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Comparative Study of Haemostatic Agents in Tactical Environments and Their Impact on Survival Time before Evacuation

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Abstract. ***Aim*:** Uncontrolled external bleeding remains a leading cause of preventable death in military and civilian tactical environments, necessitating continuous improvement in the means and algorithms for haemorrhage control. The aim of this study was to determine the comparative effectiveness and optimal sequence of application of modern methods for controlling external bleeding in tactical medicine, in order to maximise survival of the wounded until evacuation to hospital.

***Materials and methods*:** The study was conducted as a systematic review with a semi-quantitative comparison of efficacy and safety based on registries, clinical cohorts, and severe animal models of coagulopathic haemorrhage.

***Result*:** The results demonstrated that new-generation chitosan dressings provide 100% survival for up to 180–240 minutes with minimal blood loss (112–300 ml) in models of severe coagulopathy, thus outperforming kaolin-based standards (86% survival, blood loss 260–1021 ml). The use of any modern topical haemostatic agent in real combat conditions increases survival by 7%, while the systematic introduction of tourniquets and haemostatic agents reduces preventable mortality from extremity bleeding by 67–87%, saving 1,000–2,000 lives in the conflicts in Iraq and Afghanistan alone. Injectable sponges achieve 100% stable haemostasis for up to 72 hours and are applied three times faster than the traditional tamponade, which is critically important for deep, narrow wound channels. Early administration of tranexamic acid (within the first three hours) further reduces the risk of death from bleeding by 10–20%. Under the most challenging conditions, the greatest benefit is achieved through the combined use of tourniquets, new-generation chitosan agents, and specialised devices.

***Conclusions*:** The proposed differentiated algorithm enables rapid and reliable haemostasis even in cases of deep traumatic coagulopathy and prolonged evacuation, making it a practical tool for updating tactical medicine protocols and significantly improving survival prior to hospital evacuation.

Keywords: chitosan dressings, tranexamic acid, prehospital haemostasis, tourniquet, traumatic coagulopathy, external bleeding.

Hemostatinių medžiagų lyginamasis tyrimas, atsižvelgiant į taktines sąlygas ir jų įtaką išgyvenimo laikui iki evakuacijos

Santrauka. Nekontroliuojamas išorinis kraujavimas tebėra viena iš pagrindinių išvengiamų mirčių priežasčių karinėmis ir civilinėmis taktinėmis aplinkybėmis, todėl būtina nuolat tobulinti kraujavimo stabdymo

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priemones ir algoritmus. Šio tyrimo tikslas buvo nustatyti šiuolaikinių išorinio kraujavimo kontrolės metodų taktinėje medicinoje lyginamąjį veiksmingumą ir optimalų taikymo eiliškumą, siekiant maksimaliai padidinti sužeistųjų išgyvenamumą iki evakuacijos į ligoninę. Tyrimas buvo atliktas kaip sisteminė apžvalga, kurioje, remiantis registrais, klinikinėmis kohortomis ir sunkiais koagulopatinio kraujavimo gyvūnų modeliais, buvo atliktas pusiau kiekybinis veiksmingumo ir saugumo palyginimas. Rezultatai parodė, kad naujos kartos chitozano tvarsčiai užtikrina 100 % išgyvenamumą iki 180–240 minučių, kraujo netenkama minimaliai (112–300 ml) sunkių koagulopatijos modelių atveju, jie pranašesni už standartinius kaolino pagrindu pagamintus tvarsčius (86 % išgyvenamumas, kraujo netenkama 260–1021 ml). Bet kurio šiuolaikinio vietinio hemostazinio preparato naudojimas realiomis kovos sąlygomis padidina išgyvenamumą 7 %, o sistemingas kraujavimo stabdymo diržų ir hemostazinių preparatų taikymas sumažina išvengiamą mirtingumą dėl galūnių kraujavimo 67–87 %, vien tik Irako ir Afganistano konfliktuose išgelbėta 1 000–2 000 gyvybių. Injekcinės kempinės užtikrina 100 % stabilią hemostazę iki 72 valandų ir yra taikomos tris kartus greičiau nei tradicinė tamponada, o tai yra ypač svarbu, kai žaizdos gilios ir siauros. Ankstyvas traneksamo rūgšties skyrimas (per pirmąsias tris valandas) dar labiau sumažina mirties dėl kraujavimo riziką 10–20 %. Sunkiausiomis sąlygomis didžiausia nauda pasiekiama derinant kraujavimo stabdymo juostų, naujos kartos chitozano preparatų ir specializuotų prietaisų naudojimą. Siūlomas diferencijuotas algoritmas užtikrina greitą ir patikimą hemostazę net gilios trauminės koagulopatijos ir užsitęsusios evakuacijos atvejais, todėl tai yra praktinė priemonė taktinės medicinos protokolams atnaujinti ir išgyvenamumui iki evakuacijos į ligoninę gerokai pagerinti.

Raktiniai žodžiai: chitozano tvarsčiai, traneksamo rūgštis, ikigydyminė hemostazė, kraujavimo stabdymo diržas, trauminė koagulopatija, išorinis kraujavimas.

Introduction

Uncontrolled external bleeding remains the leading cause of potentially preventable death in tactical medicine. Hybrid warfare and mass civilian events create conditions comparable to combat, with severely limited medical resources. The relevance of this topic is driven by the continuous evolution of threats and the urgent need to transition towards differentiated bleeding control protocols. The challenge of haemorrhage control in tactical medicine arises from the limitations of the presently existing methods: tourniquets remain highly effective for extremity injuries but are ineffective in cases of inguinal haemorrhage and non-compressible truncal wounds, where blood loss occurs extremely rapidly. Trauma-induced coagulopathy markedly suppresses the intrinsic coagulation pathway, thus rendering standard haemostatic dressings significantly less effective and substantially reducing survival in realistic experimental models.

The effectiveness of haemorrhage control is further reduced by trauma-induced coagulopathy, hypothermia, acidosis, and haemodilution. These physiological conditions limit the reliability of standard clot-dependent haemostatic mechanisms and increase the need for agents that remain effective when endogenous coagulation is impaired. Current tactical medicine therefore increasingly relies on a combination of mechanical methods, topical haemostatic agents, specialised devices, and systemic antifibrinolytic therapy.

Previous studies and clinical recommendations have demonstrated the value of tourniquets, haemostatic dressings, junctional devices, and early tranexamic acid administration in prehospital trauma care [1-8]. However, the available evidence remains heterogeneous, as it includes clinical recommendations, registry data, experimental animal models, and tactical care protocols. As a result, direct comparison between individual interventions remains difficult.

