Impede the Bleed: Tranexamic Acid for Surgical and Traumatic Bleeds

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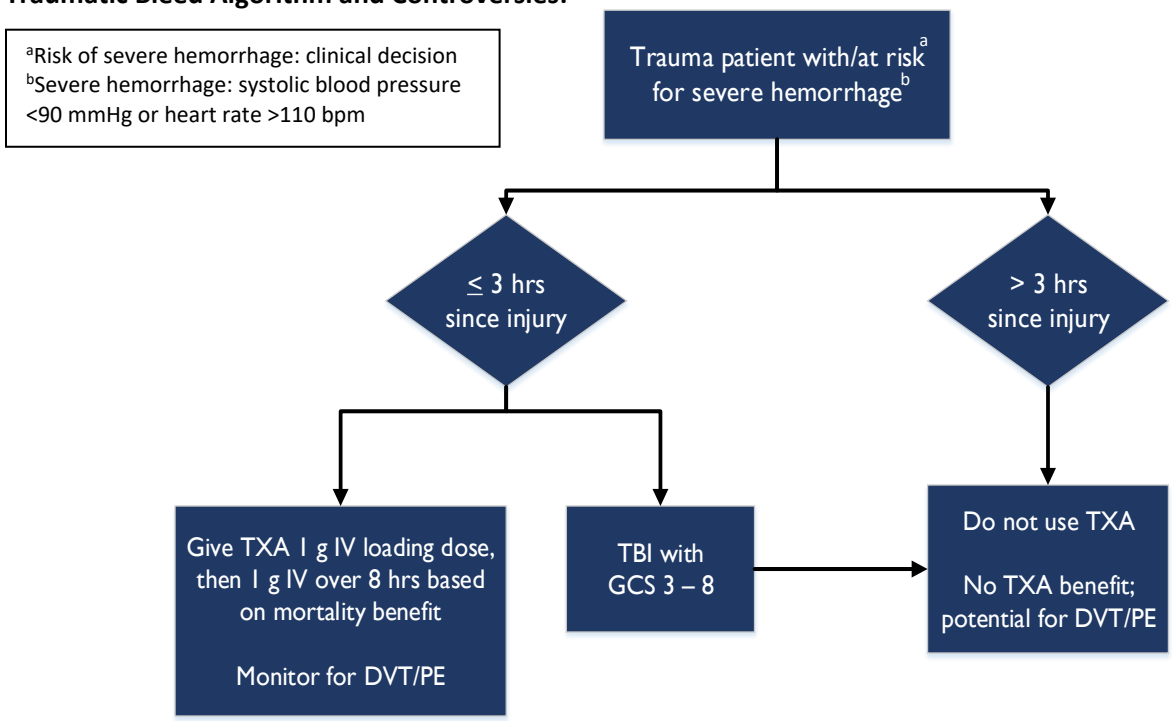
Learning Objectives:

1. Describe the risks and benefits of tranexamic acid (TXA) use in trauma and surgical patients
2. Explain the clinical controversies and unanswered questions behind the use of TXA

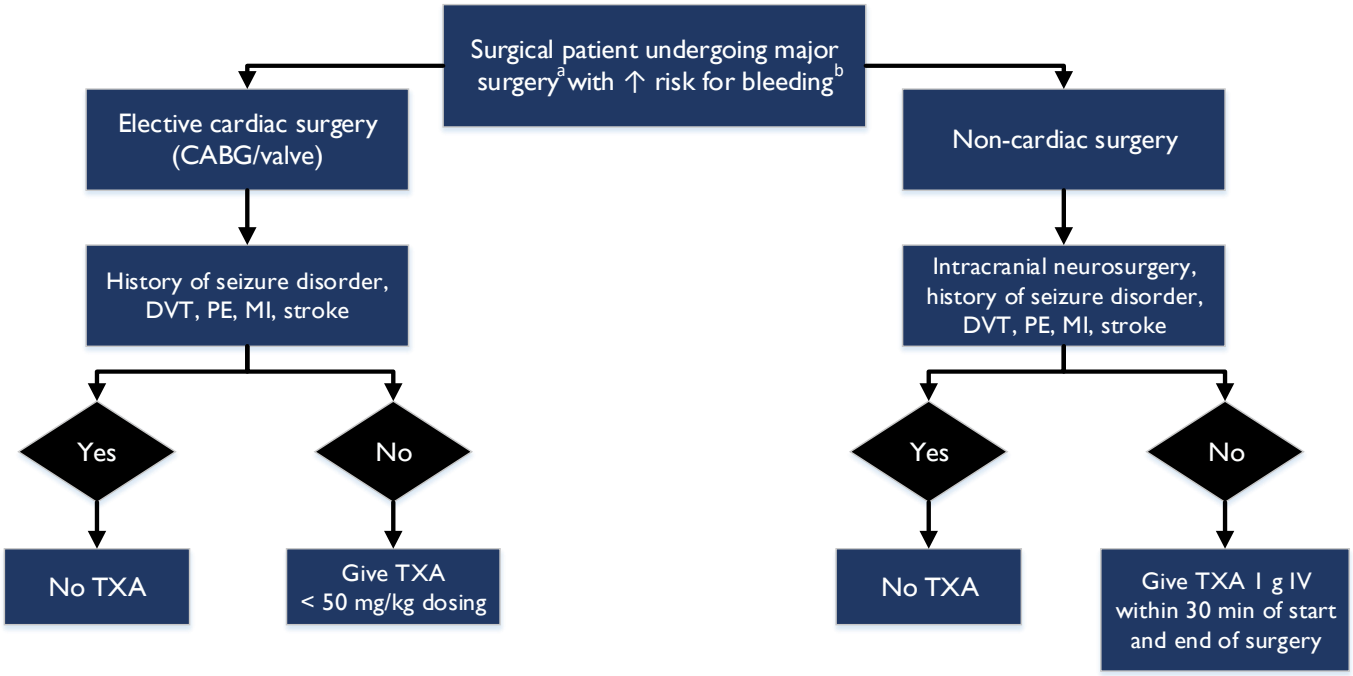
TXA Traumatic Bleed Algorithm and Controversies:[1-4]



