

Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial

The CRASH-3 trial collaborators*

Summary

Background Tranexamic acid reduces surgical bleeding and decreases mortality in patients with traumatic extracranial bleeding. Intracranial bleeding is common after traumatic brain injury (TBI) and can cause brain herniation and death. We aimed to assess the effects of tranexamic acid in patients with TBI.

Methods This randomised, placebo-controlled trial was done in 175 hospitals in 29 countries. Adults with TBI who were within 3 h of injury, had a Glasgow Coma Scale (GCS) score of 12 or lower or any intracranial bleeding on CT scan, and no major extracranial bleeding were eligible. The time window for eligibility was originally 8 h but in 2016 the protocol was changed to limit recruitment to patients within 3 h of injury. This change was made blind to the trial data, in response to external evidence suggesting that delayed treatment is unlikely to be effective. We randomly assigned (1:1) patients to receive tranexamic acid (loading dose 1 g over 10 min then infusion of 1 g over 8 h) or matching placebo. Patients were assigned by selecting a numbered treatment pack from a box containing eight packs that were identical apart from the pack number. Patients, caregivers, and those assessing outcomes were masked to allocation. The primary outcome was head injury-related death in hospital within 28 days of injury in patients treated within 3 h of injury. We prespecified a sensitivity analysis that excluded patients with a GCS score of 3 and those with bilateral unreactive pupils at baseline. All analyses were done by intention to treat. This trial was registered with ISRCTN (ISRCTN15088122), ClinicalTrials.gov (NCT01402882), EudraCT (2011-003669-14), and the Pan African Clinical Trial Registry (PACTR20121000441277).



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For the Chinese translation of the abstract see [Online](#) for appendix 2

For the French translation of the abstract see [Online](#) for appendix 3

For the Hindi translation of the abstract see [Online](#) for appendix 4

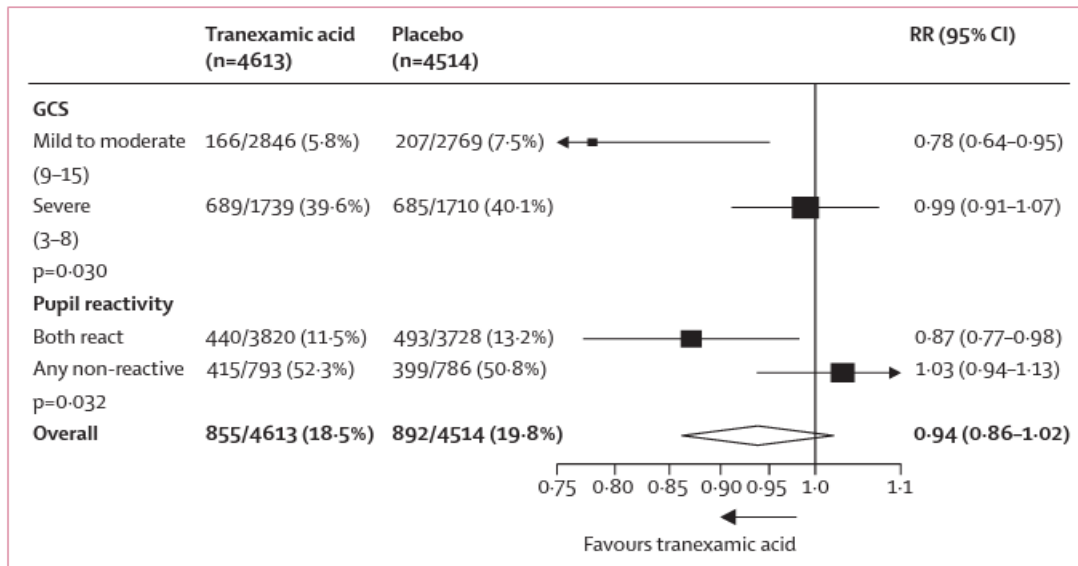


Figure 3: Effect of tranexamic acid on head injury-related death stratified by baseline severity in patients randomised within 3 h of injury
RR=risk ratio. GCS=Glasgow Coma Scale.

