Reviewer's report

Title: Changes of liver enzymes and bilirubin during ischemic stroke. Mechanisms and possible significance

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Reviewer: Paul Welsh

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Muscari et al have investigated the association between liver enzymes and infarct volume in 180 acute IS patients. They report that, as is well know, that CRP and WBC are associated with infarct volume, but they also report GOT and GPT were correlated with IV apparently independently of inflammation.

The manuscript generally well written, and the authors are experienced in this area of research. The data probably do add some information to what is already known. However, I do think the manuscript would benefit from the authors being a little more careful and circumspect in some places.

Major revisions:

1. The aim of your study, as stated, is exploratory. All of your data are based on simple correlations and regression models. I would therefore hesitate to conclude figure 1 is valid – it is very speculative at best. I believe it would be better to delete this and drop most of the speculation as to pathways – the main conclusion being that GOT is independent of CRP, and not a lot of other conclusions can be drawn.

2. You have chosen by and large to present “all data available” rather than to exclude all subjects with missing data, which would be the more accepted epidemiological practice. Given that this would lead to large amounts of missing data, I would suggest that you perform a sensitivity analysis to test whether you can state “when analyses were restricted to those with complete data, the overall conclusions were unchanged” or similar. It would also validate the “random” comment on page 5.

3. Table 3, rather than being based on simple correlations, would be better presented using linear regression, and also including a more complete adjustment model (as a separate model) adjusting for patient demographics and clinical characteristics, as well as all the biomarkers adjusted for each other. This would tell us whether the associations you observe are truly independent. For instance on page 6 you have not included WBC in the multivariable model. Using a systematic approach avoids the question as to what should be included.

4. I struggle to believe that table 5 really tells us much, as the cutoffs used to determine rising on non-rising GOT is really completely arbitrary, and excludes an arbitrary number of patients from the analysis. I would delete this, or at the very least make it more systematic e.g. compare the upper half with the lower half of changes in GOT.
5. Please state the power calculation used in study design, and how the figure of 180 patients was arrived at. Was the study designed specifically to address the present question?

Minor essential revisions
6. Table 4 needs all data included, not just data you feels warrants presentation.
7. Table 2 has some data presented as non-parametric, and in table 3 it is presented as parametric, please check normality assumptions and make presentation consistent.
8. In the abstract “The correlation of IV….day 14”. You don’t show this. Please delete.
9. In the abstract conclusion – i don’t think the “(toxic glutamate?)” adds anything
10. Please state the software used for stats
11. In the limitations section discuss the use of IV as an outcome rather than a more clinical endpoint such as Rankin score, or death/disability.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests