Resuscitation Outcomes Consortium

A Two Gram Bolus of Tranexamic Acid Improves Survival After Traumatic Brain Injury in Patients with Intracranial Hemorrhage

Martin A. Schreiber MD FACS
COL, MC, USAR
Professor of Surgery
Oregon Health & Science University

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

*CRASH-2 trial collaborators**

Summary

Background Tranexamic acid can reduce bleeding in patients undergoing elective surgery. We assessed the effects of early administration of a short course of tranexamic acid on death, vascular occlusive events, and the receipt of blood transfusion in trauma patients.

Methods This randomised controlled trial was undertaken in 274 hospitals in 40 countries. 20 211 adult trauma patients with, or at risk of, significant bleeding were randomly assigned within 8 h of injury to either tranexamic acid (loading dose 1 g over 10 min then infusion of 1 g over 8 h) or matching placebo. Randomisation was balanced by centre, with an allocation sequence based on a block size of eight, generated with a computer random number generator. Both participants and study staff (site investigators and trial coordinating centre staff) were masked to treatment allocation. The primary outcome was death in hospital within 4 weeks of injury, and was described with the following categories: bleeding, vascular occlusion (myocardial infarction, stroke and pulmonary embolism), multiorgan failure, head injury, and other. All analyses were by intention to treat. This study is registered as ISRCTN86750102, Clinicaltrials.gov NCT00375258, and South African Clinical Trial Register DOH-27-0607-1919.

Findings 10 096 patients were allocated to tranexamic acid and 10 115 to placebo, of whom 10 060 and 10 067, respectively, were analysed. All-cause mortality was significantly reduced with tranexamic acid (1463 [14·5%] tranexamic acid group *vs* 1613 [16·0%] placebo group; relative risk 0·91, 95% CI 0·85–0·97; p=0·0035). The risk of death due to bleeding was significantly reduced (489 [4·9%] *vs* 574 [5·7%]; relative risk 0·85, 95% CI 0·76–0·96; p=0·0077).

Interpretation Tranexamic acid safely reduced the risk of death in bleeding trauma patients in this study. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients.

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Lancet 2010; 376: 23–32

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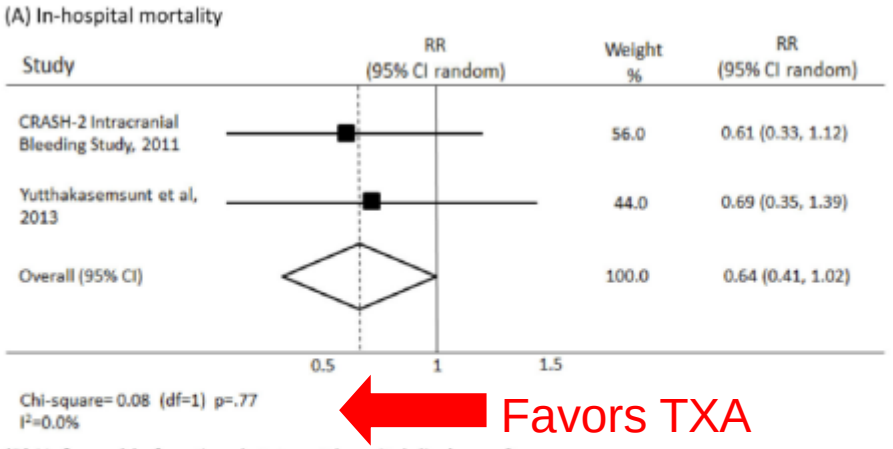
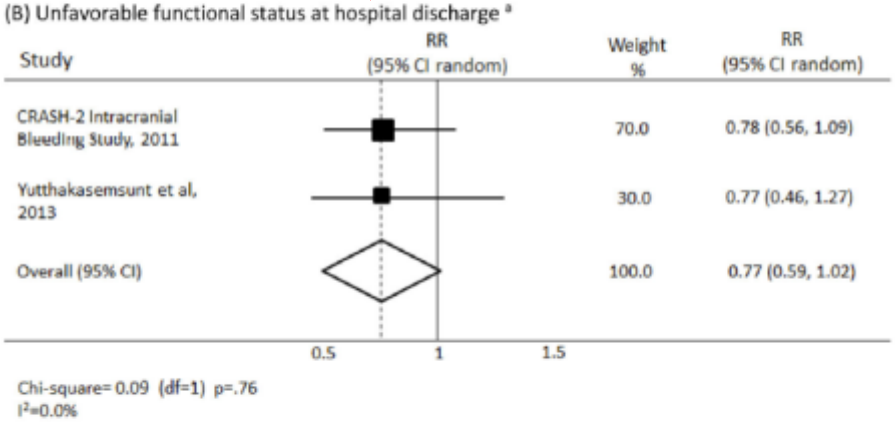
See Comment page 3

