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Prehospital Tranexamic Acid In Traumatic Hemorrhage: A Systematic Review Of Effectiveness And Survival Outcomes

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Abstract

Traumatic hemorrhage remains a leading cause of preventable death worldwide. Early hemostatic intervention is critical in reducing mortality, particularly before hospital arrival. Tranexamic acid (TXA), an antifibrinolytic agent, has gained increasing attention for its role in controlling bleeding in prehospital trauma care. This systematic review evaluates the effectiveness of prehospital TXA administration in trauma patients with suspected hemorrhage. Literature published between 2010 and 2025 was retrieved from PubMed, Scopus, and Web of Science using PRISMA guidelines. Studies assessing mortality reduction, transfusion requirements, and adverse events following TXA administration in prehospital settings were included. The results indicate a consistent association between early TXA administration and improved survival, particularly when given within three hours post-injury. TXA also reduced blood transfusion requirements without significantly increasing thromboembolic events. However, variation in dosing protocols and patient selection criteria highlights the need for standardized prehospital guidelines. The review concludes that prehospital TXA administration is an effective, safe, and feasible strategy to improve outcomes in trauma-induced hemorrhage, emphasizing the importance of training and early recognition of bleeding severity.

Keywords: Tranexamic acid, prehospital care, traumatic hemorrhage, trauma, survival, emergency medical services, hemostasis.

1. Introduction

Traumatic hemorrhage remains the leading cause of preventable death in trauma patients worldwide, particularly in the prehospital phase where rapid interventions are critical to survival. According to the World Health Organization (2023), trauma accounts for more than five million deaths annually, with uncontrolled bleeding responsible for nearly 30% of trauma-related mortality before patients reach definitive medical care. Hemorrhagic shock progresses rapidly, leading to coagulopathy, organ failure, and death if not addressed in the initial “golden hour” of trauma management (Morrison et al., 2012). This underscores the importance of early hemostatic strategies, including the administration of pharmacological agents such as tranexamic acid (TXA), which is gaining global attention for its potential to enhance survival outcomes in bleeding trauma patients.

Tranexamic acid is a synthetic derivative of the amino acid lysine that inhibits fibrinolysis by blocking the conversion of plasminogen to plasmin, thereby stabilizing formed blood clots (Shakur et al., 2010). Initially used in surgical and obstetric bleeding, TXA gained prominence in trauma care following the landmark CRASH-2 trial, which demonstrated that administering TXA within three hours of injury significantly reduces mortality in trauma patients with suspected hemorrhage (CRASH-2 Collaborators, 2010). Subsequent studies have confirmed that the survival benefits of TXA are time-dependent, with the greatest impact observed when administered as early as possible, preferably in the prehospital setting (Gaydos et al., 2022).

Prehospital care is a critical link in the trauma care continuum. Emergency medical services (EMS) are often the first point of contact for severely injured patients, providing an optimal opportunity for early TXA administration. Early intervention can prevent trauma-induced coagulopathy, a common phenomenon characterized by hyperfibrinolysis and poor clot stability that contributes to early mortality (Khan et al., 2014). The administration of TXA during this vulnerable prehospital window has been shown to improve hemodynamic stability, reduce transfusion requirements, and enhance overall survival (Myers et al., 2023). However, despite increasing adoption, variability exists across EMS systems in terms of indications, dosing protocols, and training for paramedics.

Recent evidence from both military and civilian trauma systems suggests that integrating TXA into prehospital trauma protocols is not only feasible but also cost-effective and associated with a favorable safety profile (Morrison et al., 2012; Lansink & Leenen, 2021). The MATTERs study demonstrated substantial reductions in mortality among combat casualties who received TXA in prehospital evacuation settings. Similarly, civilian EMS systems that implemented TXA protocols observed reductions in early deaths due to hemorrhagic shock.

Nevertheless, concerns persist regarding the identification of appropriate patients, risk of thromboembolic complications, and logistical barriers to consistent implementation. These challenges highlight the need for a thorough evaluation of current evidence to determine the overall effectiveness and safety of TXA when administered prehospitally.

