

Christian Fang, Chetan Pradhan

Should tranexamic acid (TXA) be administered pre-hospital in patients with open fractures with active bleeding?

Recommendation

Prehospital administration of a 1–2 g intravenous TXA bolus within 60 minutes of injury is recommended for patients with open fractures who have active hemorrhage or clinical signs of hemorrhagic shock, particularly when additional bleeding injuries are suspected. In these circumstances, the potential benefits of early TXA use outweigh the risk of adverse events.

Overview

1. This review addresses whether tranexamic acid (TXA) should be administered in the prehospital setting to patients presenting with open fractures and active bleeding.
2. Direct evidence for open fractures is low, but the indirect evidence for bleeding trauma is sufficiently consistent to support a conditional recommendation.
3. **No randomized trial has specifically enrolled "prehospital open fracture with active bleeding" as its target population.** The evidence is therefore assembled from three overlapping streams
 - Landmark trauma-hemorrhage RCTs that included, but were not restricted to, bleeding limb injuries. The open fracture with active bleeding is best understood not as a distinct indication but as one clinical route into the broader category of the bleeding trauma patient, which is the population these RCTs studied (CRSH-2, PATCH, STAAMP)
 - Prehospital-specific trials, cohorts, and syntheses in trauma at risk of hemorrhage;
 - Peri-operative orthopaedic/fracture-specific TXA studies, which are not prehospital.
4. Prehospital TXA should be given to actively bleeding open-fracture patients as part of a hemorrhage-control bundle, ideally as early as possible and preferably within 90 minutes, while remaining within the established 3-hour maximum window.
5. Future research should report open-fracture subgroups separately, including Gustilo grade, limb vascular injury, amputation, transfusion requirement, thromboembolic events, infection, flap coverage and union outcomes.
6. CRASH-2, PATCH and STAAMP established that early TXA reduces death from bleeding in a broad trauma population, and its timing analysis created 3-hour / 90 minutes rule, applicable to resource-limited and high-income

regions. Secondary timing studies demonstrated benefits when TXA is given early.

7. Meta-analyses consistently show a reproducible early (24-h) or 1-month mortality reduction with a good safety profile, but a neutral effect on longer-term and functional outcomes, and occasional harm signals (infection, VTE) when observational data are pooled.
8. TXA may convert some deaths into survival with severe disability or infection rather than into good recovery.
9. Non RCT studies vulnerable to confounding by indication.
10. Orthopaedic fracture-specific evidence is almost entirely perioperative and in-hospital, addressing surgical blood loss and transfusion in hip, femur, pelvic, and acetabular fractures rather than prehospital haemorrhage control. It shows TXA generally reduces transfusion (strongest for proximal femur) with no consistent excess thromboembolism, but with conflicting / neutral results in pelvic-acetabular ORIF. This can weakly transfer to prehospital open-fracture scenario.
11. Overall safety profile shows negligible excess VTE risks.
12. Major guidelines converges on a conditional recommendation: give prehospital TXA to trauma patients with significant bleeding (lack of definition) or haemorrhagic shock (typically SBP <90 mmHg and/or HR >110), within 3 hours, using either 1 g IV/IO (+1 g/8 h) or a 2 g IV/IO regimen. Prehospital TXA not reflexively indicated for every open fracture. For a stable, normotensive patient with an isolated low grade open fracture and controllable bleeding and short transport time, the incremental benefit of prehospital TXA is not established.

Literature Table

Study / Guideline	Type of Study	Level of Evidence	Sample Size
CRASH-2, Roberts et al. 2010–2013(1)	Multicentre double-blind placebo-controlled RCT	Level I	20211
CRASH-2 timing analysis, Roberts et al. 2011(2)	Prespecified subgroup analysis of RCT	Level I (subgroup)	20211 (subgrouped)
PATCH-Trauma, NEJM 2023(3)	Multicentre double-blind placebo-controlled prehospital RCT	Level I	1310
Ali et al, 2026 PATCH-Trauma timing analysis (4)	Multicentre double-blind placebo-controlled prehospital RCT – exploratory analysis	Level I	1310
JAMA Surgery STAAMP, Guyette et al. 2020(5)	Multicentre double-blind placebo-controlled prehospital RCT	Level I	927 (903 analysed)
STAAMP + PATCH harmonised analysis, Mazzei et al. 2024(6)	Secondary analysis of two harmonised RCTs	Level II	~2,200 combined
Cal-PAT, Neeki et al. 2017(7)	Multicentre prospective observational cohort with retrospective comparison	Level III	724 (128 TXA)
Wafaisade et al. (ADAC Air Rescue) 2016(8)	Retrospective propensity-matched registry cohort	Level III	258 matched pairs
Chen et al. 2024 SR/MA with TSA(9)	Systematic review & meta-analysis with trial sequential analysis	Level I	Pooled RCTs/cohorts
Li et al. 2025 SR/MA(10)	Systematic review & meta-analysis	Level I	Pooled trials

Acharya et al. 2023 SR/MA (RCTs only)(11)	Systematic review & meta-analysis restricted to RCTs	Level I	Pooled RCTs
Alhenaki et al. 2021 SR/MA(12)	Systematic review & meta-analysis	Level I	Pooled studies
Benipal et al. 2019 (post-CRASH-2 SR)(13)	Systematic review of post-CRASH-2 studies	Level II–III	Pooled cohorts/RCTs
Girardello et al. 2024 (state-wide observational)(14)	State-wide retrospective observational study	Level III	Injured patients (BATT-scored)
Almuwallad et al. 2023 (nationwide adherence)(15)	Nationwide retrospective cohort	Level III	National registry
Ageron et al. 2022 (severe vs non-severe)(16)	Reanalysis of RCT data (CRASH-2/-3 derived)	Level II	Large pooled
Kunze-Szikszay et al. 2016 (ROTEM study)(17)	Prospective observational mechanistic study	Level IV	27 patients
Fenwick et al. 2022 (proximal femur)(18)	Retrospective comparative study	Level III	Proximal femur fracture cohort
Shu et al. 2021 (pelvic/acetabular SR/MA)(19)	Systematic review & meta-analysis	Level I	Pooled ORIF patients
Kim et al. 2022 (pelvic/acetabular ORIF SR/MA)(20)	Systematic review & meta-analysis	Level I	Pooled Pelvic Acetabular ORIF patients
Fenwick et al. 2025 (femoral neck, topical)(21)	Retrospective comparative study	Level III	Femoral neck arthroplasty cohort
Barret et al, NAEMSP, ACEP, ACS-COT, 2025 (22)	Guideline / position statement	Guideline	N/A
EAST Practice Management Guideline 2025 update(23)	Guideline (systematic review + GRADE)	Guideline	N/A
IAEM Clinical Guideline (TXA in Trauma)(24)	Guideline	Guideline	N/A
European guideline on management of major bleeding (Rossaint et al., Grade recommendations)(25)	Guideline	Guideline	N/A