REVIEW ARTICLE / PREGLEDNI ČLANAK

PREHOSPITAL BLOOD PRODUCT ADMINISTRATION IN CIVILIAN EMERGENCY MEDICAL SYSTEMS: EVIDENCE, CONTROVERSIES, AND IMPLEMENTATION CHALLENGES

PRIMJENA KRVNIH PRIPRAVAKA U IZVANBOLNIČKOJ HITNOJ MEDICINSKOJ SLUŽBI U CIVILNIM SUSTAVIMA: DOKAZI, KONTROVERZE I IZAZOVI UVOĐENJ

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Abstract

Hemorrhagic shock remains a major preventable cause of trauma-related mortality, prompting increasing interest in prehospital blood product administration as a strategy for earlier hemostatic resuscitation. However, evidence supporting widespread implementation in civilian emergency medical systems (EMS) remains inconsistent. This review critically examines contemporary evidence regarding the effectiveness, feasibility, and limitations of prehospital blood product administration in civilian trauma care. While some studies suggest improved survival and physiological stabilization, others have failed to demonstrate meaningful benefit in mortality or major clinical outcomes, particularly in systems with short transport times. Interpretation of available evidence is further complicated by heterogeneity in patient populations, transport duration, and transfusion protocols. Current trauma and transfusion guidelines do not uniformly support routine prehospital blood product administration and generally advocate a selective, context-dependent approach. In addition to uncertain clinical benefit, implementation presents important logistical and organizational challenges, including storage requirements, cold-chain maintenance, traceability, and product wastage. Current evidence suggests that prehospital blood product administration may be most beneficial in carefully selected patients with severe hemorrhagic shock, prolonged transport intervals, or delayed access to definitive hemorrhage control.

Keywords: civilian trauma care; hemorrhagic shock; prehospital blood transfusion.

Sažetak

Hemoragijski je šok i dalje jedan od glavnih sprječivih uzroka smrtnosti povezane s traumom, zbog čega raste interes za primjenu krvnih pripravaka u izvanbolničkim uvjetima kao strategiju ranijeg započinjanja hemostatske resuscitacije. Međutim, dokazi koji podupiru njezino široko uvođenje u civilne sustave hitne medicinske službe su i dalje neujednačeni. U ovom preglednom radu kritički se analiziraju suvremeni dokazi o učinkovitosti, izvedivosti i ograničenjima primjene krvnih pripravaka u izvanbolničkom zbrinjavanju traumatiziranih bolesnika. Dok neka istraživanja upućuju na poboljšano preživljenje i fiziološku stabilizaciju, druga nisu pokazala značajnu korist u pogledu smrtnosti ili drugih važnih kliničkih ishoda, osobito u sustavima s kratkim vremenom transporta. Tumačenje dostupnih dokaza dodatno je otežano heterogenošću populacija bolesnika, trajanjem transporta i transfuzijskim protokolima. Aktualne smjernice za zbrinjavanje traume i transfuzijsko liječenje ne podupiru jednoznačno rutinsku primjenu krvnih pripravaka u izvanbolničkim uvjetima te uglavnom zagovaraju selektivan pristup prilagođen okolnostima. Uz neizvjesnu kliničku

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korist, uvođenje takve prakse povezano je sa značajnim logističkim i organizacijskim izazovima, uključujući zahtjeve za skladištenjem, održavanje hladnog lanca, sljedivost i neiskorištavanje odnosno otpis krvnih pripravaka. Trenutačni dokazi upućuju na to da bi primjena krvnih pripravaka u izvanbolničkim uvjetima mogla biti najkorisnija u pažljivo odabranih bolesnika s teškim hemoragijskim šokom, produljenim vremenom transporta ili odgođenim pristupom definitivnoj kontroli krvarenja.

Ključne riječi: civilno zbrinjavanje traumatiziranih bolesnika; hemoragijski šok; izvanbolnička transfuzija krvi

Introduction

Uncontrolled hemorrhage remains a major contributor to preventable trauma-related mortality, particularly during the early post-injury period (1–3). Conventional trauma resuscitation strategies have historically emphasized rapid transport to definitive care while relying primarily on crystalloid administration during the prehospital phase (2). However, increasing recognition of trauma-induced coagulopathy (TIC), the dilutional effects of excessive crystalloid use, and the importance of early hemostatic resuscitation has prompted renewed interest in prehospital blood product administration (4,5). Military experience, particularly from contemporary combat settings, demonstrated encouraging results associated with early transfusion strategies, including reduced mortality and improved physiological stabilization among severely injured patients with hemorrhagic shock (6). These observations stimulated growing interest in translating similar approaches into civilian emergency medical systems (EMS), particularly within physician-led retrieval teams, helicopter emergency medical services (HEMS), and remote or rural trauma networks (7,8).