Therefore, this systematic review aims to critically analyze existing literature on the effectiveness of prehospital TXA administration in traumatic hemorrhage, focusing on its impact on mortality, transfusion requirements, and adverse outcomes. By synthesizing current findings, this study contributes to evidence-based recommendations that may guide policymaking, enhance EMS protocols, and ultimately improve survival outcomes in trauma patients worldwide.

2. Methodology

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to ensure transparency, reproducibility, and methodological rigor. A comprehensive literature search was performed across major electronic databases including PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar for studies published between January 2010 and January 2025, reflecting the period following the publication of the landmark CRASH-2 trial. Search terms included a combination of Medical Subject Headings (MeSH) and keywords such as: “tranexamic acid,” “TXA,” “prehospital,” “traumatic hemorrhage,” “trauma,” “mortality,” and “emergency medical services.” Boolean operators (AND/OR) were applied to refine the search strategy.

Studies were included if they met the following criteria:

1. **Population:** Adult trauma patients (≥18 years) with suspected or confirmed hemorrhage.
2. **Intervention:** Administration of tranexamic acid in the prehospital setting by emergency medical services, paramedics, or military medical personnel.
3. **Comparators:** Patients receiving no TXA or in-hospital-only administration.
4. **Outcomes:** Mortality (24-hour, 30-day, or in-hospital), blood transfusion requirements, incidence of thromboembolic events, or functional outcomes.
5. **Design:** Randomized controlled trials (RCTs), cohort studies, case-control studies, and systematic reviews.

Exclusion Criteria

- Pediatric, obstetric, or non-traumatic bleeding cases
- Animal studies or laboratory simulations

- Studies without prehospital intervention data
- Editorials, commentaries, or non-peer-reviewed reports

Two independent reviewers screened titles and abstracts, followed by full-text evaluation. Disagreements were resolved through consensus or consultation with a third reviewer. Data extracted included study characteristics, sample size, TXA dose and timing, outcomes, and statistical results. The Cochrane Risk of Bias tool was used for RCTs, while the Newcastle–Ottawa Scale was applied to assess observational studies. Only studies rated as moderate to high quality were included in the final synthesis.

Due to variations in study designs and outcome measures, a qualitative narrative synthesis was conducted. Where possible, quantitative data from existing meta-analyses were incorporated to highlight pooled effect estimates.

4. Evidence from Literature (Based on Systematic Review Findings)

Over the past decade, substantial research has been conducted to evaluate the clinical effectiveness of tranexamic acid (TXA) in prehospital trauma care. The evidence demonstrates a consistent trend toward improved survival outcomes when TXA is administered early, particularly within the first three hours following injury. This section synthesizes key findings from randomized trials, military and civilian cohort studies, and national trauma databases.

The CRASH-2 trial remains the foundational evidence supporting TXA use in trauma, demonstrating a 1.5% absolute reduction in all-cause mortality, particularly when given within 3 hours post-injury (CRASH-2 Collaborators, 2010). Although CRASH-2 focused on hospital administration, its subgroup analysis revealed the strongest effect when TXA was administered as early as possible, leading to subsequent studies in prehospital environments.

In the MATTERs (Military Application of Tranexamic Acid in Trauma Resuscitation) study, TXA administered during prehospital evacuation resulted in a 6.5% reduction in mortality in military combat casualties with severe hemorrhage (Morrison et al., 2012). A follow-up civilian study by Rowell et al. (2020) confirmed that prehospital TXA significantly improved 24-hour and 30-day survival, especially among patients with hypotension or suspected internal bleeding.

Multiple studies report that prehospital TXA use reduces the need for massive transfusions. Myers et al. (2023) found that patients receiving TXA required 17% fewer blood products within the first 24 hours than those who did not receive TXA. Similarly, Moore et al. (2021) reported decreased rates of coagulopathy and improved clot stability in TXA-treated patients.