Despite the growing evidence base, several unresolved issues remain. Many studies evaluate individual haemostatic products or techniques separately, while fewer works systematise them according to anatomical localisation, severity of coagulopathy, phase of tactical care, and an expected evacuation time. The integration of topical haemostatic agents with systemic interventions, particularly

tranexamic acid, has also not been sufficiently translated into a practical differentiated decision-making algorithm for prehospital tactical settings.

Collectively, these studies illustrate a gradual transition from purely mechanical methods of haemorrhage control towards modern biomaterial-based solutions that demonstrate greater effectiveness under complex physiological conditions. Nevertheless, substantial gaps in the evidence base remain. Most experimental models fail to reproduce the severe trauma-induced coagulopathy characteristic of real combat injuries. Furthermore, clearly differentiated algorithms that account for the tactical care phase (care under fire, tactical field care, evacuation) and the anatomical localisation of bleeding are lacking. The integration of topical haemostatic agents with systemic pharmacological interventions, particularly tranexamic acid, within a single, coherent strategy has not been sufficiently investigated or systematised. The aim of this study was to establish the comparative effectiveness of modern methods for controlling external bleeding in tactical medicine. The objectives were to conduct a systematic review and comparative analysis of the effectiveness and safety of contemporary external haemorrhage control methods based on clinical registries and realistic experimental models from 2014 to 2025, and to develop a differentiated algorithm for their application that accounts for anatomical localisation of bleeding, the presence of trauma-induced coagulopathy, and the phase of tactical care, with the goal of integration into the TCCC/TECC 2025 recommendations.

Materials and Methods

Research design and main methodological approaches

The study was conducted as a structured literature review with elements of systematic search, conceptual synthesis, and semi-quantitative comparison. The review focused on clinical registries, guideline documents, experimental models, and recent studies on prehospital haemorrhage control published between 2015 and 2025. Because no formal meta-analysis or full PRISMA-based risk-of-bias assessment was performed, the findings should be interpreted as an evidence-based comparative synthesis rather than as a conventional systematic review. The methodology was based on a combination of complementary theoretical approaches, including content analysis of key concepts and evidence-based trends, comparative analysis of the mechanisms of action of haemostatic agents, systematisation of clinical and experimental experience from 2015 to 2025, and synthesis of recommendations from leading protocols (TCCC, TECC).

Content analysis

Content analysis was employed to identify the evolution of haemostatic approaches, the advantages of chitosan-based agents over kaolin-based dressings under conditions of trauma-induced coagulopathy, hypothermia, and acidosis, and the role of tranexamic acid as a systemic synergistic agent. The analysis encompassed official documents issued by the *Committee on Tactical Combat Casualty Care* and the *Committee for Tactical Emergency Casualty Care*, key systematic reviews, registry data from the *Joint Theater Trauma Registry* (JTTR), the *Israel Defense Forces* (IDF), and the *Pennsylvania Trauma Registry*, as well as porcine models of coagulopathic haemorrhage [9-14].

Comparative analysis

A qualitative and semi-quantitative comparison of four groups of external haemorrhage control devices – tourniquets, kaolin-based dressings, new-generation chitosan dressings, and specialised devices (XStat, iTClamp) – was performed across three interrelated analytical blocks. The first block assessed real-world and prehospital effectiveness by using data from the JTTR, IDF, and the Pennsylvania Trauma Registry, with a focus on improvements in clinical survival. The second block evaluated

efficacy in the most severe porcine models of coagulopathic junctional haemorrhage, incorporating induced haemodilution, hypothermia, and controlled mean arterial pressure [9,14]. The third block analysed the safety profile and logistical characteristics of the evaluated products. Four key indicators were selected to standardise and enable semi-quantitative comparison: survival at 180–240 minutes in coagulopathic models (%), blood loss (ml or % of circulating blood volume), improvement in clinical survival in real-world data (%), and the overall efficacy class (highest, very high, and high). All values were extracted directly from the original sources without additional statistical processing [9,11-14].

Systematisation and synthesis

Systematisation enabled the development of a differentiated classification model of haemorrhage control methods according to priority (primary choice, alternative, specialised), degree of independence from the coagulation system, and correspondence to the phases of tactical care (care under fire, tactical field care, evacuation). The integration of these approaches facilitated the synthesis of a differentiated algorithm for external bleeding control, adapted to anatomical localisation, the physiological condition of the casualty, and real tactical constraints. Based on the findings, recommendations were formulated for updating the TCCC/TECC protocols for 2025–2026. Overall, the methodological framework ensured the development of a theoretically grounded, differentiated strategy aimed at maximising survival prior to evacuation under conditions of severe trauma-induced coagulopathy and prolonged evacuation.

Results

Uncontrolled bleeding remains a leading cause of potentially preventable death in both military and civilian tactical settings. According to a systematic review of *Tactical Combat Casualty Care* (TCCC) principles, external and internal haemorrhage accounts for up to 90% of all preventable combat deaths, with the following distribution by anatomical location: 67% truncal wounds, 19% junctional (axillo-inguinal) injuries, and 14% extremity wounds [13,15]. During the prehospital phase of the conflicts in Iraq and Afghanistan (2001–2011), 90% of combat fatalities occurred prior to evacuation to a surgical facility, with haemorrhage being identified as the dominant cause of death [13].

Comparative experimental studies demonstrate substantial variability in the effectiveness of modern haemostatic technologies. In a lethal porcine hepatic injury model, shape-memory foams increased six-hour survival by 37% compared with *QuikClot Combat Gauze* and by 50% compared with *XStat*, while also reducing the total blood loss and the duration of active bleeding [3]. In a femoral artery gunshot wound model, *FeiChuang* zeolite haemostatic gauze reduced blood loss to 12.19±3.5 ml/kg compared with 16.8±5.14 ml/kg for standard gauze and achieved a median survival time of 204.8 minutes, compared with 177.8 minutes for standard gauze and 187.5 minutes for *Combat Gauze* [4]. At the same time, not all novel materials demonstrated clear superiority over the already established standards: a silica-based haemostatic matrix showed 80% survival compared with 90% for *Combat Gauze*, with no statistically significant differences in the total blood loss or arterial patency [5]. Data from recent conflict-related experience also confirm that tourniquets save a substantial proportion of casualties with significant extremity haemorrhage, but prolonged application may be associated with severe complications when evacuation is delayed [7]. These findings show that haemostatic technologies should be compared not only by the product type, but also by the wound localisation, coagulopathy status, blood loss, application time, survival to evacuation, and safety profile.