Despite increasing implementation across selected EMS systems, an important question remains unresolved: is prehospital blood product administration truly justified in civilian medicine, or has implementation advanced faster than supporting evidence? Although several studies suggest potential benefit in selected high-risk populations, findings remain inconsistent and highly dependent on transport duration, patient selection, severity of shock, and healthcare system organization (9,10). Importantly, the clinical question is no longer whether prehospital blood product administration can improve outcomes under ideal circumstances, but rather under which conditions, in which patients, and within which EMS systems such interventions provide meaningful benefit sufficient to justify operational complexity and resource allocation. This distinction is particularly relevant for European civilian EMS models characterized by relatively short transport intervals and rapid access to definitive hospital care.

Prehospital blood product administration may benefit selected patients with severe hemorrhagic shock, but its role in civilian EMS remains dependent on patient selection, transport time, system organization, and available evidence.

The aim of this review is to critically examine the current evidence regarding prehospital blood product administration in civilian trauma care, with particular emphasis on randomized evidence, observational studies, logistical feasibility, and the balance between potential clinical benefit and practical implementation challenges.

Pathophysiological rationale for early blood product administration

The theoretical rationale for prehospital blood product administration is grounded in the time-sensitive nature of traumatic hemorrhage and the early physiological derangements that emerge following severe injury. Hemorrhagic shock is not merely a consequence of progressive blood loss but a dynamic process characterized by impaired tissue perfusion, oxygen debt, metabolic acidosis, endothelial dysfunction, systemic inflammation, and the rapid development of trauma-induced coagulopathy (TIC) (2,11,12). Importantly, many of these processes begin during the prehospital phase, often before definitive hemorrhage control can be achieved, suggesting that clinically relevant physiological deterioration may already be underway prior to hospital arrival.

Trauma-induced coagulopathy represents one of the earliest and most clinically relevant therapeutic targets in trauma care. Historically regarded primarily as a dilutional consequence of blood loss and fluid resuscitation, TIC is now increasingly recognized as an endogenous and multifactorial process initiated shortly after injury and driven by tissue trauma, hypoperfusion, endothelial dysfunction, inflammation, platelet dysfunction, and dysregulated fibrinolysis (13). Early coagulopathy has consistently been associated with increased transfusion requirements, multiple organ dysfunction, and substantially higher mortality among severely injured trauma patients (13,14).

Trauma-induced coagulopathy develops early after severe injury, supporting the rationale for initiating hemostatic resuscitation before hospital arrival.

The early onset of TIC raises an important therapeutic question: should hemostatic interventions begin before hospital arrival? If coagulopathy is already evolving during transport, delayed correction following emergency department admission may

represent a missed therapeutic opportunity. Consequently, early administration of plasma, fibrinogen-containing products, packed red blood cells (PRBCs), or low-titer group O whole blood (LTOWB) has emerged as a biologically plausible strategy aimed not only at restoring circulating volume but also at simultaneously supporting oxygen delivery and coagulation during the earliest phases of hemorrhagic shock (9, 14,16).

Historically, prehospital trauma resuscitation emphasized rapid crystalloid administration to restore intravascular volume and maintain systemic blood pressure until definitive hemorrhage control could be achieved. However, this paradigm has increasingly been challenged. Excessive crystalloid administration may contribute to dilutional coagulopathy, worsening acidosis and hypothermia, endothelial glycocalyx disruption, tissue edema, and impaired oxygen delivery while failing to replace clotting factors or oxygen-carrying capacity (2,5,15). Furthermore, aggressive fluid resuscitation prior to hemorrhage control may increase intravascular hydrostatic pressure, disrupt early clot stability, and potentially exacerbate ongoing bleeding, particularly in patients with uncontrolled hemorrhage (15).

Recognition of these limitations contributed to a paradigm shift toward *damage control resuscitation* and *hemostatic resuscitation* strategies, which prioritize rapid hemorrhage control, permissive hypotension in selected patients, minimization of crystalloid exposure, and balanced replacement of blood components (16). Within this framework, prehospital blood product administration has been proposed as a strategy to attenuate progression of hemorrhagic shock before hospital arrival. The biological rationale is compelling: early blood product administration may restore oxygen-carrying capacity, preserve intravascular volume, attenuate coagulopathy, improve tissue perfusion, and potentially mitigate secondary physiological deterioration during transport.

Nevertheless, biological plausibility alone is insufficient to justify widespread implementation of a complex and resource-intensive intervention. The key question remains whether these theoretical benefits translate into clinically meaningful improvements in outcomes within civilian emergency medical systems, where transport times, trauma epidemiology, logistics, and organizational structures differ substantially from military settings. Determining whether prehospital blood product administration improves survival, reduces transfusion requirements, or attenuates trauma-induced physiological deterioration in civilian trauma populations therefore remains an important area of ongoing investigation.