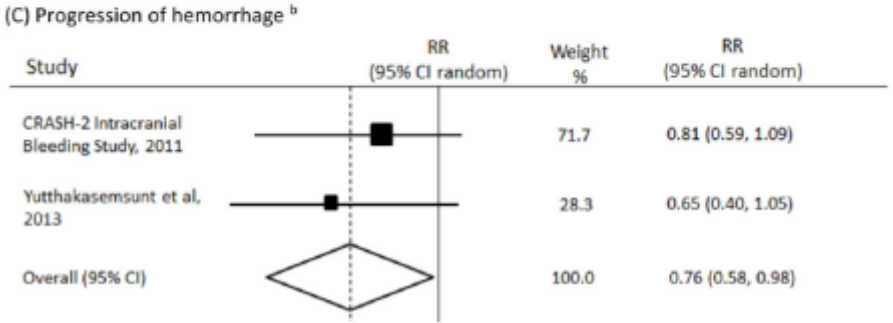
*Members listed at end of p

Correspondence to: Clinical Trials Unit, London School of Hygiene and Trop Medicine, Keppel Street, Lo WC1E 7HT, UK crash@lshtm.ac.uk

Meta–analysis (2 Studies)







510 patients overall

1 gram bolus, 1 gram infusion

Zehtabchi et al.
Am J Emerg Med
2014;32:1503 –1509.

TCCC Guidelines

- Casualty anticipated to need significant transfusion
- Administer 1 gram ASAP
- Administer 1 gram infusion after initial resuscitation
- No indication for TBI

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Methods

- 3-arm randomized trial (1:1:1)
- Multi-center, multi-national
- Double-blinded
- Key coded kits placed on rigs and replaced at trauma center when used

Primary Aim

To determine the effects of two dosing strategies of TXA on outcome following moderate to severe TBI

Subject Selection

Inclusion Criteria

- Blunt or penetrating TBI
- GCS = 3 - 12
- Prehospital SBP $\geq$ 90 mmHg
- Age ≥15 y/o, or ≥50 kg, if age unknown
- IV placed
- Planned transport to participating hospital

Exclusion Criteria

- GCS = 3 with no reactive pupil
- > 2 hours from time of injury or time unknown
- Any prehospital CPR
- Seizures, MI, stroke, dialysis
- Known or suspected prisoners
- Known/suspected pregnancy
- Drowning or hanging
- Burns >20% TBSA
- TXA or pro-coagulant drug
- Opt out

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Randomization Groups

- 2 gram PH bolus, 8 hour IH placebo infusion
  - BO
- 1 gram PH bolus, 8 hour IH 1 gram infusion
  - BM
- Placebo PH bolus, 8 hour IH placebo infusion
  - PB

Results

- Enrollment from May 2015 – Mar 2017
- 967 patients randomized and received drug
  - 346* BO
  - 312 BM
  - 309 PB

