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E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 13814
Title: The importance of imaging and recent developments in diagnosis of nonalcoholic fatty liver disease
Reviewer code: 02462225
Science editor: Fang-Fang Ji
Date sent for review: 2014-09-02 20:34
Date reviewed: 2014-09-10 14:43

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

COMMENTS TO AUTHORS

The review submitted by Koplay et al. focuses on the noninvasive imaging methods to graduate and establish a diagnosis of nonalcoholic fatty liver disease. All methods of imaging were discussed clearly. One major point is missing concerning the controlled attenuation parameter (CAP) which is a recent method for non-invasive assessment of steatosis with transient elastography. Moreover the two-hits hypothesis is currently controversed, this point must be discussed.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 13814
Title: The importance of imaging and recent developments in diagnosis of nonalcoholic fatty liver disease
Reviewer code: 02462531
Science editor: Fang-Fang Ji
Date sent for review: 2014-09-02 20:34
Date reviewed: 2014-09-11 16:45

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

COMMENTS TO AUTHORS

The aim of this manuscript is to provide an up-to-date review of the recent developments in the field of NAFLD imaging, under the general framework of an improved noninvasive diagnosis for this widespread metabolic liver disorder. The topic is surely of broad general interest. Unfortunately, the paper has some major issues that need to be carefully addressed as outlined in the comments below. Major points. 1. A number of recent studies have questioned two-hit hypothesis of NASH development. There is growing evidence that this hypothesis is likely incorrect, because simple fatty liver and NASH are probably two distinct clinical entities. Please refer to Curr Hepatol Rep. 2014 Jun 1;13(2):151-158.and Aliment Pharmacol Ther. 2012 Nov;36(9):815-23. Just because a theory is popular does not mean that it is correct. 2. Reference 5 on vitamin B12 is cited like a kind of afterthought and seems to be out of place. Please delete. 3. Biopsy is probably not the gold standard, but only the best standard for the diagnosis of NASH. Non expert physicians and patients are waiting for an almost perfect noninvasive test, which is a biomarker with less than 10% of false positive or false negative results and more than 99% applicability. This is not possible, even with liver biopsy. Therefore, it is an illusion to wait for an almost perfect biomarker with an adjusted AUROC greater than 90% for the diagnosis of NASH. This point must be explained in the paper. This is crucial for physicians interested in NAFLD imaging. 4. It is regrettable that the authors did not mention the Controlled Attenuation Parameter (CAP), an elastography-derived parameter, for the noninvasive assessment of

hepatic steatosis. It is currently a hot topic with several papers to be cited (see J Gastroenterol Hepatol. 2014 Jul;29(7):1470-6). Notably, CAP is a promising marker as it can detect steatosis even in subjects who are negative on ultrasound (see Eur J Gastroenterol Hepatol. 2013 Nov;25(11):1330-4). 5. The paper lacks a critical discussion of the pros and cons of the reviewed imaging modalities. The authors should add a final paragraph outlining the main advantages as well as caveats of the various imaging methods. Need also to add a section discussing cost-effectiveness of each modality. Otherwise the manuscript is purely narrative and does not present any point of discussion for anyone involved in the clinical aspects of NAFLD. 6. The authors should critically discuss the possible organizing principles for the future of NAFLD imaging. 7. This manuscript could make use of tables to summarize approaches to NAFLD imaging. This would unclutter the review and allow greater focus on concepts and issues. 8. The paper needs to be edited by a native English speaker because there are several spelling errors.