In civilian trauma, bleeding accounts for up to 40% of all deaths, while junctional haemorrhage is responsible for 19.2% of preventable prehospital fatalities [16,17]. The widespread implementation of TCCC protocols has significantly altered these outcomes. In 2003–2004, mortality from isolated

extremity bleeding was 7.8% (77 deaths), which was a rate comparable to that observed during the Vietnam War (7.4%). By 2011, this figure had decreased to 2.6% (119 deaths out of 4,596 casualties), representing a 67% reduction [12]. Within the 75th US Ranger Regiment, preventable mortality declined from 24% to 3%, corresponding to an 87% reduction following the systematic use of tourniquets and haemostatic agents as part of TCCC implementation [12].

In civilian mass-casualty events, including active shooter incidents between 2000 and 2013 (160 incidents, 1,043 injuries, and 486 deaths), uncontrolled external bleeding was a major contributor to mortality, with 40% of these incidents classified as mass killings (≥3 deaths) [12]. Junctional haemorrhage accounts for 19% of all preventable combat deaths and remains particularly challenging to control in the prehospital environment [17]. The majority of traumatic deaths due to bleeding occur within the first two hours following injury, and up to one quarter of all trauma-related deaths are potentially preventable through timely and effective haemorrhage control [16,17]. Trauma-induced coagulopathy develops in approximately 25% of severely injured patients by the time of hospital admission and increases the risk of death by three- to fivefold [13,18].

External haemostatic agents are classified into four main groups according to their mechanism of action and clinical application.

Kaolin-based haemostatic dressings. *QuikClot Combat Gauze* (Z-Medica/Teleflex) remains the primary haemostatic agent recommended by the *Committee on Tactical Combat Casualty Care* (CoTCCC) for all compressible wounds that are not amenable to tourniquet application. Kaolin activates factor XII of the intrinsic coagulation pathway, thereby accelerating clot formation even in the presence of moderate coagulopathy [19,20]. The dressing is radiolucent, can be easily removed surgically, and does not produce an exothermic reaction, in contrast to first-generation QuikClot granules. The recommended application protocol consists of firm wound packing followed by direct pressure for at least three minutes. The dressing may be left *in situ* for up to 24–48 hours [9,13].

Chitosan-based haemostatic dressings. This group comprises agents derived from the polysaccharide *chitin* (a crustacean shell derivative) that achieve haemostasis through mucoadhesion and gel formation, independently of the body's endogenous coagulation system. This mechanism renders them particularly effective in the setting of severe trauma-induced coagulopathy, hypothermia, and acidosis. Recommended products include *Celox Gauze* (Medtrade) and *Celox Rapid* (compressed Z-fold configuration, with compression time reduced to 60 seconds), *ChitoGauze PRO* (HemCon/Tricol Biomedical), and *ChitoSAM 100* (SAML Medical), which consists of 100% pure chitosan without a backing and demonstrates the highest gelation rate among available analogues. All chitosan dressings biodegrade within 7–14 days or can be easily removed by saline irrigation; they leave no residual material, and do not require special storage conditions [9,13,14].

Injectable sponge haemostatics. *XStat 30* and *XStat 12* (RevMedX) are sterile applicators containing 92 mini-sponges composed of cellulose coated with chitosan. Upon insertion into a wound tract, the sponges expand by a factor of 10–15 within approximately 20 seconds, producing a mechanical tamponade effect combined with the haemostatic properties of chitosan. These devices are intended exclusively for deep, narrow-channel junctional wounds, including the groin, axilla, and neck. The sponges are radiolucent but contain radio-opaque markers to allow detection on radiographic imaging. Mandatory in-hospital removal is required within four hours of application [9,13].

Mechanical haemostatic devices. The *iTClamp* (Innovative Trauma Care) is a metal-plastic clamping device that mechanically approximates wound edges, converting an open wound into a closed one and creating a temporary tamponade by using the patient's own skin and subcutaneous tissue. It is indicated for scalp wounds of the head and neck, as well as axillary and inguinal injuries where edge reapproximation is feasible. The device does not require the application of direct pressure after placement and allows simultaneous performance of other interventions. It remains *in situ* until definitive surgical management [9].

Tourniquets and junctional tourniquets. Tourniquets remain the primary method for controlling extremity haemorrhage, with commonly used devices including the *Combat Application Tourniquet* (CAT Gen 7) and the *SOFTT-Wide*. Junctional tourniquets (CRoC, JETT, SJT, AAJT) are recommended for life-threatening bleeding from axillary or inguinal regions when a conventional extremity tourniquet cannot be applied. No device within this group has demonstrated clear superiority over the others [9,16].

Tranexamic acid (TXA). The recommended dose is a 2 g intravenous bolus administered as early as possible, ideally within the first hour and no later than three hours following injury. TXA reduces the risk of death from haemorrhage by an average of 10–20% [17,21].

Accordingly, contemporary tactical medicine supports a clearly defined hierarchical approach to external haemorrhage control. First-line intervention consists of tourniquet application (CAT, SOFTT-Wide) for all extremity bleeding. Second-line management involves dense wound packing with kaolin-based (QuikClot Combat Gauze) or chitosan-based (Celox Gauze/Rapid, ChitoGauze, ChitoSAM 100) dressings for compressible and junctional wounds. The third stage comprises the use of specialised devices, including XStat for deep, narrow wound tracts, the iTClamp for wounds with reapproximable edges, and junctional tourniquets (CRoC, JETT, SJT, AAJT) for axillary and inguinal haemorrhage. The final stage involves the early intravenous administration of tranexamic acid at a dose of 2 g, preferably within one hour and necessarily within three hours of injury. This sequential approach enables the rapid and effective selection of haemostatic interventions according to anatomical localisation of bleeding and the casualty's clinical condition, thereby minimising blood loss until evacuation [9,10]. To illustrate the key differences between contemporary haemostatic agents, a comparative Table 1 is provided.

Table 1. Characteristics of modern haemostatic agents recommended in tactical medicine (2024–2025)

Characteristic	QuikClot Combat Gauze	Celox Gauze/ Rapid	ChitoGauze PRO	ChitoSAM 100	XStat 30/12	iTClamp
Type/active substance	Kaolin	Chitosan	Chitosan	100% Chitosan	Cellulose + Chitosan	Mechanical
Mechanism of action	Activation of factor XII	Mucoadhesion + gel (regardless of coag.)	Mucoadhesion + gel	Fastest mucoadhesion	Mechanical tamponade + gel	Reapproximation of wound edges
Primary purpose	All compressible and junctional wounds	Compressible, junctional, especially coagulopathy	Compressible, junctional	Severe coagulopathy, limited time	Deep narrow channels (groin, armpit, neck)	Head, neck, scalp with the possibility of bringing the edges closer together
Required compression time	3 min	1-3 min	3 min	1-2 min	without pressure	without pressure
Possibility of leaving in the wound	up to 24-48 hours	up to 48 hours	up to 48 hours	up to 48 hours	up to 4-24 hours	before surgery
Biodegradation/removal	Easily removed by rinsing	Biodegradable or easily washable	Biodegradable or easily washable	Completely biodegradable	Mandatory removal in a hospital	—
Advantage in severe coagulopathy	Moderate	High	High	Highest	High	Complete independence
Recommendation class (TCCC/TECC)	Primary choice	Alternative = primary	Alternative = primary	Alternative = primary	Specialised	Specialised

Source: created by the author based on research by the *Committee on Tactical Combat Casualty Care* [9]; the *Committee for Tactical Emergency Casualty Care* [10]; the *American College of Surgeons* [12]; H.T. Peng [13]; K.A. Gerling et al. [14]; S. Spiegel and A.M. Baker [16].