Controversy	CRASH-2 Trial	MATTERS Trial	CRASH-3 Trial
Dose and Frequency	1 g IV then 1 g IV over 8 hrs	Mean (SD) dose: 2.3 (1.3) g	1 g IV then 1 g IV over 8 hrs
Timing	≤3 hrs: benefit >3 hrs: risk	32.7% received within 1 hr	≤3 hrs: benefit in GCS 9-15 >3 hrs: no ↑ mortality
Mortality Benefit	Yes	Yes	Head injury-related death if mild/moderate GCS
Bleeding/ Transfusions	↓ death due to bleeding, but no difference in transfusion	↑ transfusions in TXA group (more severely injured)	-
Seizures/ Thrombosis	Seizures not assessed/ No difference in MI/stroke/PE	Seizures not assessed/ ↑ VTE	Seizures/thrombosis outcomes not powered
Quality of Evidence:	Low quality of evidence	Moderate quality of evidence	High quality of evidence

Abbreviations: IV: intravenous; SD: standard deviation; GCS: Glasgow Coma Scale; MI: myocardial infarction, PE: pulmonary embolism; VTE: venous thromboembolism; TBI: traumatic brain injury; DVT: deep vein thrombosis

TXA Surgical Bleed Algorithm and Controversies:[5-8]



[a]Major surgery: cardiac, intraperitoneal, intrathoracic, retroperitoneal, or major orthopedic surgery (hip arthroplasty, internal fixation of hip or femur, pelvic arthroplasty, knee arthroplasty, above-knee amputation, or amputation below the knee but above the foot)
[b]Risk for bleeding: >70 years old, female, use of low-molecular weight heparin/antiplatelet drug <5 days before surgery, renal impairment (eGFR, <60 ml/min), insulin-dependent diabetes, liver disease, prior major bleeding or hemophilia, uncontrolled hypertension (systolic blood pressure >160 mmHg)

Controversy	Cochrane Review Non-Urgent	Cochrane Review Urgent	ATACAS Trial Cardiac	POISE-3 Trial Non-cardiac
Dose and Frequency	Dosing varied between trials	10-15 mg/kg bolus +/- second dose	Not to exceed 50 mg/kg	1 g IV bolus
Timing	-	-	>30 min after start of anesthesia	Start and end of surgery
Mortality Benefit	No benefit	No benefit (Wide CI)	No benefit/mortality not ↑	↓ death by bleeding, not all-cause
Bleeding/ Transfusions	↓ bleeding (414 mL) ~1 unit/patient saved	↓ transfusions (uncertain volume)	↓ reoperation; ~1 unit/patient saved	↓ major bleeding ↓ ≥1 unit pRBCs
Seizures/ Thrombosis	Seizures not assessed; No difference in MI/stroke/VTE	Seizures not assessed; uncertain MI/stroke/VTE risk	↑ seizures; no ↑ MI/stroke/PE	Thrombosis: not noninferior, seizures uncertain (Wide CI)

Quality of Evidence: Low quality of evidence | Moderate quality of evidence | High quality of evidence

Abbreviations: IV: intravenous; CI: confidence interval; pRBC: packed red blood cell; MI: myocardial infarction; VTE: venous thromboembolism; CABG: coronary artery bypass; DVT: deep vein thrombosis; PE: pulmonary embolism; GCS: Glasgow Coma Scale

Appendix:

- Injury Severity Score (ISS):[9]
  - ISS is a score that describes severity of traumatic injury in literature
  - ISS is the sum of the squares of the three most severely injured body region AIS values
  - ISS ranges 1-75, with a higher ISS indicating a higher severity of injury and mortality risk
- Abbreviated Injury Scale (AIS):[10]
  - The AIS describes the severity of injury of each body region
  - There are nine body regions that are grouped into six to calculate the ISS: head or neck, face, chest, abdominal or pelvic contents, extremities or pelvic girdle, and external
  - AIS ranges from 1-6 for each body region, with AIS of 6 being maximum injury
  - If a single body region has an AIS of 6, an ISS of 75 is automatically assigned
- Glasgow Coma Score (GCS):[11]
  - GCS is an assessment of level of consciousness and is used to describe severity of injury
  - GCS is the sum of the Glasgow Coma Scale results: eye opening (1-4), verbal response (1-5), best motor response (1-6)
  - GCS ranges from 3-15: severe injury (3-8), moderate injury (9-12), mild injury (13-15)
- Trial definitions:
  - ATACAS risk of major complications: age ≥70, left ventricular impairment (fractional area change <20%, ejection fraction <40%, or at least moderate impairment on ventriculography), concomitant valvular or aortic surgery, left ventricular aneurysmectomy, repeat cardiac surgery, COPD, renal impairment <45 ml/min, obesity (BMI >25), pulmonary htn (mPAP >25), peripheral vascular disease
  - POISE-3 major bleeding: bleeding that resulted in a postoperative hemoglobin ≤7 g/dL; a transfusion of ≥1 unit of red blood cells; or led to an intervention

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