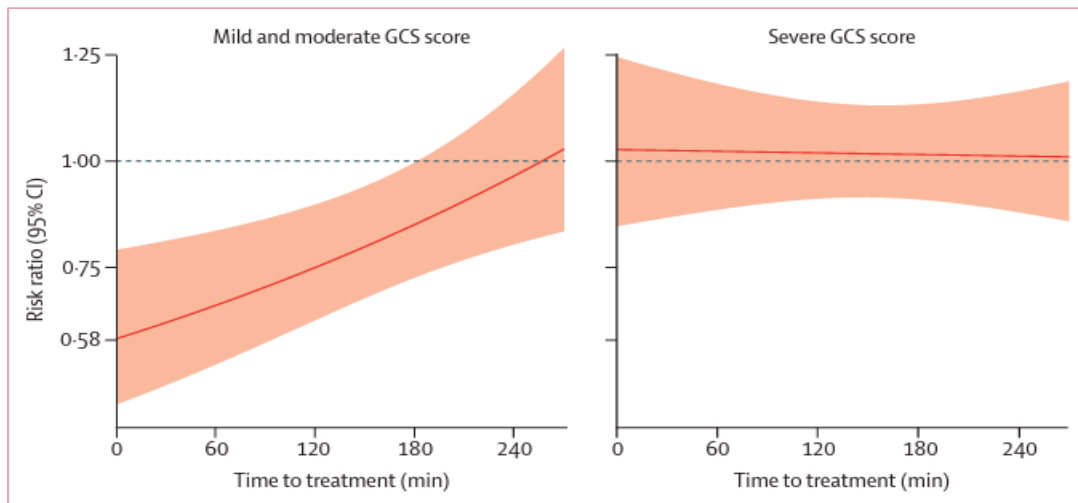


Figure 4: Effect of tranexamic acid on head injury-related death by severity and time to treatment in all patients
The models were adjusted for GCS score, age, and systolic blood pressure. 537 patients with mild and moderate GCS scores (9-15) and 918 patients with severe GCS scores (4-8), excluding those with a GCS score of 3 and those with no reactive pupils, died because of head injury. GCS=Glasgow Coma Scale.