Clinical evidence for prehospital blood product administration

Despite strong pathophysiological rationale supporting early hemostatic resuscitation, clinical evidence regarding the effectiveness of prehospital blood product administration in civilian trauma care remains inconsistent. Over the past decade, several randomized controlled trials, observational cohort studies, and registry analyses have attempted to determine whether early transfusion strategies improve survival and physiological outcomes in patients with traumatic hemorrhagic shock. However, interpretation of available evidence remains challenging because of substantial heterogeneity in study design, patient selection, transport duration, injury severity, and the type of blood products administered.

Among the most influential randomized investigations, Sperry et al. reported an association between prehospital plasma administration and lower 30-day mortality among severely injured trauma patients transported by helicopter over prolonged distances (9). Patients at risk of hemorrhagic shock who received thawed plasma during transport experienced lower mortality compared with standard care. Importantly, the observed benefit appeared greatest among patients with prolonged transport intervals and more severe physiological derangement, suggesting that timing of hemostatic intervention may be clinically relevant (9).

In contrast, Moore et al. failed to demonstrate a mortality benefit from prehospital plasma administration in an urban emergency medical system characterized by relatively short transport intervals (17). Although plasma administration was feasible and safe, no significant differences were observed in mortality or major clinical outcomes between intervention and standard care groups. These findings raised important questions regarding the influence of transport duration and healthcare system organization on the effectiveness of prehospital blood product administration, suggesting that benefit may be context-dependent rather than universal (17).

Similarly, Crombie et al. evaluated prehospital administration of packed red blood cells and lyophilized plasma compared with standard crystalloid resuscitation in trauma patients at risk of hemorrhagic shock and failed to demonstrate significant improvement in the primary composite outcome of mortality or lactate clearance (18). Although some physiological benefits were observed, interpretation of these findings was complicated by heterogeneity in injury severity, variability in timing of intervention, and relatively short transport intervals within participating trauma systems (18).

The benefit of prehospital blood product administration appears to be context-dependent, with greater potential benefit in patients with severe hemorrhagic shock, prolonged transport times, and delayed access to definitive hemorrhage control.

Taken together, randomized evidence does not uniformly support routine implementation of prehospital blood product administration across all civilian emergency medical systems. Rather, available findings suggest that effectiveness may depend on factors such as transport duration, severity

of hemorrhagic shock, timing of intervention, and patient selection. Importantly, studies conducted within systems characterized by rapid access to definitive trauma care have generally demonstrated less consistent benefit than those involving prolonged prehospital intervals (9, 17,18).

In addition to randomized evidence, several observational studies and trauma registry analyses have reported associations between prehospital blood product administration and improved hemodynamic stabilization, reduced markers of shock severity, and lower mortality among selected high-risk trauma populations (19,20). Military experience has also substantially influenced enthusiasm for early transfusion strategies, with multiple combat-based studies reporting improved survival among severely injured patients receiving blood products early in the resuscitative process (21,22). However, translation of these findings into civilian systems remains challenging because of substantial differences in injury mechanisms, evacuation times, resource availability, and organizational structure.

More recently, growing interest has focused on the prehospital use of low-titer group O whole blood, which may offer both physiological and logistical advantages compared with conventional component therapy. By simultaneously providing red blood cells, plasma, and platelets in a single product, whole blood more closely approximates balanced hemostatic resuscitation while potentially simplifying transfusion logistics and reducing product complexity (23).

Observational studies have reported encouraging safety profiles and a potential survival benefit associated with low-titer group O whole blood use in selected trauma populations, although high-quality randomized evidence remains limited and important questions regarding patient selection, storage logistics, and comparative effectiveness remain unresolved (22,23)

Overall, current evidence suggests that prehospital blood product administration may confer clinically meaningful benefit in carefully selected trauma patients, particularly those with severe hemorrhagic shock, prolonged transport intervals, or delayed access to definitive hemorrhage control. Nevertheless, findings remain heterogeneous and insufficient to support universal implementation across all civilian emergency medical systems. Consequently, the question has increasingly shifted from whether prehospital blood products should be administered to under which conditions, in which patients, and within which systems such interventions provide sufficient benefit to justify operational complexity and resource utilization.

Current guideline perspective, implementation challenges, and future directions

Despite increasing interest and implementation of prehospital blood product administration in selected EMS systems, current international guidelines do not recommend its routine use in civilian trauma care. The available evidence is characterized by substantial heterogeneity in study design, patient selection, transport duration, healthcare system organization, and transfusion protocols, making universal recommendations difficult (2,4,5).

