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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 32378 (33866)

Title: Clinical profile of acute-on-chronic liver failure in a multi-ethnic Asian city

Reviewer's code: 03645178

Reviewer's country: Spain

Science editor: Jing Yu

Date sent for review: 2017-01-19

Date reviewed: 2017-01-20

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

COMMENTS TO AUTHORS

The manuscript overall is of interest and the results are enlightening. Maybe you should reformulate the core tip, since your data show that while APASL may identify well patients with chronic liver disease decompensations, EASL criteria is stronger in detecting patients with high short-term mortality. Also, maybe you would like to rephrase your aims in the abstract, since the main goal is to describe the clinical profile of patients with ACLF, above exploring applicability of either set of criteria.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 32378 (33866)

Title: Clinical profile of acute-on-chronic liver failure in a multi-ethnic Asian city

Reviewer’s code: 03700007

Reviewer’s country: United Kingdom

Science editor: Jing Yu

Date sent for review: 2017-01-19

Date reviewed: 2017-01-25

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 checked="" 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

General Comments This retrospective cohort study analyses patients with acute on chronic liver failure in Singapore, using two well recognised criteria to define their cohort in terms of demographics, precipitants, and outcome, and essentially attempts to validate these criteria in their cohort. The article could be of interest to readers of the World Journal of Gastroenterology. The article could be improved by consideration of the comments below, and would benefit from a review of the English grammar used throughout; however at this stage I am unclear how this study advances our knowledge of acute of chronic liver failure. Note: I cannot see an Acknowledgments section in the copy of the manuscript I have - this will need to be added. Title I would suggest incorporating the use of the APASL and EASL criteria into the title, as this will attract more readers. Abstract This would benefit from a review of English grammar and language. For example, the aim would be better worded as ‘to explore the applicability of the APASL and EASL guidelines for ACLF in profiling patients and determining



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outcomes'. In results, the term 'acute liver injury' should be changed to 'liver injury'.
Introduction As a Western reader, it would be helpful to have demographic information about the Singapore population presented in a figure. It would also be useful to include a sentence detailing the differences between decompensated CLD and AOCLF, as this is very topical. The figures reported in the results section detail 3 month mortality; therefore it would be more relevant to report 3 month mortality in the introduction rather than 28 day mortality. Figure 1 is excellent and very useful, but I think the manuscript would also benefit from the inclusion of a table detailing the main differences in the APASL and EASL criteria- most readers will be more familiar with one set of criteria than the other. The first paragraph in the discussion section would be well placed in the introduction and consideration should be given to moving this. Patients and Methods Again, this section would benefit from a review of English grammar and language. Results A flowchart should be provided of the study population. In Table 1, I am not sure that race or the presence of diabetes mellitus is relevant. Information about racial population in Singapore could be presented in an earlier figure as advised. The % is missing in the infection' EASL only' cohort. It is unsurprising that bacterial infection is a more common precipitant in the EASL group, when the ASAPL criteria dictate that the acute precipitating event must be hepatic in origin. It is interesting to note that despite the fact the patients meeting ASAPL criteria can be non cirrhotic (and only 42.9% of this group are non-cirrhotic), that the MELD score is higher in this group than those who meet the EASL criteria alone or both criteria. Potential reasons for this should be postulated in the discussion. Similarly I am not surprised to see that patients meeting both sets of criteria were more likely to die during admission, or be dead at 3 months, or that mortality increases with the number of organ failures. Not much can be made from the transplant data as the numbers are very small. Table 3- only includes details for 70 out of 78 patients. Could you explain why the rest are not included? Table 4- male gender, diabetes mellitus, and previous hepatic decompensation should be removed from the RACE section of the table and presented separately. Where p values are not significant, it is not necessary to report them to their decimal point (p = NS). Discussion Again, this section would benefit from review of English grammar and language. Further consideration needs given as to what new information this study adds to our understanding of AOCLF, and what studies need to be undertaken in the future to further advance our knowledge.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 32378 (33866)

Title: Clinical profile of acute-on-chronic liver failure in a multi-ethnic Asian city

Reviewer's code: 02860625

Reviewer's country: Italy

Science editor: Jing Yu

Date sent for review: 2017-02-04

Date reviewed: 2017-02-07

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 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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear Author, I've read with interest this paper on ACLF. ACLF is a life-threatening condition of hi interest in hepatology. Diagnostic and prognostic criteria have been deeply debated recently. This paper represent, even thou retrospective, a great overview (and for some reson even an external validation) of different ACLF criteria applied to a multicultural population. The methods are clear and the results are comprehensive. Moreover the discussion is clear and goes streight to the main topics on ACLF. In conclusion I do support the pubblication of this paper, and I strongly suggest to apply the idea on a prospective design.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 32378 (33866)

Title: Clinical profile of acute-on-chronic liver failure in a multi-ethnic Asian city

Reviewer's code: 03567380

Reviewer's country: United States

Science editor: Jing Yu

Date sent for review: 2017-02-04

Date reviewed: 2017-02-15

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
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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 report by Rajoo et al. describes a retrospective study investigating ACLF in patients from Singapore. The study compared the EASL and APASL ACLF guidelines in patients with an acute decompensation of liver disease. Of the patients screened, 78 patients with ACLF were identified with 49 fulfilling both EASL and APASL criteria. These 49 patients were found to have worse outcomes with increased age also being a poor prognostic factor. Meeting the APASL criteria, but not the EASL criteria, was shown to lead to better survival rates, probably due to the requirement of liver cirrhosis for the EASL criteria. Overall, the study was performed well and the study is important in this field. That being said, there are some areas the authors could improve this report which are summarized below: 1) Do the authors believe that both EASL and APASL guidelines should be evaluated in developed/developing Asian patient populations? What would the authors recommend as a change to current clinical practice, if any? Please describe this in the discussion. 2) Is the observation that the



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APASL patients have a higher MELD score and lower mortality expected? Please describe in the discussion why this might occur. 3) More studies should be referenced in this report (whether it is in the discussion or introduction)? For example, other studies have investigated ACLF in other populations and found different results (PMID: 27194893). More discussions on recent ACLF papers investigating pathology and etiology would also improve this study (PMID: 28185839 and 28130311). 4) What do the numbers next to APASL and EASL criteria represent in Figure 1? 5) Table 1 does not have value for Hepatitis B flare for EASL only. Some percentages are not included. Why are the numbers listed higher than the n for same columns? For example, APASL only on cause of acute liver injury has a higher n than 14 (21 reported in this case). Please review this table for accuracy. 6) Wording/grammar errors exist in the publication. For example, "It describes a condition in which two hepatic insults liver operate simultaneously....". Please proofread and edit manuscript accordingly.