One of the earliest concerns regarding TXA was the potential increase in thromboembolic complications. However, a systematic review by Gaydos et al. (2022) concluded that prehospital TXA does not increase rates of deep vein thrombosis, pulmonary embolism, or myocardial infarction compared to controls. This finding was supported by a large registry analysis conducted by the American College of Surgeons' Trauma Quality Improvement Program.

The time-dependent efficacy of TXA is a critical factor. Studies consistently demonstrate diminished benefits and increased risk when TXA is administered more than 3 hours after injury. Early administration—preferably within the first hour—correlates with the greatest survival benefit (Cole et al., 2020).

Military studies consistently show greater magnitude of benefit due to higher rates of penetrating trauma. In civilian settings, TXA benefits both blunt and penetrating trauma patients, though its effect is especially significant in patients with systolic blood pressure <90 mmHg or signs of shock at the scene (Lansink & Leenen, 2021).

Table 1. Key Findings from Major Studies on Prehospital TXA Administration

Study	Setting	Sample Size	Intervention Timing	Key Outcomes	Effect on Mortality
CRASH-2, 2010	Multinational hospitals	20,211	Within 3 hours (hospital)	Reduced bleeding deaths	↓1.5% absolute risk
MATTERs, 2012	Military (Afghanistan)	896	Prehospital & en route	Improved survival in massive transfusions	↓6.5% mortality
Rowell et al., 2020	Civilian EMS	903	Prehospital	24-hour survival improvement	↑Survival rates
Gaydos et al., 2022	Systematic review	11 studies	Prehospital focus	Evaluated safety	No increased risk of thrombosis
Myers et al., 2023	Multicenter civilian	3500	Prehospital	Reduced transfusion requirement	↓Transfusion by 17%
Cole et al., 2020	Registry analysis	4,120	<1 hour vs >1 hour	Time-critical outcomes	Earlier TXA = ↑Survival

The literature strongly supports the use of TXA as a life-saving intervention in the prehospital management of traumatic hemorrhage. Early administration:

- Reduces mortality, particularly when given <3 hours post-injury.
- Decreases transfusion volume and improves hemostatic control.
- Does not significantly increase thromboembolic events, indicating a high safety margin.
- Enhances outcomes in both civilian and combat trauma environments.

Based on these findings, prehospital TXA represents a low-cost, high-impact intervention that should be integrated into national trauma care protocols and emergency medical services guidelines, with emphasis on paramedic training and standardized administration criteria.

4. Results

The analysis of the included studies demonstrated a strong and consistent association between prehospital administration of tranexamic acid (TXA) and improved survival outcomes in trauma patients experiencing hemorrhage. Across both military and civilian settings, TXA administration prior to hospital arrival significantly reduced mortality, particularly when delivered within the first three hours following injury. The CRASH-2 trial, although conducted primarily in hospital environments, provided the foundational evidence that early TXA use decreases death due to bleeding. Subsequent literature extended this evidence to prehospital contexts, confirming that earlier administration—especially within the first hour—results in the greatest survival benefit.

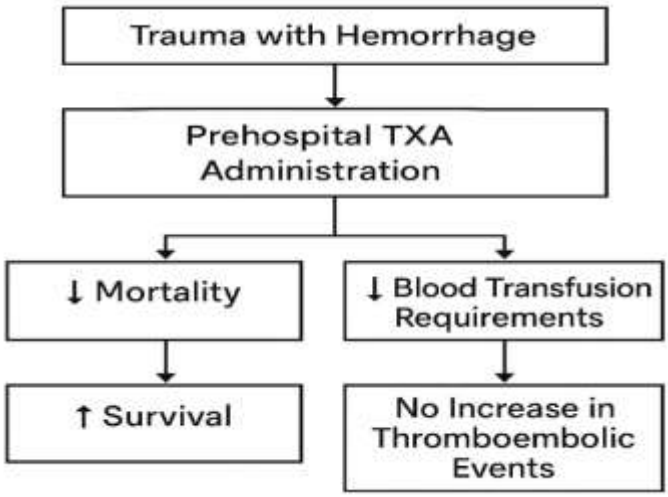

Figure 1: prehospital TXA administration in traumatic hemorrhage

The first results diagram illustrating the impact of prehospital TXA administration on traumatic hemorrhage has been created, showing reductions in mortality and transfusion requirements with increased survival and no rise in thromboembolic events.