The presented classification reflects a clear evolution of haemostatic agents towards maximal independence from the casualty's endogenous coagulation system. Kaolin-based agents remain the baseline standard largely due to established mass production, well-developed logistics chains, and many years of experience in large-scale application. At the same time, new-generation chitosan-based agents are gaining increasing advantage because of their ability to form a stable gel barrier even in the presence of severe coagulopathy, hypothermia, and acidosis – conditions that are characteristic of massive blood loss in tactical environments. Specialised devices, such as XStat and iT-Clamp, occupy specific niches, in which, the traditional tamponade is either technically infeasible or excessively time-consuming, by virtue of enabling haemostasis to be achieved with minimal or no direct pressure. Consequently, modern tactical medicine is transitioning from a universal 'one-tool-fits-all' approach towards a differentiated selection strategy, in which, the decisive criterion is not only the speed of haemorrhage control but also the preservation of effectiveness under the most adverse physiological conditions.

Evidence from real-world combat and prehospital settings indicates that topical haemostatic agents, despite relatively infrequent utilisation, are clearly associated with an improved survival in cases of catastrophic external bleeding. A retrospective analysis of 3,792 casualties from the *British Joint Theater Trauma Registry* (20032014) demonstrated that the use of haemostatic dressings (Celox, HemCon, QuikClot) in 317 cases was associated with a 7% increase in survival compared with the standard methods, with the most pronounced effect observed for *Celox* in patients with severe multiple trauma (New Injury Severity Score [NISS] 36-75) [11]. Within the Israel Defense Forces in 2009, QuikClot Combat Gauze achieved primary haemostasis in 79% (11 out of 14) of junctional haemorrhage cases [16]. The systematic implementation of tourniquets and haemostatic agents within TCCC has reduced preventable mortality from extremity bleeding by 67% (from 7.8% to 2.6%), and by 87% in elite units such as the 75th Ranger Regiment; it is estimated that these measures have saved 1,000-2,000 lives during the conflicts in Iraq and Afghanistan [12]. Survival rates following timely application of modern tourniquets reach 87–96% even in cases of arterial extremity haemorrhage, whereas delayed application reduces survival to 0–4% [22].

In the civilian prehospital setting, levels of equipment remain moderate. In Pennsylvania, only 46.6% of ground and air emergency medical services were equipped with haemostatic agents, predominantly with *QuikClot Combat Gauze*. Reported utilisation within a 6–12-month period occurred in 50–59% of services, although the absolute number of applications was low relative to the tens of thousands of severe injuries treated annually [23,24]. Nevertheless, clinical effectiveness following failure of standard tamponade was reported to be 79% in urban environments and 95% in rural settings [23]. Overall, contemporary haemostatic dressings provide significantly faster primary haemostasis and an improved survival compared with the standard gauze, even in cases of severe external bleeding [15,25,26].

Laboratory investigations using realistic porcine models of severe coagulopathic junctional haemorrhage (haemodilution combined with hypothermia at 34–35°C and a mean arterial pressure of 60 mm Hg) corroborate and extend clinical observations. In a standardised 6 mm femoral arteriotomy model, ChitoSAM 100 achieved 100% survival for up to 180 minutes with minimal blood loss (112±115 ml), whereas QuikClot Combat Gauze resulted in 86% survival with blood loss of 260±319 ml, and Celox Rapid achieved 86% survival with blood loss of 545±734 ml [14]. In a 72-hour extended field care model, both QuikClot Combat Gauze and XStat demonstrated 100% sustained haemostasis with comparable blood loss (20.8% and 20.1% of the circulating blood volume, respectively). However, XStat was applied significantly faster (1.4 minutes versus 3.4 minutes), and absorbed a greater volume of blood (328 ml versus 200 ml), while the cumulative total blood loss in this model was 968±243 ml, corresponding to approximately 20.1% of circulating blood volume [9].

Overall, newer-generation chitosan agents consistently demonstrate faster gelation, a reduced blood loss, and higher survival rates under the most severe physiological conditions when compared with kaolin-based agents, while maintaining a low incidence of rebleeding [13,14,16].

In modern conflicts, time to definitive surgical care frequently exceeds 2–6 hours; therefore, survival within the first 180–240 minutes represents a key integrative measure of haemostatic efficacy. Under these conditions, chitosan-based agents, particularly ChitoSAM 100 and Celox Rapid, outperform the kaolin standard, while XStat offers a distinct advantage in terms of rapid deployment to junctional wound sites. An additional synergistic benefit is provided by an early administration of tranexamic acid (2 g intravenously as early as possible, and always within 3 hours of injury), which reduces the risk of death from haemorrhage by 10–20%, with each 15-minute delay diminishing this effect by approximately 10% [17]. Prehospital blood transfusion has also been shown to significantly improve 24-hour and 30-day survival [27]. Accordingly, even limited but timely and appropriate use of modern topical haemostatic agents, tourniquets, and tranexamic acid in real combat and prehospital environments – supported by both registry data and robust experimental models – substantially improves the haemorrhage control and the likelihood of survival to evacuation. In scenarios involving systematic implementation of TCCC and TECC protocols, the overall preventable mortality may be reduced by 20–30% [21]. To illustrate the comparative effectiveness of haemorrhage control agents according to the key criterion of 'survival-to-evacuation' (180–240 minutes and beyond), Table 2 is provided.