This uncertainty is reflected in contemporary international trauma guidelines. Importantly, no major contemporary guideline currently recommends routine prehospital blood product administration for all civilian trauma patients. The most recent European guideline on the management of major bleeding and coagulopathy following trauma recognizes the potential role of prehospital blood product administration within the concept of damage control resuscitation but does not recommend its routine use in civilian prehospital care because the available evidence remains limited and heterogeneous (2). Likewise, the recent Position Statement and Resource Document of the National Association of EMS Physicians (NAEMSP) emphasizes early recognition of life-threatening hemorrhage, minimization of excessive crystalloid administration, and rapid transport to definitive care, while acknowledging that evidence supporting universal prehospital transfusion strategies is still insufficient (5). Similarly, the most recent systematic review and clinical practice guideline update concluded that current data do not justify routine implementation and highlighted the need for further high-quality studies before stronger recommendations can be made (4).

Logistical barriers, including cold-chain maintenance, product availability, wastage, traceability, and coordination with transfusion services remain major challenges to widespread civilian implementation.

Consequently, the major challenge is no longer determining whether blood products can be administered safely in the prehospital environment, but rather identifying the patients and healthcare systems in which such an approach provides meaningful clinical benefit. Patients with severe hemorrhagic shock, prolonged transport intervals, remote geographical locations, or delayed access to definitive hemorrhage control appear to be the most plausible candidates; however, reliable tools for their early identification remain limited (9,17,18). Implementation also requires considerable logistical and organizational resources. Maintaining an uninterrupted cold chain, ensuring product availability, minimizing wastage, guaranteeing traceability, and coordinating transfusion services with emergency medical systems all represent substantial operational challenges. These factors may significantly influence the cost-effectiveness and feasibility of widespread implementation, particularly in civilian EMS systems characterized by short transport times and rapid access to trauma centers (4,5).

Growing interest in low-titer group O whole blood may partially overcome some of these limitations by simplifying transfusion logistics and providing balanced hemostatic

resuscitation through a single product. Nevertheless, important questions regarding optimal patient selection, storage protocols, comparative effectiveness, and economic sustainability remain unanswered (6,22,23).

Therefore, the current debate is no longer whether prehospital blood product administration is biologically plausible, but whether sufficient clinical evidence exists to justify its routine implementation in civilian emergency medical systems. At present, both the available evidence and contemporary guidelines support a selective, individualized, and system-dependent approach rather than universal adoption.

Importantly, this position is reinforced by the most recent randomized trials published in 2026, which have not demonstrated a clear clinical benefit of prehospital whole blood transfusion. The SWiFT trial (24) showed that, among patients with life-threatening hemorrhage, prehospital transfusion of two units of whole blood was not superior to standard care in reducing the risk of death or massive transfusion within 24 hours. Similarly, the TOWAR trial (25) found that, in injured patients with hemorrhagic shock, the use of whole blood for prehospital transfusion did not result in lower 30-day mortality compared with blood component therapy. Several factors may explain the neutral findings observed in these trials. Both studies included heterogeneous trauma populations treated within mature trauma systems, where relatively short transport intervals and rapid access to definitive care may have reduced the opportunity for prehospital transfusion to influence clinical outcomes. These findings therefore do not necessarily exclude a benefit in carefully selected patients experiencing prolonged transport or delayed hemorrhage control. These contemporary findings further suggest that, despite a strong biological rationale and encouraging observational data, current evidence does not support the routine universal implementation of prehospital blood product administration. Future research should therefore focus on identifying the patients most likely to benefit, optimizing transfusion strategies, and determining the organizational settings in which prehospital blood product administration provides clinically meaningful and cost-effective improvements in outcomes (2,4,5).

Conclusion

Prehospital blood product administration represents a promising strategy for the early management of traumatic hemorrhagic shock and is supported by a strong pathophysiological rationale. However, current clinical evidence remains heterogeneous and does not support its routine implementation across all civilian emergency medical systems. Moreover, the most recent randomized trials published in 2026 have also failed to demonstrate a clear clinical benefit of prehospital whole blood transfusion, further emphasizing the uncertainty regarding its universal use. Contemporary guidelines therefore advocate a selective, individualized, and system-dependent approach rather than routine implementation. Future research should focus on identifying the patients most likely to benefit, optimizing transfusion strategies, and determining the healthcare systems and organizational settings in which prehospital transfusion provides clinically meaningful, logistically feasible, and cost-effective improvements in outcomes. Until such evidence becomes available, a selective and evidence-based implementation tailored to local resources and patient populations appears to be the most appropriate strategy for civilian emergency medical systems.

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