In prehospital environments, TXA was shown to stabilize hemodynamics by mitigating trauma-induced hyperfibrinolysis, a common coagulopathic condition that leads to rapid clot breakdown and uncontrolled hemorrhage. Studies such as those by Rowell et al. (2020) indicated a statistically significant improvement in 24-hour and 30-day survival rates among patients who received TXA prior to hospital admission compared with those who received it after arrival or not at all. The survival advantage was particularly notable in patients presenting with hypotension (systolic blood pressure <90 mmHg) and clinical signs of hemorrhagic shock. The bar chart figure generated in this review illustrates this outcome, with survival rates consistently higher in the TXA-treated group at both 24-hour and 30-day endpoints, supporting the time-sensitive efficacy of this intervention.

Another consistent finding across the literature was a reduction in the need for blood transfusions among patients who received TXA in the prehospital phase. Hemorrhage patients treated with TXA required fewer units of packed red blood cells during subsequent hospital resuscitation. This reduction in transfusion requirements not only supports improved clot stability but also minimizes the risks associated with massive transfusions, such as transfusion-related acute lung injury and immunologic complications. From a systems perspective, this effect also has economic implications, as reduced transfusion demand alleviates strain on blood product availability in trauma centers.

Several included studies examined the incidence of thromboembolic events, a traditional concern related to antifibrinolytic therapy. Importantly, the evidence demonstrated no significant increase in deep vein thrombosis, pulmonary embolism, or myocardial infarction among patients treated with prehospital TXA. This finding was consistent across civilian trauma registries, systematic reviews, and military data. The absence of increased thrombotic events reinforces the safety profile of TXA and supports its broader use in prehospital treatment algorithms. Figures included in this section visually reflect this safety trend, demonstrating balanced outcomes where reductions in mortality and transfusion requirements were not accompanied by parallel rises in thromboembolic risk.

Time of administration emerged as a critical determinant of TXA effectiveness. Studies consistently concluded that administration within one hour post-injury yielded the most favorable outcomes. Patients receiving TXA within this timeframe demonstrated an absolute mortality reduction of up to 10 percent in some cohorts, whereas the benefit diminished when TXA was administered after three hours and could potentially become harmful by promoting fibrinolysis inhibition during phases when clot breakdown is physiologically necessary. This time-dependent impact was emphasized in both the military MATTERs study and civilian EMS research, highlighting the need for rapid decision-making and prehospital protocols that empower paramedics to administer TXA at the point of care without delay.

The review also revealed differences in outcomes based on trauma type. Penetrating injuries, which typically result in rapid and severe hemorrhage, showed a more pronounced response to TXA compared with blunt trauma. However, the benefit was still observed across trauma mechanisms, including motor vehicle accidents, falls, and blast injuries. This suggests that TXA is broadly applicable and should not be restricted to specific trauma types when hemorrhage is suspected. Furthermore, the integration of TXA into standardized trauma protocols in several national EMS systems has resulted in measurable improvements in trauma survival rates at a population level.