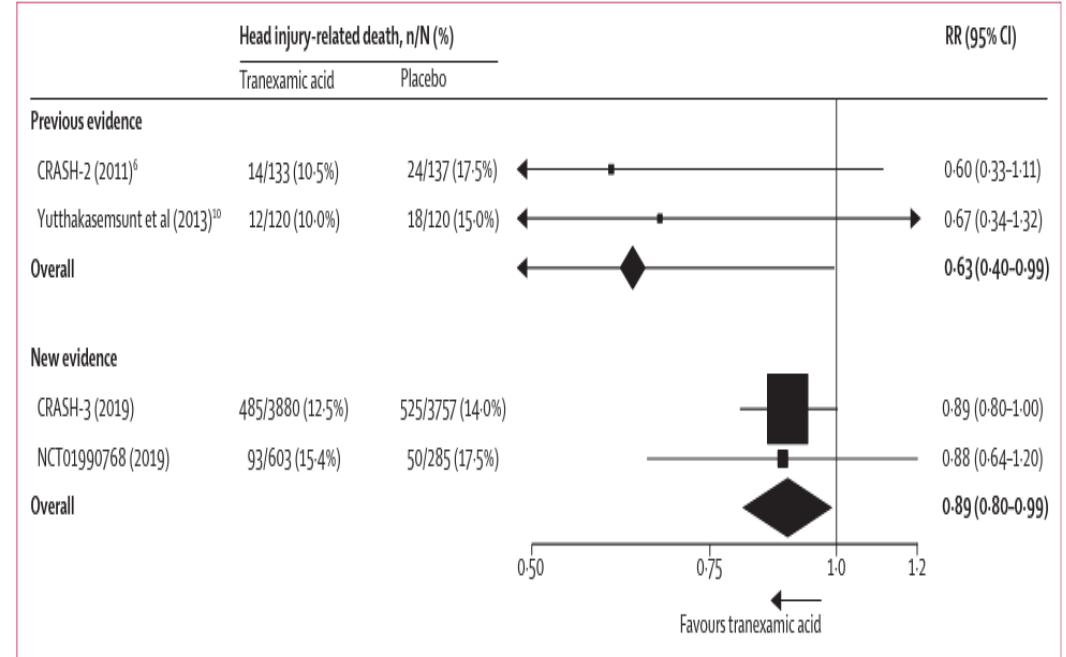
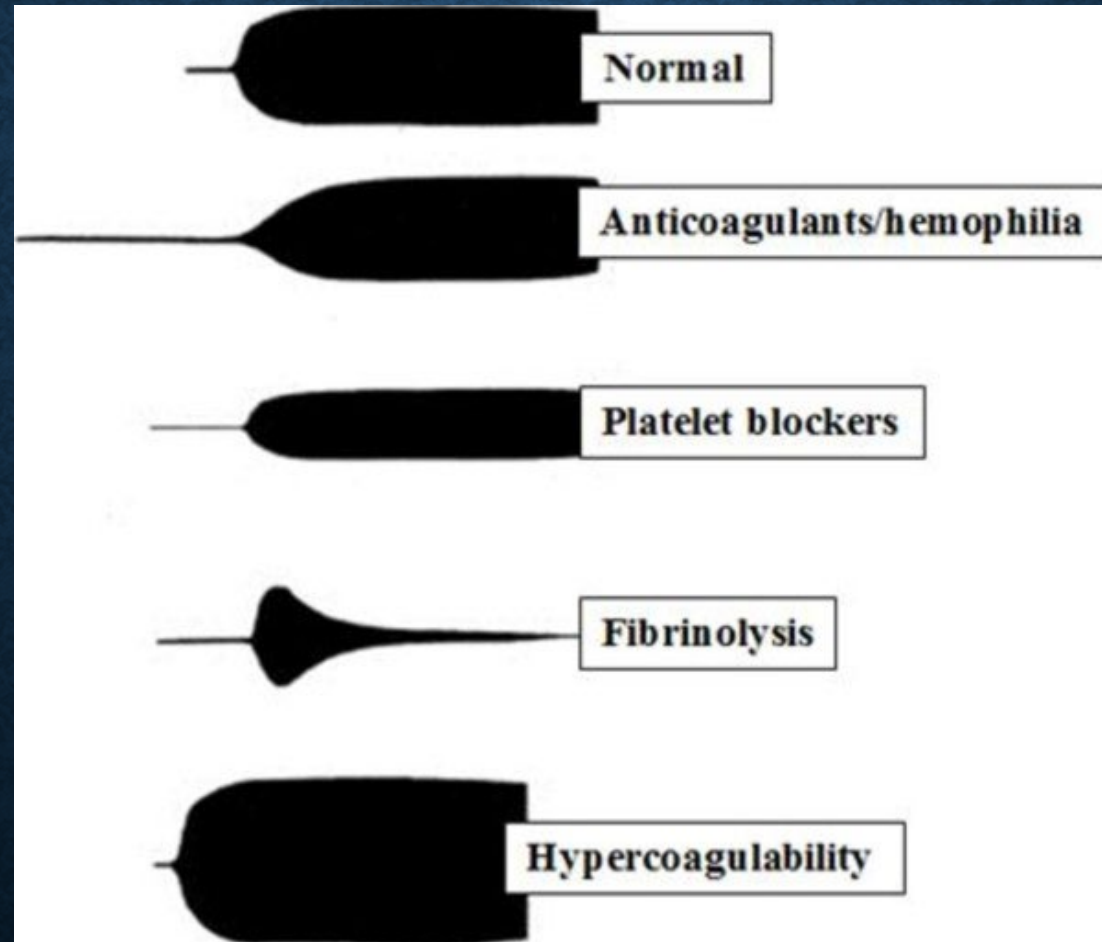


Figure 5: Evidence on the effect of tranexamic acid on head injury-related death
RR=risk ratio.

ROTEM/TEG



ACIDOSIS
HYPTHERMIA
COAGULOPATHY

CALCIUM