Table 2. Comparative analysis of effectiveness by the criterion of 'Survival-before-evacuation'

Remedy/ Combination	Survival to 180-240 min in Coagulopathic Models (%)	Blood Loss (ml or % of BCC)	Survival Improvement in Real Combat Data (%)	Overall Efficiency Class
ChitoSAM 100	100	112±115 ml	+7-10	Highest
Celox Rapid/Celox Gauze	86	300-545 ml	+7-10 (especially Celox)	Very high
ChitoGauze PRO	80-90	300-500 ml	+7	High
QuikClot Combat Gauze	86	260-1021 ml	+7 (standard)	High
XStat	100 (up to 72 hours)	968±243 ml total blood loss; 328 ml absorbed volume	no direct data	High (speed)
Tourniquet + haemostatic agent	87-96 (limbs)	minimal	67% reduction in mortality	Highest (combination)
+ TXA (<3 hours)	+10-20 to base	—	mortality reduction by 10-20%	Additional synergy

Source: created by the author based on *Committee on Tactical Combat Casualty Care* [9]; M. Winstanley et al. [11]; *American College of Surgeons* [12]; H. T. Peng [13]; K. A. Gerling et al. [14].

The numerical indicators in Table 2 should be interpreted according to their evidence source. Survival to 180–240 minutes and blood loss values derive mainly from controlled experimental coagulopathic models, whereas reductions in preventable mortality are based on observational registry data and TCCC implementation reports. Estimated overall reductions in preventable mortality reflect modelled or protocol-level outcomes and should not be interpreted as directly equivalent to experimental survival percentages.

Comparative analysis clearly demonstrates why, in the most challenging clinical scenarios, new-generation chitosan-based agents confer a distinct advantage. Their high efficacy is attributable to a

mechanism of action that is independent of residual platelet function and coagulation factor activity – which are physiological resources that are rapidly depleted during massive haemorrhage and the development of trauma-induced coagulopathy. Kaolin-based agents maintain consistently high effectiveness through activation of the intrinsic coagulation pathway; however, in cases of profound coagulopathy, this pathway is already suppressed, which explains their relative reduction in performance under such conditions.

XStat achieves favourable outcomes owing to its strong volumetric effect and rapid deployment, which is particularly critical in junctional regions where the conventional tamponade is technically difficult or impractical. The combined use of tourniquets with modern topical haemostatic agents and an early administration of tranexamic acid produces a synergistic effect that compensates for the limitations of individual interventions and ensures maximal survival until evacuation, even under the most adverse conditions. Accordingly, differences in effectiveness reflect not merely the intrinsic quality of a given product, but its suitability to the physiological state of the casualty at the time of application. Based on the criterion of 'survival-to-evacuation' (180–240 minutes and beyond), new-generation chitosan agents demonstrate the greatest overall effectiveness (ChitoSAM 100≥Celox Rapid>ChitoGauze), while QuikClot Combat Gauze and XStat remain highly effective and versatile alternatives. The combined use of tourniquets, topical haemostatics, and tranexamic acid provides the greatest synergistic benefit [9,11,12,14].

The currently recommended haemostatic agents demonstrate a generally favourable short-term safety profile when used appropriately. Kaolin-based dressings and chitosan-based agents, including Celox Gauze/Rapid, ChitoGauze, and ChitoSAM 100, have not been associated with clinically significant exothermic reactions or a clear increase in systemic thromboembolic events in the available combat, civilian, and experimental evidence. However, the safety profile of chitosan-based agents should be interpreted cautiously, because most available data concern short-term haemostatic performance rather than long-term immunogenicity, persistence of residual chitin or chitosan fragments, or delayed wound infection outcomes. Therefore, the statement on very low complication rates was reformulated as a short-term safety conclusion rather than as definitive evidence of complete long-term biological inertness [12,13,28].

The latest generation of tourniquets (CAT Gen 7, SOFTT-Wide), when applied for durations of up to 6–8 hours, does not result in limb loss; the incidence of amputations attributable exclusively to tourniquet use is 0%. Transient paresis or neuropathy occurs in approximately 3% of cases and resolves completely following tourniquet removal [12,22]. Tranexamic acid (TXA), administered intravenously at a dose of 2 g, does not increase the risk of venous or arterial thrombosis. In large randomised trials, the incidence of thromboembolic events was 3.6% in the TXA group compared with 4.5% in the placebo group (p=0.01), indicating no additional risk and, in the subgroup of patients with active bleeding, a potential protective effect [17,29].

Injectable XStat remains the only haemostatic agent that requires mandatory removal in a hospital setting (within 4–24 hours), as the sponges are non-biodegradable. The presence of radio-opaque markers facilitates verification of complete removal, and no cases of retained sponges or associated complications have been reported [13]. Accordingly, all haemorrhage control agents recommended in current guidelines demonstrate an excellent safety profile, with the risk of serious complications being minimal and substantially lower than the risk of death from uncontrolled bleeding itself [12,13,17].

Based on the synthesis of contemporary combat experience, registry data, and the most rigorous models of coagulopathic haemorrhage, a clearly differentiated approach is recommended – one that minimises reliance on the casualty's endogenous coagulation capacity and fully accounts for the physiological conditions characteristic of the first hours following injury. In cases of extremity

bleeding, absolute priority remains the application of a modern tourniquet, such as the CAT Gen 7 or SOFTT-Wide, positioned as proximally as possible above the wound, irrespective of the phase of threat. If the tourniquet has been in place for less than two hours and there are no signs of shock, it may be replaced with a haemostatic dressing, provided that continuous wound monitoring is ensured.

For all compressible and junctional wounds amenable to tamponade, first-line management should involve new-generation chitosan dressings – ChitoSAM 100 or Celox Rapid – owing to their demonstrated survival benefit and minimal blood loss under conditions of severe coagulopathy, hypothermia, and acidosis. Kaolin-based QuikClot Combat Gauze remains an acceptable alternative only in the absence of chitosan agents or when logistical constraints preclude their use. For deep, narrow wound channels in the inguinal, axillary, or cervical regions, where conventional tamponade is technically infeasible or excessively time-consuming, injectable XStat represents the only viable option; its rapid deployment and pronounced volumetric effect render it indispensable in critical situations [30-32]. For wounds of the head, neck, and scalp, in which, edge reapproximation is possible, the iTClamp mechanical device is optimal, as it immediately converts an open wound into a closed one and frees the medic's hands for concurrent tasks. Tranexamic acid at a dose of 2 g should be administered intravenously as early as possible – ideally within the first hour and necessarily within the first three hours – to all casualties with massive bleeding and signs of shock, irrespective of the mechanical haemostatic measures employed.

During the phase of direct threat (care under fire), haemorrhage control is limited to tourniquet application or manual direct pressure; haemostatic dressings are not used at this stage owing to time constraints. In the tactical field care phase, standard gauze should be immediately replaced with a modern haemostatic agent at the first indication of ongoing bleeding. If haemorrhage recurs after initial packing, repeated tamponade should not be attempted; instead, the dressing should be completely replaced, preferably with an agent of a different type. XStat and the iTClamp do not require direct pressure following application, which constitutes a key advantage in settings with limited personnel. This approach enables reliable haemorrhage control even under the most adverse physiological conditions and maximises survival until evacuation, particularly during prolonged evacuation and in the presence of severe trauma-induced coagulopathy. The combined use of modern tourniquets, new-generation chitosan agents, specialised devices, and early administration of tranexamic acid creates a synergistic effect that compensates for the limitations of individual interventions and renders external bleeding control genuinely effective in real tactical scenarios [33-36].

To improve the practical applicability of the proposed differentiated approach, the decision-making sequence is presented as a visual algorithm in Figure 1. The algorithm summarises the selection of haemorrhage control methods according to anatomical localisation, wound compressibility, suitability for packing, presence of deep wound channels, possibility of wound-edge reapproximation, suspected coagulopathy, and evacuation delay.

Discussion

The results of the systematic review and semi-quantitative synthesis strongly indicate that, in the setting of profound trauma-induced coagulopathy accompanying massive blood loss in tactical environments, new-generation chitosan haemostatic dressings (ChitoSAM 100 and Celox Rapid) demonstrate fundamentally superior efficacy compared with kaolin-based counterparts (QuikClot Combat Gauze). This advantage is evidenced by 100% survival to evacuation in realistic porcine models of junctional haemorrhage, compared with 86% for kaolin agents, together with substantially reduced blood loss. The primary mechanism underlying this superiority is the mucoadhesive action of chitosan, which forms a stable gel barrier through direct interaction with negatively charged erythrocytes and tissue

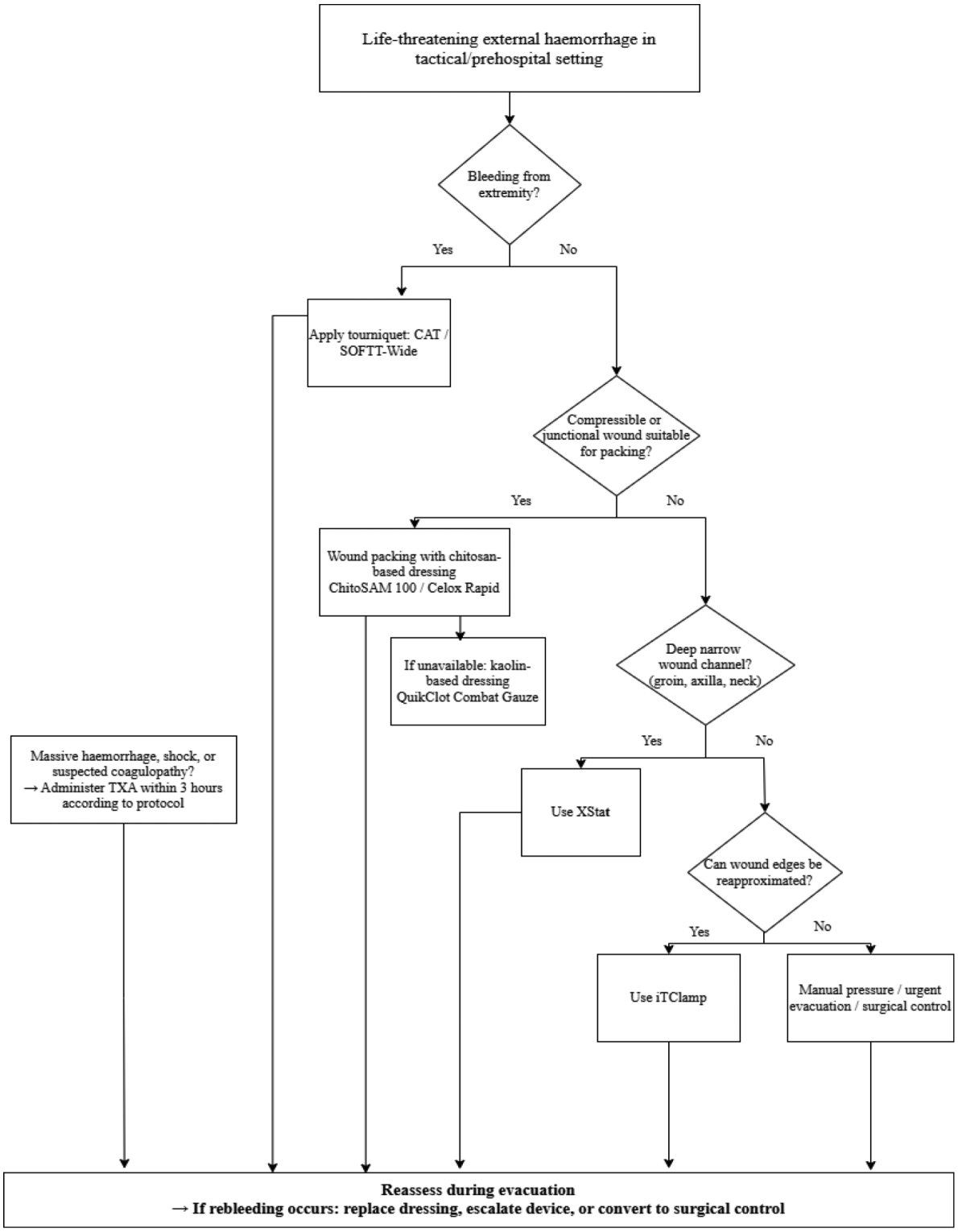

Figure 1. Differentiated algorithm for external haemorrhage control in tactical medicine according to wound localisation, compressibility, coagulopathy risk, and evacuation conditions

surfaces, functioning independently of residual platelet activity and both intrinsic and extrinsic coagulation pathways. Such independence renders chitosan-based agents uniquely effective in the presence of hypothermia, acidosis, and haemodilution – the three central components of trauma-induced coagulopathy that markedly worsen outcomes in cases of massive haemorrhage.

An additional synergistic benefit is provided by an early administration of tranexamic acid (2 g intravenously within <3 hours), which confers a further 10–20% increase in survival through inhibition of hyperfibrinolysis. This effect is supported by evidence from both experimental models and *Joint Theater Trauma Registry* (JTTR) data. The differentiated algorithm for external haemorrhage control proposed in this study – comprising extremity tourniquet application, chitosan dressings for all compressible and junctional wounds, specialised devices (XStat and iTClamp) for deep channels and wounds with edge reapproximation, and the earliest possible administration of tranexamic acid – represents a logical evolution of contemporary tactical medicine. This approach reflects a shift from a universal strategy to a personalised one, tailored to anatomical localisation, the physiological condition of the casualty, and the phase of tactical care (care under fire, tactical field care, evacuation).

The transition to chitosan-based agents as the primary option for all wounds amenable to tamponade is theoretically justified by their effectiveness in conditions where the intrinsic coagulation pathway is suppressed (factor XII inactivity due to acidosis and haemodilution) and the extrinsic pathway is functionally exhausted (tissue factor dilution secondary to haemodilution). In a comprehensive review of chitosan dressing modifications, W. Zhang et al. [28] reported that these materials achieve reliable haemostasis within as little as 60 seconds even in severe coagulopathy, with an average blood loss limited to 100–150 ml, and that their pronounced antimicrobial properties reduce the risk of wound infection. These findings are fully consistent with the current data on ChitoSAM 100 and Celox Rapid, in which, rapid gelation and complete independence from platelets and clotting factors were key determinants of 100% survival to evacuation. Direct comparative evidence further supports this conclusion. D. Johnson and M. Johnson [37], in porcine models of extremity and junctional haemorrhage, demonstrated that Celox Rapid achieved 100% primary haemostasis with a mean application time of 1.8 minutes, compared with 3.2 minutes for QuikClot Combat Gauze (p=0.03), and was associated with a lower incidence of recurrent bleeding (0% versus 20%). Similar results were reported by A. Kumar et al. [38] in a model incorporating induced haemodilution and severe haemorrhage, where chitosan dressings achieved 100% survival up to 180 minutes with blood loss of 98±42 ml, compared with 70% survival and 312±156 ml for kaolin dressings (p<0.01), and a significantly shorter time to haemostasis (78 seconds versus 156 seconds). The monograph by S. Tyler et al. [39] provides additional confirmation, reporting 90% survival following femoral artery transection and 100% haemostasis in hepatic injury models in heparinised pigs treated with chitosan-based agents. While a systematic review by M. Welch et al. [40] encompassing 17 prehospital studies found no statistically significant differences in the overall efficacy between haemostatic agent types, data from more recent studies (2023–2024) clearly differentiate chitosan-based agents in the most severe coagulopathic models. Collectively, this body of evidence provides strong justification for replacing kaolin-based dressings with chitosan-based agents as the standard first-line option for topical haemorrhage control in tactical medicine.

Nevertheless, the superiority of chitosan-based dressings in coagulopathic haemorrhage should be balanced against the current limitations of the safety evidence. Most studies focus on immediate haemostasis, survival to evacuation, blood loss, and short-term complications, whereas long-term immunogenicity, local tissue response to residual chitin or chitosan fragments, and delayed infection rates remain insufficiently characterised. For this reason, the present algorithm recommends chitosan-based dressings as first-line agents for severe compressible and junctional bleeding, but also recognises the need for further prospective follow-up studies assessing wound healing, infection, biodegradation, and immune response after field application.

For deep, narrow wound channels and non-compressible anatomical regions, the algorithm prioritises the use of specialised devices. W. Wu et al. [41], using a realistic *Tactical Combat Casualty Care* (TCCC) model of junctional haemorrhage, demonstrated that a modified chain-based sponge

dressing achieved significantly faster haemostasis, reduced the total blood loss, and denser wound channel packing compared with the standard gauze, with more favourable vital signs during follow-up. These findings were corroborated by W. Yang et al. [42] in a groin gunshot wound model, in which, the chain-based sponge achieved 100% primary haemostasis with a mean application time of 38.75 seconds and a survival time of 120 minutes, compared with 62.25 minutes for the standard gauze ($p<0.05$). Similarly, N. Ali-Mohamad et al. [43] reported 90–100% survival using a self-expanding gauze combined with low-dose thrombin and systemic tranexamic acid, with the total blood loss below 200 ml. In a 72-hour prolonged field care model, G. A. Pratt et al. [44] found that XStat was superior to Combat Gauze in terms of the speed of application and the volume of blood absorption, although the final haemostasis and the overall survival were equivalent between the two agents. In the most extreme hemicorporectomy model, R. B. Schwartz et al. [45] demonstrated a 100% immediate haemostasis and a 90% three-hour survival with the Abdominal Aortic and Junctional Tourniquet, compared with 0% survival for Combat Gauze, with a blood loss of 0.3 L versus 2.1 L, respectively. Collectively, these findings strongly support the prioritisation of volumetric devices and junctional tourniquets for haemorrhage control in anatomical regions inaccessible to the conventional tamponade.

Fibrin-, thrombin-, gelatin-, and oxidised-cellulose-based agents, including *Surgicel Nu-Knit* and *Floseal*, were not included in the main algorithm because they are primarily surgical haemostatic adjuncts used under direct visualisation in controlled operative settings. The proposed algorithm focuses on prehospital tactical haemorrhage control, where rapid wound packing, minimal equipment requirements, limited visibility, and prolonged evacuation are decisive. Therefore, these agents are acknowledged as relevant hospital-based comparators but not as direct replacements for TCCC-oriented dressings and devices.

For wounds in which reapproximation of wound edges is feasible, particularly in the head, neck, and scalp, the algorithm recommends the use of the iTClamp device. This recommendation is supported by the findings of S. M. Stuart et al. [46], who demonstrated that iTClamp achieved primary haemostasis 75% faster than the standard tamponade, irrespective of adjunctive haemostatic agents, and maintained a 100% success rate after 60 minutes of observation. Therefore, iTClamp should be considered a specialised option for anatomically suitable wounds where rapid mechanical closure can create a temporary tamponade and free the medic's hands for concurrent interventions.

The stability of haemostatic dressings during patient movement and prolonged evacuation represents a critical determinant of success in prolonged field care. G. D. Landers et al. [47], in a porcine model incorporating simulated limb movement, reported recurrent bleeding rates of 25–58% at 30 minutes after tamponade and 0–42% at 270 minutes, depending on the type of dressing used. These findings underscore the substantial challenges associated with all gauze-based haemostatic agents under real-world evacuation conditions and highlight the necessity for regular wound reassessment. Accordingly, the proposed differentiated algorithm explicitly states that, at the earliest suspicion of recurrent bleeding or prior to the initiation of transport, the dressing should be immediately replaced with a new one – preferably of a different type – or converted to a specialised device such as XStat or iTClamp, which does not require continuous pressure and remains stable during movement. This strategy minimises the risk of sudden catastrophic haemorrhage during evacuation and enhances the survival prospects in austere and resource-limited environments.

Synergy with tranexamic acid (TXA) represents a key component of contemporary strategies for controlling massive haemorrhage in tactical medicine, as this antifibrinolytic agent inhibits excessive plasminogen activation and thereby prevents premature clot degradation under conditions of hyperfibrinolysis typical of severe trauma. The apparent variation in reported TXA effects reflects differences in the study design, outcome definition, timing of administration, and patient severity.

In the present review, a 10–20% reduction in death from bleeding is used as the conservative overall estimate for early TXA administration within three hours of injury. Higher estimates reported in combat anaesthesiology and damage-control resuscitation literature, including the 25% survival increase and broader 20–40% mortality reduction ranges, are interpreted as context-specific findings related mainly to casualties with haemorrhagic shock, severe coagulopathy, or massive transfusion requirements [48,49]. Therefore, these higher figures are not presented as the general effect size for all trauma patients but as evidence that TXA may provide greater benefit in selected high-risk subgroups. Consequently, early TXA administration should be regarded as an integral element of any modern algorithm for external haemorrhage control, irrespective of the local haemostatic agent employed.

The suggestion to give chitosan-based agents the priority should also be considered in light of practical implementation limitations. Haemostatic efficacy alone cannot justify the worldwide replacement of kaolin-based dressings, despite the reviewed experimental and registry-based evidence supporting their superior performance in coagulopathic haemorrhage. Prior to protocol-wide implementation, factors such as procurement costs, availability in military and civilian supply chains, shelf-life stability under high temperature and humidity, storage requirements, replacement cycles, and the expense of retraining medics must be taken into account. As a result, the suggested algorithm does not suggest that kaolin-based dressings should be immediately replaced everywhere. Instead, it advocates for a phased and context-sensitive approach wherein kaolin-based dressings may still be appropriate in situations where implementation is limited by cost, supply continuity, or training capacity, while chitosan-based agents are prioritized for junctional wounds, severe coagulopathy, massive bleeding, and prolonged evacuation. Cost-effectiveness analysis, procurement modelling, shelf-life comparison, and supply-chain resilience evaluation should all be included in future field research.

Collectively, all 15 studies published between 2019 and 2024 consistently indicate the same hierarchy of effectiveness: new-generation chitosan dressings represent the primary choice for compressible and junctional wounds; specialised devices (XStat, iTClamp, AAJT, chain-based sponge systems) are indicated for deep wound channels and injuries amenable to edge reapproximation; and kaolin-based dressings serve as alternatives only in the absence of chitosan-based agents. The differentiated algorithm proposed in this study fully integrates this body of evidence, minimises reliance on residual coagulation capacity, and optimises the sequence of interventions according to anatomical localisation, the physiological condition of the casualty, and the phase of tactical care. As such, it is suitable for immediate incorporation into the 2025–2026 TCCC/TECC recommendations and has the potential to substantially reduce preventable mortality from external haemorrhage in modern conflicts characterised by prolonged evacuation times.

Several limitations should be considered when interpreting the findings. First, the review was based on heterogeneous evidence, including guideline documents, retrospective registries, clinical cohorts, and animal models, which limits direct comparability between the presently covered studies. Second, the numerical indicators were not generated through pooled meta-analysis; therefore, survival rates, blood loss values, and mortality reductions should be interpreted according to their original study context. Third, many data on chitosan-based products derive from experimental or short-term prehospital evidence, while long-term immunogenicity, wound infection, biodegradation, cost, training requirements, and supply-chain feasibility remain insufficiently studied. Finally, the proposed differentiated algorithm requires prospective field validation before it can be adopted as a universal protocol.

Conclusions

A systematic review and semi-quantitative comparative analysis of contemporary methods for controlling external bleeding in tactical medicine (2015–2025) enabled the establishment of a clear hierarchy of effectiveness based on the criterion of survival to evacuation under conditions of trauma-induced coagulopathy. New-generation chitosan haemostatic dressings (ChitoSAM 100, Celox Rapid) demonstrated the highest survival rates (86–100%) and the lowest blood loss (112–545 ml), attributable to their mucoadhesive mechanism of action, which is entirely independent of the residual coagulation system function. Kaolin-based dressings (QuikClot Combat Gauze) were inferior in these parameters, with the survival of 86% and the blood loss ranging from 260 to 1,021 ml. Specialised devices, including XStat and iTClamp, achieved 100% stable haemostasis in deep, narrow wound channels and in areas amenable to edge reapproximation, while significantly reducing the application time and eliminating the need for sustained external pressure. Early administration of tranexamic acid (2 g intravenously within <3 hours) provided an additional 10–20% survival benefit through inhibition of hyperfibrinolysis. The synthesised differentiated haemorrhage control algorithm – comprising extremity tourniquet application, chitosan dressing (ChitoSAM 100 or Celox Rapid) for all compressible and junctional wounds, XStat for deep narrow channels or iTClamp for wounds with edge reapproximation, and the earliest possible administration of tranexamic acid – minimises dependence on the casualty's physiological condition, optimises intervention timing across the phases of care, and has the potential to reduce preventable mortality by 20–30% compared with universal, non-differentiated approaches.

The practical significance of this work lies in the readiness of the proposed algorithm for immediate incorporation into the TCCC/TECC 2025–2026 recommendations as an updated standard for prehospital external haemorrhage control. It is recommended to prioritise chitosan-based dressings as first-line agents for high-risk compressible and junctional haemorrhage, particularly in casualties with suspected coagulopathy or delayed evacuation, while retaining kaolin-based dressings as acceptable alternatives where the procurement cost, shelf life, supply-chain availability, or training capacity limit immediate replacement. Study limitations include the predominance of data derived from porcine models and retrospective registry analyses, the absence of large randomised clinical trials in real combat settings after 2022, and the limited number of studies addressing prolonged evacuation exceeding 24 hours. Future research should focus on prospective field validation of the proposed algorithm in contemporary conflicts, assessment of logistical considerations (shelf life and cost), and the development of hybrid devices combining the volumetric effect of XStat with the complete biodegradability of chitosan-based materials.

Conflicts of interest

The author declares no conflicts of interest.

List of abbreviations

AAJT – Abdominal-Aortic and Junctional Tourniquet; CAT – Combat Application Tourniquet; CoTCCC – Committee on Tactical Combat Casualty Care; CRoC – Combat Ready Clamp; IDF – Israel Defense Forces; iTClamp – Innovative Trauma Care Clamp; JETT – Junctional Emergency Treatment Tool; JTTR – Joint Theater Trauma Registry; LMWH – Low-Molecular-Weight Heparin; MARCH – Massive Haemorrhage, Airway, Respiration, Circulation, Hypothermia; NISS – New Injury Severity Score; BCC – Circulating Blood Volume; SJT – SAM Junctional Tourniquet; SOFTT-Wide – Special Operations Forces Tactical Tourniquet Wide; TECC – Tactical Emergency Casualty Care; TCCC – Tactical Combat Casualty Care; TXA – Tranexamic Acid; VTE – Venous Thromboembolism; OR – Odds Ratio; CI – Confidence Interval.

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