Author’s response to reviews

Title: Midline shift in relation to thickness of traumatic acute subdural hematoma predicts mortality. A retrospective cohort study.

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Version: 3
Date: 30 August 2015

Author’s response to reviews: see over
Dear Dr Vespa,

We thank you very much to submit a revised manuscript. We address all comments subsequently following the comments/remarks of the successive reviewer to whom we want to express our gratitude for their very valuable contributions. In the revised document the revisions are marked grey.

Editorial request: the name of the ethics committee have been introduced in the Methods section (p 12, l 9)

Reviewer 1: We agree with the general comment on sensistivity and specifity. However, a prediction with a high specifity could be very beneficial regarding statement towards the family considering the prognosis. In this case a specificity of 1.0 meant that none of the patients survived for whom was (retrospectively (!) otherwise we could have been accused of a self fullfilling prophecy) predicted that they would die. Larger studies to confirm this are indeed needed. However, the main purpose of this study was to address attention to this very important predictor.
1) We have addressed our major objection against measuring the volume of the hematoma itself on page 13. Since it is (at this moment) not possible to measure the volume of the midline shift, we do not think it is appropriate to compare a volume with a distance since it can always be discussed at which level this distance should be measured. We also think that the parenchymal injury is very important for the outcome, and that it is represented through the difference in midline shift and thickness of the hematoma.

2) All patients had a decompressive craniotomy with evacuation of the hematoma with initial replacement of the bone flap except when massive brain swelling was present. (p9, l 12-15).

3) We added the mean mortality rates corresponding to the different measurements of the observers (p16, l 5-8). We think that the sample was too small to define a reliable continuous variable through standard regression techniques. Therefore, we did not introduce it.

4) We removed the part of the sentence that introduced the confusion (thanks for attending us).

5) NCV was indeed a miswriting. It should be TH and has been changed.

6) We added our motivation to use the described technique. (p10, l 24-29)

Reviewer 2

1) We agree with the reviewer that the relation is an indicator for the severity of the brain injury. The main purpose was to draw attention to this important predictor that in our opinion did not receive proper attention. From this sample, we thought that further analysis through regression techniques would not be appropriate resulting in very wide confidence intervals and distracting the
attention of the subject. We can not say how it would rank, since they items the reviewer mentioned correlate obviously. This would be a great subject for a large study, like the European Center TBI study.

2) For this study we did not addressed confounders. As we explained above we wanted to focus on the difference between MLS and TH. We found a positive correlation, and therefore it can be used as a separate item in future prognostic modelling our analysis of large groups. In these studies it could probably be more predictive than only the volume of the hematoma, since the brain swelling factor is taken into account. It should certainly not be used as a standalone factor! We added that in the conclusion of the discussion.

3) We added the CRASH calculations for the patient that died and had a MLS exceding the TH by 3mm or more (p16, L3-5).

4) We determined PPV per rater session since as the reviewer suggested the PPV would be of a mean of measurements. If clinically used this will not be a problem, but since we focussed on these measurements we thought it would be more appropriate to calculate it for each rater session.

5) We took indeed the measurements at the same slices (the slide in which the TH was largest) since we thought the MLS would correspond very well with the TH but also with the impact on the brain at that level if the same slice was used. We used the level of the frontal horns for the measurement of the TH since the impact on the brain will be expressed by a MLS exceeding the TH at the same level. This has been added (p10 – L 24-29).

6) All minor suggestions for minor revisions have been done, we thank you for attending us to these matters.
Reviewer 3

1) we thank Professor Oertel very much for his kind and supportive comments.

2) we changed all the minor issues according to his suggestions.

Thank you very much for your considerations. We are very anxious about your decision.

Sincerely yours,

Ronald H.M.A. Bartels, M.D., Ph.D.