Reviewer’s report

Title: Post-operative re-bleeding in patients with hypertensive ICH is closely associated with the CT blend sign

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Reviewer: Robbert-Jan van Hooff

Reviewer's report:

Hematoma expansion after intracerebral hemorrhage is a frequently encountered problem. As it is associated with poor clinical outcome, limiting the risk of hematoma expansion is key. Recently the novel blend sign has been introduced as a new imaging marker for the prediction of (spontaneous) hematoma growth. Authors aim to examine a possible relation between the presence of the blend sign and post-operative re-bleeding in a small population.

Although attempts have been made to reduce hematoma expansion in several clinical trials, all have failed to demonstrate improved outcome. In this light, the presented study is of interest. However, the manuscript could benefit from some improvements.

Introduction:

I would suggest to rephrase 'At present, there are no effective medical or surgical treatments for ICH, despite...'

Methods:

- Informed consent was obtained only from the 'authorized representatives of the patients'. Was obtaining informed consent from participating patients directly in no case possible? If so, the reason(s) should be mentioned. Based on given GCS scores at least some patients should have been able to give informed consent.

- Authors write that the presence of the blend sign was evaluated by two experienced reviewers. I'd suggest that the background/experience of these reviewers (neuroradiologist, neurosurgeon,...) is added.

- Patients receiving prior anticoagulant therapy were excluded from the study. What about the prior use of anti platelet drugs? Anti platelet drugs use prior to ICH might be associated with higher risks of post-operative bleeding.
Authors define an intracranial re-hemorrhage as 'an increase in the hematoma volume of >33% compared to previous CT scan or the hyper-density appeared again in the focal region of the follow-up CT scan after it disappeared following surgery'. To which previous CT scan do authors refer? Was a control CT-scan systematically performed (immediately?) after surgery? And if so, what were hematoma volumes at this time point?

Results:
- Assessing the inter observer reliability of a novel sign is indeed of importance for the value of this relatively new sign. Even though authors mention in the Methods section to have performed this analysis, no results of this analysis are given in the manuscript.
- Table 2 shows data of the post-operative re-hemorrhage vs. non re-hemorrhage group. Being n=33 and n=96 respectively, this would add up to a total 129 patients. However, based on Table 1 the sum of included patients would be 126 patients. This should be changed.
- Authors state that significant differences were found between the re-hemorrhage vs. non re-hemorrhage groups for the baseline hematoma volume, the GCS score and, most importantly because of the hypothesis, the presence of blend sign on initial CT scan. For the baseline hematoma volume and the GCS score p-values were of 0,045, for the presence of blend sign a p value of <0,001 is found. These values are more likely a reflection of the small study populations rather than a real statistical significant difference. I would recommend that these results should be interpreted with caution.
- A positive predictive value of only 58,5% was found by authors. In my opinion, I would classify this to be low. Therefore, a comment on this should be mentioned in the Discussion section. Furthermore, the PPV is lower than the one found by Qi Li et al. (reference 9); could the authors give an explanation for this difference?

Discussion:
- The time to baseline CT in both groups (i.e. blend sign positive and blend sign negative) is quite long. According to the authors, might this factor have been of influence on the results? As hematoma expansion is most frequently seen in the first 6 hours after onset, the possible presence of the blend sign at 11/12 hours after onset, might be of limited value. Similarly, there are also indications to think that the frequency (and therefore importance) of the spot sign reduces over time.
- The novel blend sign could be an interesting imaging marker to predict hematoma expansion after ICH. To my knowledge, this sign has until now only been evaluated in small cohorts.
Why did authors prefer to examine this sign in a small cohort with an intervention, instead of a larger cohort without any surgical intervention?

- Aiming to avoid hematoma expansion after initial ICH is indeed key, obviously because of its negative influence on clinical outcome. To what extent was the presence of post-operative re-bleeding accompanied by clinical deterioration? As the mean post-operative volumes (3.56 vs. 3.40 ml) were quite small, I doubt that this was necessarily accompanied by clinical deterioration. It might therefore interesting to add clinical neurological parameters (i.e. NIHSS at 24 hours, etc.).

- To which extent have authors ruled out the possibility that the possibly found correlation between prior blend sign and post-operative hemorrhage is for example not simply a reflection of the performed intervention? If I'm not mistaken all patients received a CT-scan prior to surgical intervention (performed at 24 hours). Was any hematoma expansion examined between initial CT and CT at 24 hours?

- Authors conclude quite firmly that the CT blend sign could predict postoperative re-bleeding in patients with ICH that underwent MIS. Due to the very small groups (only 41 patients with positive blend sign on initial CT) and above mentioned comments authors should be careful in drawing conclusions. In general, I feel authors could elaborate more on the limitations of their presented study.

**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

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