver steatosis. Patients with NAFLD must have > 5% of hepatocytes with liver fatty associated with no alcohol abuse or use of few drugs that lead to steatosis. In addition, other chronic liver diseases must be excluded. According to Bedogni et al (BMC 2006), Fatty Liver Index (FLI) was not developed to diagnosis of NAFLD. It was validated using abdominal ultrasound as the reference to diagnosis fatty liver. Thus, authors should not state in the paper that NAFLD was or not associated with severe outcomes. In my point of view, the better is to evaluate the prognostic value of the FLI instead of NAFLD. 2. Alcohol consumption is crucial point in NAFLD and its evaluation should be better

described (lines 137-138). Does the authors used a validated questionnaire, such as CAGE or AUDIT, or estimated alcohol use in g/day ? 3. Population sample (lines 118-130): The original study of the cohort (Turkish Adult Risk Factor Study, Onat Atherosclerosis 2001) had 3687 individuals. Why only half of them were evaluated in the present study (n=1822) ? Authors should include a flow-chart of eligible and included patients. 4. Definitions (lines 155-166): Authors should define CHD. Authors should describe how they have access to death information: National Death Registry ? Information with family ? Did deaths have a classification according to ICD-10 codes ? 5. Data analysis (lines 175-183): Authors should describe the use of ANOVA (applied in Table 1) and Cox regression (described in the core tip and applied in Tables 3 and 4). Did the p values on Table 1 are corrected by Bonferroni (authors stated in the footnote that in bold denote significant difference between 2 groups) ? 6. Results: Authors should provide a K-M graphic for incidence of (or survival without) diabetes and CHD and overall mortality. The Cox analysis (Tables 3 and 4) should be repeated replacing the FLI (NAFLD for the authors) by its parameters (BMI, GGT, triglycerides and waist circumference). These analyses should be provided in a Supplementary Material. Severe outcomes might be related to metabolic factors (BMI, etc) and not with fatty liver estimated by FLI. 7. Discussion: The results of the present study are contradictory with the Cremona Study (Calori Hepatology 2011) where FLI had a prognostic value for prediction of overall mortality. The Cremona Study followed more than 2,000 individuals for 15 years and collected mortality data from a National Death Registry. In the present study it was not observed using the same biomarker of liver fat. Thus authors should discuss this point more deeply than 4 lines (280-283). Authors should also discuss the prognostic value of others biomarkers of liver steatosis such as SteatoTest (Perazzo AP&T 2015) and liver fibrosis in NAFLD patients, such as NFS, FIB-4 and APRI (Kim Hepatology 2013). Limitations of the study should be discussed such as (i) FLI was not validated to NAFLD diagnosis, (ii) absence of abdominal US to detect liver fat (it is easy, can be done at the bed side and is available worldwide); (iii) co-linearity between FLI and metabolic factors (confounding factors). Minor Points - Table 2 and Fig 1 should be placed in Supp Material - In Table 1, it is obvious that BMI, tryglicerides, GGT and waist circumference will be significantly higher in patients with NAFLD, because these parameters are included in the formula of the biom

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

-Introductiion section: please report the epidemiology of NASH in Metabolic Syndrome (Masarone et al. Review on recent Clinical trials 2014). Please brief report the association between central fat mass, BMI and liver steatosis, thas was been reported in literature (Abenavoli et al. Panminerva Med 2014).
-Methods section: ultrasound assessment of the NAFLD severity, by echography and/or Fibroscan can help to better define the study. If these evaluation were not performed is necessary to clearly report in the text the reason (i.e. cost). Is also necessary to report the cardiovascular-profile of Turkish people in general or involved in the study referee n. 23.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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Title: Non-alcoholic fatty liver disease: disparate predictive ability for cardiometabolic risk and all-cause mortality
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COMMENTS TO AUTHORS

It was a population based study that aimed to investigated the association of a surrogate of non-alcoholic fatty liver disease (NAFLD) with incident type-2 diabetes, coronary heart disease and all-cause mortality. There are some questions to be considered: 1- the number of subjects: in the abstract it was 1422; in results 1661 and in the core tip and tables it was 1822. 2- Methodology: to establish the diagnosis of NAFLD is necessary to be very careful about the alcohol consumption and it is not so clear in this study; there are no data concerning medications used by the individuals and the presence of other liver diseases; there is no explanation about the diagnosis of coronary heart disease (one of the major outcomes); in statistical analysis the authors used ANOVA and hazard ratio instead of test t and relative risk; there are no information about the variables used in the logistic regression models. Results: how many individuals had diabetes, insulin resistance, hypertension and metabolic syndrome at baseline?