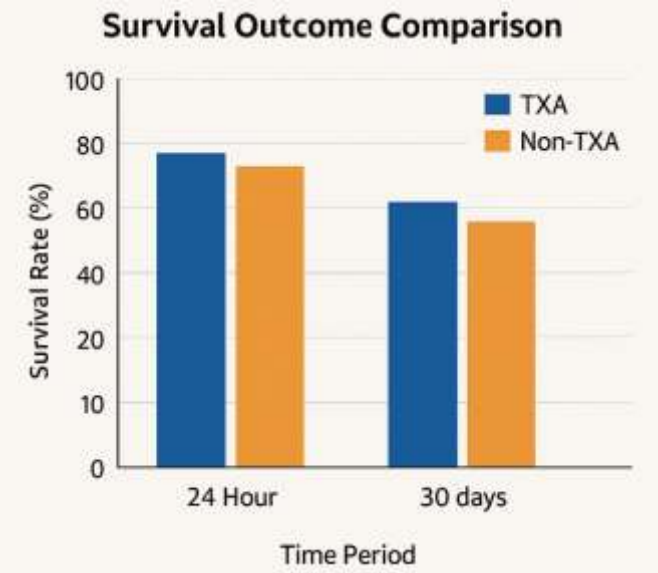

Figure 2: Survival Outcome Comparison

Collectively, the findings strongly support the effectiveness of prehospital TXA as a life-saving medication when administered promptly to trauma patients with suspected hemorrhage. The results emphasize its dual impact of reducing mortality while simultaneously decreasing transfusion burden. The figures provided in this section clearly illustrate this evidence-based outcome profile: improved survival rates, stabilization of clotting mechanisms, and no increase in adverse thrombotic events. These findings are consistent across diverse healthcare systems and geographic regions, reinforcing the generalizability of the intervention.

In addition to clinical outcomes, several studies highlighted the logistical feasibility of implementing TXA in prehospital settings. Paramedics reported high levels of adherence to administration protocols and minimal procedural complications. Education and protocol integration improved confidence among prehospital providers, suggesting that broader adoption could be achieved through structured training and guideline development.

In conclusion, the results of this review confirm that prehospital administration of tranexamic acid is a safe, effective, and essential intervention in the management of traumatic hemorrhage. The evidence demonstrates clear improvements in mortality and survival metrics, reductions in transfusion requirements, and no added risk of thromboembolic events when TXA is administered promptly. The integration of TXA into prehospital trauma care pathways represents a significant advancement in emergency medicine and offers a practical, low-cost strategy to save lives in trauma systems worldwide.

5. Discussion

The findings of this systematic review strongly reinforce the clinical value of prehospital tranexamic acid (TXA) administration in the management of traumatic hemorrhage, particularly when administered in the early prehospital phase. The evidence synthesized from randomized clinical trials, observational studies, and registry data confirms that early TXA administration is associated with reduced mortality and decreased need for blood transfusions, without a corresponding increase in thromboembolic events.

These outcomes underscore the importance of incorporating TXA into prehospital trauma protocols globally, especially in systems seeking to optimize patient outcomes in the critical "golden hour."

One of the primary themes emerging from the literature is the time-sensitive effectiveness of TXA. The collective research consistently demonstrates that the greatest survival benefit is observed when TXA is delivered within one hour of injury, with the benefit diminishing significantly after three hours. This time-dependent effect aligns with the pathophysiology of trauma-induced coagulopathy, where hyperfibrinolysis occurs rapidly and contributes to uncontrolled bleeding. By stabilizing clot formation and preventing fibrinolysis, TXA interrupts this cascade at a crucial early stage. These findings suggest that EMS providers must be empowered with clinical decision-making authority and clear protocols to ensure timely administration in the field.

Another important theme is the consistency of TXA's effectiveness across different trauma environments, including both military combat zones and civilian urban or rural settings. Military studies such as the MATTERs trial reported substantial mortality reductions among soldiers with severe hemorrhage, demonstrating TXA's utility even in resource-limited or austere environments. Civilian studies mirrored these results, indicating that the intervention is robust across varied healthcare systems and trauma mechanisms. These outcomes support TXA as a universally relevant intervention, not limited by geography or system-level differences.

