Reviewer’s report

Title: Elevated D-dimer is Associated with Increased 28-day Mortality in Acute-on-Chronic Liver Failure in China: a Retrospective Study

Version: 1 Date: 31 Jul 2018

Reviewer: giovanni capretti

Reviewer's report:

Dear authors,

first I want to thank you for the opportunity to review your interesting work.

You clearly state the drawbacks of your study design and consider them in your conclusions; this in my opinion is of a paramount importance in any proper scientific paper.

Still your work, as it is, can raise some questions:

- of your 192 patients that meets the APASL ACLF criteria 65 were excluded because the D-Dimer wasn't measured at the admission. 34% is a big percentage of lost cases. You should provide an analysis or demonstrate that this patients were theoretically similar to the cohort you analyzed; otherwise you could have a fundamental selection bias. I provide you an example, if the 65 cases without the d-dimer are the ones admitted in a specific clinical setting or in specific condition or peculiar clinical scenarios this can mislead you evaluation providing the data of a subpopulation and not on your real patients' population

- of great support to your conclusions could be an external validation cohort of your findings or at least and internal one (e.g. with a bootstrap).

- 115 cases could statistically support an extended multivariate analysis such as your adjusted models; I have some concerns if the evaluations of adjusted Odds ratios for 28-day mortality per unit increase in D-dimer in subgroups of patients could still have any statistical validity. In some cases you performe a multivariate analysis on subpopulation of 30 or less patients
the D-Dimer levels correlate in your analysis with a wide spectrum of severity scores and prognostic elements. Have you performe any test to assess how much it's measure can add to the already present elements/scores?

Please argument on these topics.

Best regards

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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