Author’s response to reviews

Title: Outcomes following administration of tranexamic acid in combat-related intracranial hemorrhage: a cohort study

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Author’s response to reviews:

Dr. Munnangi,

Thank you for the opportunity to revise our manuscript and resubmit it. Our point-by-point response to the reviewers’ comments is included below. Changes made to the manuscript have been underlined. We would like to clarify further what the 1st reviewer would like to see in the table of our multivariate analysis. Thank you.

Regards,

Pat Walker

Reviewer reports:
joel tochie, MD (Reviewer 1): Congratulations to the authors for choosing to work on a topic of tremendous importance in emergency medicine. The manuscript is original and quite interesting. Kindly find some few review comment below

comments
Title : there is not specific and it is redundant. Also the word combat is not specific to this study which includes participants of the army force. Combat can also refer to boxers, does doing catch or marchal acts. Suggested title: Outcomes of tranexamic acid administration in military trauma patients with intracranial hemorrhage: a cohort study

We have changed the title as recommended.

Methods : page 2, line 25 : change combat casualties to army force survivors
Because the casualties include members of the U.S. Army, Navy, Air Force, and Marine Corps, we have changed the term combat to military or added military to described the type of combat throughout the manuscript.

Main text
Page 4, line 15 to 31: please provide references to support your sentences

We have added a reference for this.

Page 4, line 10: change receive to received

We have changed this.

Page 5, line 7: change combat to army

We have adjusted this to military.

Page 5, line 54: you stated guidelines recommend that TXA is effective in TBI if started within 3 hours. Is it not important mentioning this time frame as your inclusion criteria?

Because our database did not include the time that TXA was administered, we were unable to use time in the inclusion criteria.

Page 6, line 12: please specify the name of the local Institutional review board and the authorization number issued by this board

We have included this.

Page 6, line 46: Please specify cerebral CT-scan and not bearly CT-scan. CT-scan was performed at what interval to follow the progression of ICH. Is it possible to know the number of barrettes of the CT-scan machine, was the CT-scan performed by residents or one or several radiologists. If by radiologists what is their average number of professional experience since qualification. All these data aims at reducing bias

We have added head CT to this portion. We do not know how many slices the CT scanners that were used had. All radiologists were staff radiologists of varying experience.

Methods:
* mention ISS as a study variable and spell it out in full before its utilisation in the result section

We have added this.
* please define TBI, ICH, casualties, massive transfusion seen in your methods

Result:
* page 8, line 49 to 59: what was the blood lost, pre-TXA hemoglobin, amount of blood unit transfused, post-TXA hemoglobin between those who received TXA and those who did not.

Unfortunately we did not have this information available in our data.

* Apart from the GCS, what was the functional outcome after TXA administration?
We included Glasgow Outcome Score to demonstrate functional outcomes.

* Did your patients with ICH present with signs of intracranial hypertension? If yes how many, what was the mean intracranial hypertension, apart from decompressive craniotomy, was mannitol used?

Unfortunately we were limited in the availability of this data once again with regard to signs of intracranial hypertension and related

Page 9, line 41: please provide a table of the multivariate analysis done for better transparency of results

Just to clarify, what would you like to see included in the table of multivariate analysis? Here is what we looked at:

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binary logistic regression</td>
<td>0.36</td>
</tr>
<tr>
<td>ISS</td>
<td>0.36</td>
</tr>
<tr>
<td>Ventilator Days</td>
<td>0.29</td>
</tr>
<tr>
<td>Total Blood</td>
<td>0.55</td>
</tr>
<tr>
<td>Pelvic Fracture</td>
<td>0.06</td>
</tr>
<tr>
<td>Lower Extremity Fracture</td>
<td>0.32</td>
</tr>
<tr>
<td>TXA Administration</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Discussion

Page 11, line 35: cite the reference studies you refer to please

The studies we refer to are included in the paragraph below.

Page 11, line 23: change more research to more prospective large-sample size randomized controlled trials

We have added this

Page 13, line 17: change TBI take to TBI to take

We have adjusted this sentence.

Page 13, line 20: change capability to facility

We have kept capability as the type of facility present in a field setting will likely be variable for the military.

References

Please your reference should not have the month and day of publication in order to be in conformity with Vancouver referencing

We have changed to the Vancouver format.

Hideharu Tanaka, (Reviewer 2): In your study, why do you think about increase in GCS improvement
with TXA?
please identify more detailed explain pathophysiology

Why TXA administration in patients with combat-related intracranial hemorrhage shows no
difference in progression of intracranial hemorrhage, need for cranial decompression, Glasgow
Outcome Score, or mortality?

Please answer to brief mechanism

As there was no difference in progression of intracranial hemorrhage that we saw between patients that
did and did not receive TXA, it is difficult to say what the exact mechanism is. Perhaps it is due to the
anti-inflammatory properties of TXA, but it is difficult to say that at this point.