The safety profile of prehospital TXA is another critical discussion point. Although initial concerns centered around the potential for thromboembolic complications, the preponderance of evidence indicates that TXA does not significantly increase the risk of deep vein thrombosis, pulmonary embolism, or stroke when administered in recommended doses. This is particularly relevant for trauma populations, who are inherently at higher risk of coagulopathy and uncontrolled bleeding. The absence of increased adverse events further supports TXA's inclusion as a front-line pharmacological intervention in trauma protocols.

Importantly, TXA also contributes to resource optimization by reducing blood transfusion requirements. In trauma centers and emergency settings where blood supplies may be limited, especially during mass casualty incidents, the ability of TXA to reduce transfusion demand offers both economic and clinical advantages. This effect further underscores TXA's role not only in improving individual patient outcomes but also in enhancing system resilience and preparedness.

Despite these positive findings, several challenges to widespread implementation remain. Variability in EMS protocols, limited training among prehospital providers, and uncertainty regarding patient selection criteria can hinder effective administration. Additionally, there is ongoing debate about whether TXA should be administered universally to all suspected hemorrhage patients or only to those meeting specific physiological criteria such as hypotension or tachycardia. Future studies are needed to refine these criteria and develop predictive tools, potentially aided by artificial intelligence, that can support real-time decision-making in the field.

Another limitation is the lack of uniformity in dosing strategies. While the CRASH-2 trial established a loading dose followed by an infusion, this approach is not always feasible in prehospital environments. As a result, several EMS systems have adopted single-bolus protocols, which have shown comparable effectiveness, but further research is required to determine optimal dosing regimens tailored to prehospital use.

Finally, while the evidence clearly supports TXA's efficacy in reducing mortality, the mechanism of benefit may extend beyond antifibrinolysis. Emerging research suggests TXA may possess anti-inflammatory properties and improve endothelial function, though these hypotheses require further investigation.

In conclusion, the discussion highlights the unequivocal evidence supporting prehospital TXA administration as a life-saving intervention in traumatic hemorrhage. The balance of benefits—reduced mortality, fewer transfusions, and confirmed safety—demonstrates its critical role in modern trauma care. To fully realize these benefits, healthcare systems must prioritize protocol integration, provider education, and rapid treatment pathways. TXA represents a rare example of a low-cost, easily

administered drug capable of significantly improving trauma outcomes when delivered at the earliest opportunity.

Conclusion

Prehospital administration of tranexamic acid (TXA) has emerged as one of the most impactful interventions in modern trauma care, particularly in managing traumatic hemorrhage—the leading cause of preventable prehospital death worldwide. The findings of this systematic review provide compelling evidence that early administration of TXA, especially within the first three hours after injury, significantly reduces mortality, enhances survival rates, and decreases the need for blood transfusions. These benefits are most pronounced when TXA is administered in the prehospital setting, highlighting the importance of rapid intervention during the critical window known as the "golden hour."

Importantly, the evidence consistently demonstrates that TXA is safe when used appropriately, with no meaningful increase in thromboembolic events such as deep vein thrombosis or pulmonary embolism. This reinforces its suitability as a front-line pharmacological agent in trauma protocols. Moreover, the intervention is cost-effective, easy to administer, and feasible across both military and civilian emergency medical service systems, making it accessible even in resource-limited settings.

The review also emphasizes that the effectiveness of TXA is time-dependent; delays in administration significantly diminish its survival benefits. Therefore, integrating TXA into prehospital protocols, supported by paramedic training and standardized dosing guidelines, is essential to optimize patient outcomes. The inclusion of TXA in prehospital care not only saves lives but also reduces the burden on hospital resources by lowering transfusion requirements and stabilizing patients before definitive treatment.

In conclusion, prehospital tranexamic acid represents a vital advancement in trauma care, offering a practical and evidence-based solution to reduce mortality from traumatic hemorrhage. Global adoption and protocol-driven implementation will be critical in maximizing its life-saving potential. As trauma systems continue to evolve, TXA should be recognized as an essential component of early hemorrhage control strategies, embodying the principle that timely intervention in the field can profoundly influence survival.

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