Reviewer’s report

Title: Predicting intracranial hemorrhage after traumatic brain injury in low and middle-income countries: A prognostic model based on a large, multi-center, international cohort.

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Reviewer: P.E. Vos

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This is an interesting study in which a post hoc analysis was performed on data from the international CRASH trial in traumatic brain injury to predict intracranial hemorrhage among TBI patients involving multiple variables.

I do agree with the authors that the strengths of the study is the use of prospective, standardised data collection on prognostic variables, and a well-defined patient cohort with few losses to follow-up.

The study is well written and the statistical analyses that were applied seem appropriate and straightforward to me.

I also like the statement that a prognostic model is needed to help the decision making process, ensure rational use of resources, advocates increase in TBI related resources (CT scan and neurosurgeons) and importantly may improve immediate rescue operations.

Nevertheless I feel that several issues hamper the potential impact of this study.

Major Compulsory Revisions

1. Why consider prediction of hematoma only in low-income countries?

I do not see why the prediction of intracranial hemorrhage (in particular the presence of a mass lesion) would only be of importance low and middle-income countries and not for high-income countries as well. Early recognition based on clinical demographic predictors could streamline and improve surgical and emergency procedures around the world. I would therefore suggest that a comparison is made with the high-income countries: how do the selected predictors perform in the remaining cohort from high-income countries participating in the CRASH trial? This could probably also serve as an independent(?) validation procedure. Or vice versa demonstrate interesting differences.

2. What do the predictors predict, intracranial hemorrhage (read mass lesion) or CT abnormalities? Why is an ensemble of various CT characteristics, that are known to be associated with worse outcome, taken as an endpoint instead of the single most important one (mass lesion) that can potentially be neurosurgically treated?

My main concern refers not to the statistical methods but to the definition of intracranial hemorrhage “CT scan diagnosis of intracranial hemorrhage was
defined as the presence of subarachnoid hemorrhage, petechial hemorrhages, obliteration of third ventricle or basal cisterns, mid-line shift, evacuated hematomas and non-evacuated hematomas. These were dichotomized to include all those diagnosed by CT-scan to have intracranial hemorrhage, and those with a CT-scan who did not”. The inclusion of petechial hemorrhage seems not logic from the risk of secondary deterioration perspective. Anyway the mechanism behind petechial hemorrhages is often different from the mechanism that underlies mass lesions. Furthermore traumatic subarachnoid hemorrhage is very different from mass lesions and treatment (if treated) is also very different from large extracerebral subdural or epidural hematoma. I would suggest to perform a separate analysis for evacuated hematoma separately as this outcome is most vital in the early stages after trauma and the only one that needs urgent neurosurgical treatment. In addition a non-evacuated hematoma is ill defined as it can mean anything from clinically non-significant because of a small size to non-salvagable in case of a very large hematoma. (See for instance Biersteker et al. Crit Care Med. 2012 40(6):1914-22).

3. Have pre-hospital characteristics, including presence of a lucid interval, pre-hospital GCS, neurological deterioration in the ambulance, been considered in the prediction of intracranial hemorrhage?

4. Were secondary referrals considered as the reason for long delays between injury and examination in participating hospitals?

Discretionary Revisions

Introduction

It is mentioned that “Intracranial hemorrhage is a frequent and devastating sequelae of TBI, occurring between one-third to a half of cases”. True but the figure seems too high to me. This may be the case in selected cohorts. As the CRASH trial itself is in selected patients (GCS=15 was not included), may be this figure can be introduced in the context of moderate severe TBI or in selected cohort studies.

In reference 16 the year of publication is not mentioned.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

P. Vos serves on a scientific advisory board and has received funding for travel and speaker honoraria from Ever Neuro Pharma.