Reviewer’s report

Title: Enhanced prehospital volume therapy does not lead to improved outcomes in severely injured patients with severe traumatic brain injury

Version: 1 Date: 04 Oct 2018

Reviewer: Endre Czeiter

Reviewer's report:

In the present manuscript the authors investigate the potential effects of the "enhanced prehospital volume therapy" to the clinical course/outcome of the severe TBI patients. The main conclusion of the manuscript is that meanwhile the "enhanced prehospital volume therapy" not improves anyhow the outcome of the patients it has a significant negative effect to the coagulation parameters (like hemoglobin (Hb) levels and prothrombin ratio) probably due to a "dilutive effect" of excessive volume therapy.

Although the hypothesis and the aims of the manuscript are clear and well defined it has major limitations and raises some major and minor concerns, reviewed as follows:

1. The authors chosen the matched-pair design for the statistical analysis. Among other parameters the 169 matched-pairs were selected according to the "Systolic blood pressure at the accident site". As the blood pressure at the accident site could be influenced by the extent of bleeding - which could determine the amount of applied volume - this method highly raise the possibility of "overmatching" which is described as the most common mistake with this statistical approach leading to potentially biased results.

2. In addition to the above the fact that beside those significant differences between group 1 and 2 described by the authors (Hb at admission to hospital; Prothrombin ratio (%) in hospital; INR; Units of fresh-frozen plasma in hospital) there were borderline significance/tendencies in such parameters as BP at accident site, Prehospital use of catecholamines, Prehospital chest tube indicating that probably those patients who received "high volume" at the prehospital stage were in worse state (probably due to the more blood loss) than those who received less volume.

In light of the above I would suggest to the authors to completely redo the analysis with a different approach (like correlation analysis between the applied prehospital volume and the in hospital coagulation parameters) especially because - as it is apparent in the "figure 1" (seemingly there were at least thousands of patients fulfilled the inclusion criteria) - the matched-pair method narrows down the number of cases in the analysis very rapidly.

Beside these there are some minor comments to the manuscript:

1. In the "background" section on the 4th page we could read the following "...no other prehospital therapeutic approaches that can improve the severity of this type of injury do exist." I would not
like to utilize any kind of "therapeutic" approach which improves! the severity of the injury - probably this just should be a typo...

2. As part of the "discussion" section in the 12th and 13th page of the manuscript the authors states the following: "Regarding a complete abandonment of volume administration, valid data is not available. Here, prospective studies are required." As the authors also admit due to the really hazardous nature to the CPP of the patients I cannot imagine an RCT for the testing of complete abandonment of prehospital volume therapy in case of severe TBI patients.

3. In case of "Figure 1" it would be worth to know the total amount of those patients (maybe as part of the figure legend) who fulfilled the inclusion criteria of the current study (see my major concern above about the amount of the "lost" cases for the analysis by the applied matched-pair method...)

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

No

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

No

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

No

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 am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an
organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal