



Strategies for the Effective Management of Bleeding in Trauma Patients: A Narrative Review

ABSTRACT

Injuries are the leading cause of death worldwide among individuals aged 1-46. Effective management strategies like preventing dilutional coagulopathy, enhancing clotting, and early bleeding cessation can reduce trauma-related mortality. A restrictive transfusion strategy is advised for trauma patients, aiming to maintain hemoglobin levels between 7-9 g/dL. Administering tranexamic acid within 3 hours of trauma is suggested for those with active bleeding or at high risk of bleeding. For patients suspected of massive bleeding in the emergency department, a platelet-to-plasma-to-pRBC ratio of 1:1:1 or 1:1:2 is recommended by guidelines. In conclusion, traumatic coagulopathy requires immediate medical intervention and personalized treatment approaches to counteract its severe, potentially fatal consequences.

Keywords: Blood coagulation, fibrinogen, focused assessment with sonography for trauma, multiple trauma

Injuries stand as the predominant cause of death worldwide for individuals between the ages of 1-46 (1). In 2013, injuries claimed the lives of 4.8 million people. The leading causes of such deaths were traffic accidents, suicides, falls, and interpersonal violence, listed in descending order (2). While most trauma-related fatalities transpire in the intensive care unit, 33.6% occur in the emergency department and 12.9% in the operating room. The primary causes of these trauma-induced deaths are detailed in Table 1. Exsanguination ranks as the second highest cause of death following traumatic brain injury and most often results from penetrating trauma, causing early-stage fatalities either pre-hospital or within the emergency department (3). Early intervention measures such as preventing dilutional coagulopathy, enhancing clotting, and halting bleeding can significantly reduce the incidence of trauma-related deaths (4).

In this review, our objective is to collate insights on bleeding management in trauma patients. We undertook a narrative review by sourcing and scrutinizing research articles from PubMed. Our search parameters encompassed key terms like trauma management, bleeding, hemorrhage, coagulopathy, bleeding management, and traumatic coagulopathy. We limited our scope to studies published exclusively in English and narrowed our database searches to articles released between 1993 and August 2023. Notably, we refrained from evaluating the risk of bias or the evidence quality given the narrative nature of this review, and no statistical analyses were performed.

1. Initial Resuscitation, Prevention of Further Bleeding, and Prompt Transportation of Trauma Patients to the Suitable Trauma Center

In 2014, the American College of Surgeons delineated criteria for trauma centers, segmenting them into various levels. Level 1 centers serve as the linchpin in trauma care, furnished with abundant resources and a proficient team primed to address every facet of trauma care, from prevention to rehabilitation. Level 2 centers largely parallel Level 1 in their clinical capacities but might be constrained when managing particular specialized traumas. Level 3 trauma centers are adept at executing initial assessments, resuscitation, and emergency surgeries. However, they can also transfer patients to higher-tier centers when

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Table 1. Primary Causes of Traumatic Deaths

1. Traumatic brain injury
2. Exsanguination
3. Physiologic collapse
4. Airway
5. Pre-trauma medical event
6. Sudden unexpected deaths

Table 2. Ventilation Strategies in Trauma Patients

1. Avoidance of hypoxemia / hyperoxemia
2. Normoventilation
3. PaCO ₂ = 35-40 mm Hg
4. Low tidal volume ventilation (6 mL/kg)

warranted. Conversely, Level 4 centers prioritize advanced life support, subsequently referring patients to more equipped centers for comprehensive care (5). For optimal trauma management, it's paramount to swiftly steer patients to the fitting trauma center. This decision hinges on factors like their vital signs, injury mechanisms, and the proficiencies of accessible hospitals (6). A meta-analysis from 2021 underscored that a robust trauma system, especially for critically injured patients, correlates with diminished mortality rates, especially when juxtaposed with Level 3 and 4 trauma centers (7).

Local Bleeding Management in Pre-hospital Settings

Open injuries to the extremities can be managed using techniques such as external digital compression or pressure bandages, with or without the inclusion of topical hemostatics (6). In situations involving penetrating neck injuries that result in life-threatening hemorrhage, and where gauze packing and manual compression fall short in halting deep tissue bleeding, the deployment of a Foley catheter balloon tamponade can provide an effective, swift, and minimally invasive means to control the bleeding (8).

A tourniquet is another viable strategy for managing extremity bleeding. A 2019 meta-analysis demonstrated that the employment of tourniquets diminishes the occurrence of hemorrhagic shock, bolsters survival rates, and reduces the demand for blood transfusions. Furthermore, when tourniquets remain in place for durations under 2 hours, the associated risks – including nerve palsy, amputation, compartment syndrome, and wound infections – are seldom encountered (9).

Airway Protection

Ensuring normoventilation and warding off hypoxia are pivotal in the management of trauma patients. When the Glasgow Coma Scale score is below 8 or in the presence of airway obstruction, hemorrhagic shock, hypoventilation, and hypoxemia, interventions such as endotracheal intubation or the use of supraglottic airway devices are warranted. It's crucial to note that hyperventilation-induced hypocapnia might result in vasoconstriction. This, in turn, can diminish cerebral blood flow, posing the risk of secondary brain injury. The specifics of ventilation in trauma patients are detailed in Table 2 (6).

Table 3. FAST-PLUS Protocole

1. Morrison's pouch with curvilinear probe
2. Pericardium in subxiphoid window
3. Splenorenal and perisplenic spaces
4. Suprapubic scan for rectovesical, rectouterine, vesicouterine pouch
5. Anterior thoracic window for pneumothorax
6. Transverse scan of pubic symphysis for symphyseal widening

2- Detection of Bleeding

In research focused on predicting traumatic hemorrhage, various parameters have been identified as significant indicators. These include systolic blood pressure, the mechanism of trauma (e.g., blunt, penetrating, amputation, crush injury), heart rate, age, hemoglobin level, lactate level, a Shock Index exceeding 0.8, and a pulse pressure less than 30 mmHg (6). A 2020 retrospective study advocated for a procedural shift: when indicators of bleeding, such as a systolic blood pressure under 90 mmHg or the onset of penetrating chest trauma, are present, it's recommended to circumvent the emergency department. Instead, patients should be directly routed to the operating room for initial evaluation and resuscitation. Adopting this «direct to operating room» strategy is believed to potentially curtail mortality rates (10).

Within the confines of the emergency department, extended focused abdominal sonography for trauma (e-FAST) is employed to spot bleeding and pinpoint conditions like tamponade, hemo-pneumothorax, and intraperitoneal fluid. Complementing e-FAST, the FAST-PLUS protocol has been developed, which incorporates scanning the transverse symphysis for the pubis open book fracture, as detailed in Table 3 (11). Nevertheless, Computed Tomography retains its position as the definitive method for determining the origin of hemorrhage in trauma cases (6).

Initial hemoglobin (Hg) and lactate measurements procured in the emergency department furnish insights into active bleeding. A diminished initial Hg suggests the patient is grappling with hemorrhagic shock. However, a standard initial reading does not necessarily negate the possibility of hemorrhage (6). Research from 2013 unveiled that a pronounced decrease of 6 units in Hct levels is a harbinger of hemorrhage in trauma patients undergoing fluid treatment (12). The tissue hypoperfusion stemming from bleeding culminates in hypoxia and anaerobic respiration. This cascade heightens lactate concentrations, prompting metabolic acidosis and subsequently elevating the base deficit. Empirical data underscores the correlation between elevated lactate and base deficit levels in trauma victims and a heightened mortality rate (13).

3- Management of Blood Pressure, Volume, and Temperature in Trauma Patients

Details regarding the management of blood pressure, volume, and temperature in trauma patients are provided in Table 4.

Target Blood Pressure

European Guidelines for managing major bleeding advocate for a mean arterial pressure (MAP) of 50-60 mmHg in patients without brain trauma. For those with brain injuries, a MAP of 80 mmHg or more is suggested (6). A systematic review from 2018 assessed

Table 4. Summarizing of Blood Pressure, Volume and Temperature Management in Trauma Patients

1. MAP should be maintained at 50-60 mm Hg. >80 mm Hg in patient with traumatic brain injury
2. In fluid resuscitation, the primary choice should be balanced crystalloids and saline.
3. If the target MAP cannot be achieved, norepinephrine should be administered.
4. Targeted hemoglobin level should be maintained between 7-9 g/dL
5. Maintaining normothermia with core temperature 36-37 C

MAP: mean arterial pressure

patients with traumatic hemorrhagic shock, comparing those under a restricted volume replacement strategy, which results in permissive hypotension, to those under aggressive fluid resuscitation commonly employed in conventional resuscitation methods. The findings revealed that the group subjected to permissive hypotension exhibited lesser blood loss, diminished requirements for blood transfusions, and better survival outcomes (14).

A 2012 review, which incorporated randomized controlled trials from the Cochrane database, indicated that to attain the desired blood pressure, using colloids did not furnish a mortality advantage over crystalloids in critically afflicted patients (15). It was also ascertained that colloids weakened clot robustness and interfered with the coagulation process by extending the clot formation duration (16). A meta-analysis that juxtaposed the clinical outcomes of patients administered balanced crystalloids (like Ringer's lactate solution and Plasma-Lyte) versus those given normal saline, discerned that those treated with balanced crystalloids exhibited lower mortality rates and reduced incidences of acute kidney injury onset. These patients also showed lesser advancement towards renal replacement therapy and decreased occurrences of hyperchloremic metabolic acidosis (17).

Considering the aforementioned studies, the 2023 European Guidelines for the Management of Major Bleeding endorse the preferential application of balanced crystalloids in fluid resuscitation strategies. When saline is utilized, its use should not surpass 1-1.5 liters. Hypotonic solutions such as Ringer's lactate ought to be eschewed in patients with head injuries, given the potential risks of inducing cerebral edema. When the targeted MAP remains unattained via a restrictive volume replacement methodology, administering norepinephrine might be considered to aim for optimal tissue perfusion (6).

Erythrocyte Transfusion

In a 2016 randomized controlled study involving 200 trauma patients, groups with hemoglobin threshold values of 7 and 10 g/dL were analyzed. Some subjects received erythropoietin and erythrocyte transfusion. Findings revealed that those in the 10 g/dL threshold group encountered more complications (18). As such, for trauma patients, it's recommended to adopt a restrictive transfusion approach, aiming to keep hemoglobin levels within the 7-9 g/dL range (6).

Intraoperative cell salvage (ICS) stands as a strategy for erythrocyte transfusion where the patient's own lost blood is gathered, treated, and then reinfused during the operation. A 2010 retrospec-

tive study evaluated trauma patients who underwent emergency surgical procedures, comparing those who utilized ICS to those receiving conventional care. The outcomes demonstrated that the ICS group necessitated fewer packed red blood cell transfusions and this approach was more economically efficient (19). Based on a Grade 2B recommendation, ICS is advocated for trauma patients experiencing intense bleeding, particularly in the abdominal, thoracic, and pelvic areas (6).

Temperature Management

Hypothermia is characterized by a core body temperature dropping below 35°C. A 2020 meta-analysis compared the clinical outcomes of trauma patients in states of normothermia and hypothermia. The study deduced that trauma patients with hypothermia showed a significantly higher mortality rate (20). Hypothermia escalates oxygen usage, induces cardiac depression, which in turn leads to hypotension, impairs platelet function, and hinders the coagulation process by obstructing enzymatic actions. Especially, the administration of unheated intravenous fluids to trauma patients can notably heighten their risk of hypothermia. To prevent hypothermia in these patients, potential measures encompass utilizing blankets, elevating room temperature, and delivering warmed IV fluids (21).

5- Prompt Management of Bleeding

Damage Control Surgery

Damage control surgery is a strategic intervention utilized for severely injured patients who might not tolerate a full surgical procedure due to limited physiological reserves. The primary goals are halting bleeding and averting abdominal contamination. The process encompasses five stages:

1. Identification: Determining suitable patients for the procedure is crucial. Those presenting the lethal triad of hypothermia, coagulopathy, and acidosis—especially when manifesting hypotension and tachycardia alongside life-threatening bleeding and penetrating injuries—are prime candidates.
2. Initial Surgery: During this phase, active bleeding is curtailed, and contamination is minimized.
3. Intensive Care Resuscitation: Following the initial intervention, patients are stabilized and resuscitated in the intensive care unit.
4. Definitive Surgery: Once the patient is physiologically stabilized, they undergo a comprehensive surgical procedure to address the injuries definitively.
5. Abdominal Reconstruction: The final phase involves reconstructing the abdominal wall (22).

A retrospective study from 1993 investigated the outcomes of definitive laparotomy versus damage control surgery in 46 patients with penetrating abdominal wounds. The results indicated that, particularly among those with major vascular and multiple visceral injuries, damage control surgery significantly diminished mortality rates (23).

REBOA (Resuscitative Endovascular Balloon Occlusion of Aorta)

REBOA offers an advanced technique to arrest severe bleeding resulting from non-compressible injuries within the thorax or abdomen. It is particularly beneficial for cases involving pronounced pelvic fractures, traumatic cardiac arrests due to bleeding, profound

hemorrhagic shocks from abdominal trauma, and penetrating injuries to the chest. By inflating a balloon either in the descending or abdominal aorta, blood flow to the lower regions is temporarily obstructed. REBOA stands as a pivotal bridge between hemodynamic collapse and attaining a definitive control over bleeding in select patients (24).

6- Management of Coagulopathy

Antifibrinolytic Agents

Antifibrinolytics play a critical role in the prevention and management of trauma-induced coagulopathy. One of the prominent antifibrinolytic agents, tranexamic acid (TXA), has demonstrated efficacy in reducing mortality in trauma patients. The CRASH-2 trial, involving a large cohort of 20,211 trauma patients, revealed the beneficial impacts of TXA in reducing both bleeding-related and overall mortality rates (25). The European Guidelines for the Management of Major Bleeding strongly advocate (Grade 1a recommendation) the initiation of TXA within the first three hours post-trauma in patients exhibiting ongoing bleeding or those at elevated risk for bleeding. Notably, these guidelines recommend not delaying TXA administration while awaiting viscoelastic test outcomes (6).

Initial Management of Massive Bleeding

Addressing massive bleeding promptly is paramount in trauma patients. The 2023 European Guidelines for the Management of Major Bleeding suggests using a transfusion ratio of platelet-to-plasma-to-packed red blood cells (pRBC) of either 1:1:1 or 1:1:2 for patients presenting with suspected massive bleeding in the emergency setting (Grade 1C recommendation) (6).

In the PROPPR Trial conducted in 2015, researchers explored the outcomes of these two massive transfusion protocols in a cohort of 680 severely traumatized patients. This study concluded that there was no discernible difference in mortality rates at both 24-hour and 30-day endpoints between the two protocols (26). Reinforcing the efficacy of these protocols, a 2020 review found that the early employment of 1:1:1 or 1:1:2 transfusion ratios in the emergency department led to marked reductions in mortality, organ failure, and related complications (27).

In essence, the prompt management of coagulopathy in trauma patients is essential for optimizing outcomes. Established guidelines and research-backed interventions, including antifibrinolytic agents and transfusion protocols, serve as guiding principles in achieving this objective.

Further Management of Coagulation

Properly managing coagulopathy in trauma patients is of paramount importance. When faced with an increased prothrombin time (PT) or activated partial thromboplastin time (aPTT), or abnormalities are detected in viscoelastic tests (like VEM, TEG/ROTEM), there is a significant indication for coagulation support. The recommended interventions, backed by a Grade 1C recommendation, include administering fresh frozen plasma (FFP) or specific coagulation factor concentrates (6).

Fibrinogen

A crucial protein in the coagulation cascade, fibrinogen levels can decrease due to several reasons, including hemorrhage, hemodilution, hypothermia, and heightened fibrinolytic activity seen in acidosis (28). A 2012 cohort study with 517 trauma patients found

a direct correlation between diminished fibrinogen levels upon hospital admission and adverse patient outcomes (29). To counteract this, if viscoelastic tests indicate a fibrinogen deficit or plasma Clauss fibrinogen level drops below 1.5g/L, the immediate course of action involves supplementing with either 3-4 grams of fibrinogen concentrate or 15-20 units of cryoprecipitate (6).

7- Management of Anticoagulant Agents

Anticoagulant management in trauma patients is a delicate balance. For those on oral Vitamin K antagonists who are bleeding:

The best approach, according to a Grade 1A recommendation, is the simultaneous administration of both Vitamin K and Prothrombin Complex Concentrates (PCC).

Specifically, an IV infusion of Vitamin K at a dose of 5-10 mg should be given slowly.

As the onset of Vitamin K action requires at least 4 hours, PCC is employed for a swift reduction of INR. The exact dose is contingent on the patient's INR: 25 IU/kg for INR between 2-4, 35 IU/kg for INR between 4-6, and 50 IU/kg for INR above 6.

For patients on dabigatran, a direct thrombin inhibitor, and faced with critical bleeding, the immediate solution is to infuse 5 grams of idarucizumab intravenously. On the other hand, for those on factor Xa inhibitors like apixaban or rivaroxaban, particularly in traumatic brain injury scenarios, the advised intervention is to administer Andexanet alfa. In cases where this is not available, 25-50 U/kg of PCC can be used as an alternative (6).

This comprehensive management strategy ensures optimal coagulopathy management in trauma patients while taking into account the different anticoagulants they might be on. Proper application of these guidelines helps optimize patient outcomes and prevent further complications.

CONCLUSION

The multifaceted challenges of traumatic coagulopathy in emergency medicine require not only keen insight but also decisive action. The cascade of events leading to traumatic coagulopathy, from hemodilution and hypothermia to acidosis and elevated fibrinolytic activity, can be a precursor to grave bleeding complications. The urgency of addressing this is paramount, as each passing moment can influence a patient's trajectory to recovery or exacerbate complications.

Modern advancements, such as point-of-care viscoelastic tests, have made it feasible to quickly discern coagulation abnormalities. This allows for timely interventions, ranging from administering crucial coagulation factors like fibrinogen to deploying PCC. Furthermore, the advent of specific reversal agents, be it idarucizumab for those on dabigatran or Andexanet alfa for patients on factor Xa inhibitors, adds another layer of precision to the management toolkit.

In the dynamic, high-pressure realm of the emergency department, where every second counts, the astute diagnosis and effective management of traumatic coagulopathy can indeed tip the scales, transforming a dire situation into a manageable one. Health professionals equipped with this knowledge and the requisite skills stand at the frontline, ready to make life-saving decisions for those in their care.

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REFERENCES

- Rhee P, Joseph B, Pandit V, Aziz H, Vercruyssen G, Kulvatunyou N, et al. Increasing trauma deaths in the United States. *Ann Surg* 2014;260(1):13-21. [\[CrossRef\]](#)
- Haagsma JA, Graetz N, Bolliger I, Naghavi M, Higashi H, Mullany EC, et al. The global burden of injury: incidence, mortality, disability-adjusted life years and time trends from the Global Burden of Disease study 2013. *Inj Prev* 2016;22(1):3-18. [\[CrossRef\]](#)
- Callcut RA, Kornblith LZ, Conroy AS, Robles AJ, Meizoso JP, Namias N, et al; Western Trauma Association Multicenter Study Group. The why and how our trauma patients die: a prospective Multicenter Western Trauma Association study. *J Trauma Acute Care Surg* 2019;86(5):864-70. [\[CrossRef\]](#)
- Cole E, Weaver A, Gall L, West A, Nevin D, Tallach R, et al. A decade of damage control resuscitation: new transfusion practice, new survivors, new directions. *Ann Surg* 2021;273(6):1215-20. [\[CrossRef\]](#)
- Committee On Trauma. Resources for Optimal Care of the Injured Patient. In: Rotondo MF, Cribari C, Smith RS, editors. Resources for Optimal Care of the Injured Patient. Chicago: American College of Surgeons; 2014.
- Rossaint R, Afshari A, Bouillon B, Cerny V, Cimpoesu D, Curry N, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. *Crit Care* 2023;27(1):80. [\[CrossRef\]](#)
- Alharbi RJ, Lewis V, Shrestha S, Miller C. Effectiveness of trauma care systems at different stages of development in reducing mortality: a systematic review and meta-analysis protocol. *BMJ Open* 2021;11(6):e047439. [\[CrossRef\]](#)
- Jose A, Arya S, Nagori SA, Thukral H. Management of life-threatening hemorrhage from maxillofacial firearm injuries using Foley Catheter Balloon Tamponade. *Craniofac Trauma Reconstr* 2019;12(4):301-4. [\[CrossRef\]](#)
- Eilertsen KA, Winberg M, Jeppesen E, Hval G, Wisborg T. Prehospital tourniquets in civilians: a systematic review. *Prehosp Disaster Med* 2021;36(1):86-94. [\[CrossRef\]](#)
- Johnson A, Rott M, Kuchler A, Williams E, Cole F, Ramzy A, et al. Direct to operating room trauma resuscitation: optimizing patient selection and time-critical outcomes when minutes count. *J Trauma Acute Care Surg* 2020;89(1):160-6. [\[CrossRef\]](#)
- Ianniello S, Conte P, Di Serafino M, Miele V, Trinci M, Vallone G, et al. Diagnostic accuracy of pubic symphysis ultrasound in the detection of unstable pelvis in polytrauma patients during e-FAST: the value of FAST-PLUS protocol. A preliminary experience. *J Ultrasound* 2021;24(4):423-8. [\[CrossRef\]](#)
- Thorson CM, Ryan ML, Van Haren RM, Pereira R, Olloqui J, Otero CA, et al. Change in hematocrit during trauma assessment predicts bleeding even with ongoing fluid resuscitation. *Am Surg* 2013;79(4):398-406. [\[CrossRef\]](#)
- Husain FA, Martin MJ, Mullenix PS, Steele SR, Elliott DC. Serum lactate and base deficit as predictors of mortality and morbidity. *Am J Surg* 2003;185(5):485-91. [\[CrossRef\]](#)
- Tran A, Yates J, Lau A, Lampron J, Matar M. Permissive hypotension versus conventional resuscitation strategies in adult trauma patients with hemorrhagic shock: a systematic review and meta-analysis of randomized controlled trials. *J Trauma Acute Care Surg* 2018;84(5):802-8. [\[CrossRef\]](#)
- Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev* 2013;(2):CD000567. [\[CrossRef\]](#)
- Schramko A, Suojäranta-Ylinen R, Kuitunen A, Raivio P, Kukkonen S, Niemi T. Hydroxyethylstarch and gelatin solutions impair blood coagulation after cardiac surgery: a prospective randomized trial. *Br J Anaesth* 2010;104(6):691-7. [\[CrossRef\]](#)
- Hammond DA, Lam SW, Rech MA, Smith MN, Westrick J, Trivedi AP, et al. Balanced crystalloids versus saline in critically ill adults: a systematic review and meta-analysis. *Ann Pharmacother* 2020;54(1):5-13. [\[CrossRef\]](#)
- Robertson CS, Hannay HJ, Yamal JM, Gopinath S, Goodman JC, Tilley BC, et al; Epo Severe TBI Trial Investigators. Effect of erythropoietin and transfusion threshold on neurological recovery after traumatic brain injury: a randomized clinical trial. *JAMA*. 2014;312(1):36-47. [\[CrossRef\]](#)
- Brown CV, Foulkrod KH, Sadler HT, Richards EK, Biggan DP, Cyszcz C, et al. Autologous blood transfusion during emergency trauma operations. *Arch Surg* 2010;145(7):690-4. [\[CrossRef\]](#)
- Rösli D, Schnüriger B, Candinas D, Haltmeier T. The impact of accidental hypothermia on mortality in trauma patients overall and patients with traumatic brain injury specifically: a systematic review and meta-analysis. *World J Surg* 2020;44(12):4106-17. [\[CrossRef\]](#)
- Tsuei BJ, Kearney PA. Hypothermia in the trauma patient. *Injury* 2004;35(1):7-15. [\[CrossRef\]](#)
- Germanos S, Gourgiotis S, Villias C, Bertucci M, Dimopoulos N, Salemis N. Damage control surgery in the abdomen: an approach for the management of severe injured patients. *Int J Surg* 2008;6(3):246-52. [\[CrossRef\]](#)
- Rotondo MF, Schwab CW, McGonigal MD, Phillips GR 3rd, Fruchterman TM, Kauder DR, et al. Damage control: an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993;35(3):375-83. [\[CrossRef\]](#)
- Castellini G, Gianola S, Biffi A, Porcu G, Fabbri A, Ruggieri MP, et al; Italian National Institute of Health guideline working group on Major Trauma. Resuscitative endovascular balloon occlusion of the aorta (REBOA) in patients with major trauma and uncontrolled haemorrhagic shock: a systematic review with meta-analysis. *World J Emerg Surg* 2021;16(1):41. [\[CrossRef\]](#)
- Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, et al; CRASH-2 trial collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet* 2010;376(9734):23-32. [\[CrossRef\]](#)
- Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, et al; PROPPR Study Group. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA* 2015;313(5):471-82. [\[CrossRef\]](#)
- Meneses E, Boneva D, McKenney M, Elkbuli A. Massive transfusion protocol in adult trauma population. *Am J Emerg Med* 2020;38(12):2661-6. [\[CrossRef\]](#)
- Moore EE, Moore HB, Kornblith LZ, Neal MD, Hoffman M, Mutch NJ, et al. Trauma-induced coagulopathy. *Nat Rev Dis Primers* 2021;7(1):30. [\[CrossRef\]](#)
- Rourke C, Curry N, Khan S, Taylor R, Raza I, Davenport R, et al. Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes. *J Thromb Haemost* 2012;10(7):1342-51. [\[CrossRef\]](#)