* 1 excluded from analysis because enrolled while in police custody

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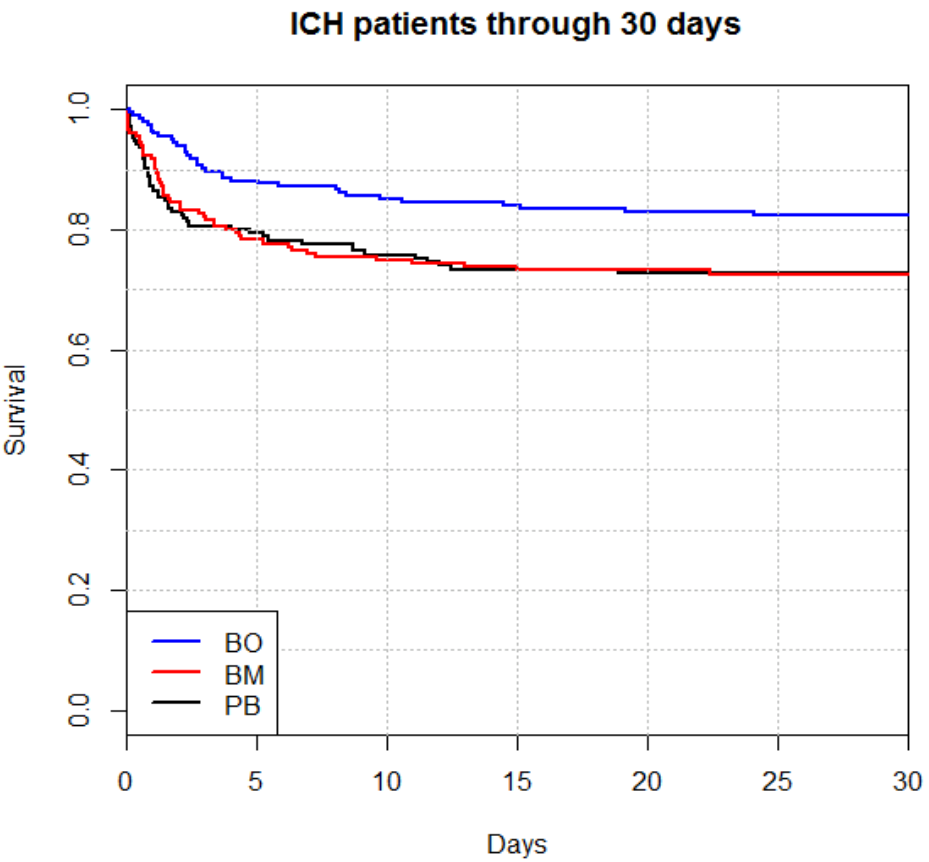
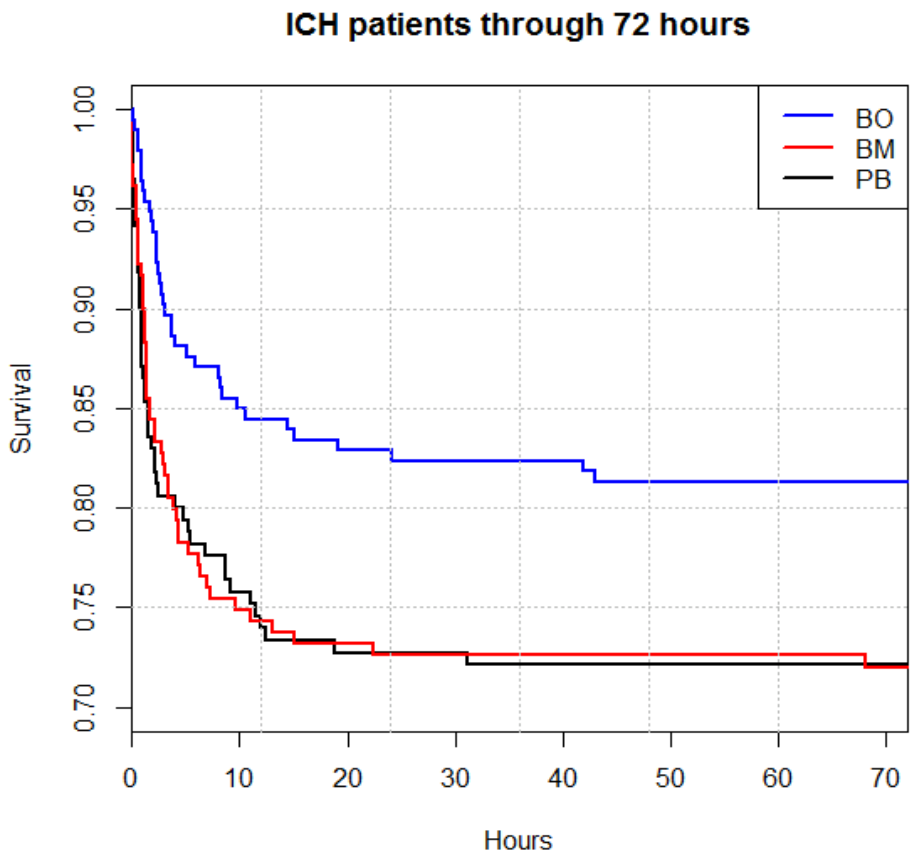
Mortality





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Conclusions

- Prehospital TXA use is feasible
- Does not result in favorable GOSE at 6 months
- Does not affect TEG on admit
- 2 grams prehospital TXA results in improved 28 day survival in patients with ICH
- 1st therapeutic with evidence for benefit in acute TBI
- What about hemorrhagic shock?

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