

## **Navigating Complex Coagulopathies: A PBM Approach to Trauma and Major Surgery**

Mihai Ștefan<sup>†</sup>, Afak Nsiri and Tae Yop Kim

<sup>†</sup>Correspondence email: mihai.stefan@umfcd.ro

### **Abstract**

Coagulopathy is a major determinant of morbidity and mortality in trauma and major surgery, driven by interacting effects of tissue injury, haemorrhagic shock, inflammation, haemodilution, and iatrogenic factors, and it is worsened by hypothermia, acidosis, and hypocalcaemia. Across trauma, cardiac surgery, and obstetric haemorrhage, shared mechanisms include endothelial dysfunction, platelet impairment, early fibrinogen depletion, impaired thrombin generation, and dysregulated fibrinolysis, creating dynamic phenotypes that fixed-ratio transfusion or delayed laboratory testing may not adequately address. A patient blood management (PBM) approach frames haemostatic failure as time-critical and multifactorial, prioritising early recognition, physiological stabilisation, and deficit-specific therapy. Conventional tests remain useful but are static and slow; viscoelastic testing can rapidly characterise clot formation, strength, and fibrinolysis when embedded in structured algorithms. PBM-guided treatment integrates early antifibrinolytics, fibrinogen replacement, selective factor concentrates, appropriate platelet therapy, and optimisation of temperature, pH, and calcium to reduce unnecessary allogeneic transfusion and improve outcomes.

**Key words:** trauma, coagulopathy, haemorrhage, patient blood management, major surgery

### **INTRODUCTION**

Coagulopathy is a major determinant of adverse outcomes in trauma and major surgery. Triggered by tissue injury, haemorrhagic shock, inflammation, haemodilution, hypothermia, pre-existing anticoagulation, and time-dependent physiological deterioration, dysregulated haemostasis rapidly amplifies bleeding and perpetuates systemic instability.<sup>1–3</sup> The clinical consequences are substantial: uncontrolled haemorrhage remains a leading cause of preventable death after trauma, while major surgical procedures frequently challenge even experienced teams with complex, evolving coagulation disturbances. At the same time, transfusion—long regarded as the default response to bleeding—has well-recognised limitations. Reliance on empirical or ratio-based transfusion strategies may fail to correct specific haemostatic defects, expose patients to avoidable risks, and contribute to significant resource strain. Modern perioperative and acute care therefore demands a shift from product-centred resuscitation toward personalised haemostatic management.

Patient blood management (PBM) provides a unifying framework for this shift. PBM aligns haemostatic care with broader goals of patient safety, physiological

stabilisation, and resource stewardship, because it integrates optimisation of red blood cell (RBC) mass, minimisation of blood loss, and targeted correction of coagulopathy.<sup>4</sup> Within this framework, the management of complex coagulopathies requires timely recognition of haemostatic abnormalities, rapid point-of-care assessment when available, and the use of therapies that address specific deficits rather than relying on nonselective transfusion.

This article explores how PBM principles can be applied to trauma and major surgery to improve bleeding management, enhance clinical decision-making, and support a more rational, outcome-driven approach to haemostasis. Through a synthesis of pathophysiology, diagnostic strategies, and therapeutic options, we propose a clinically pragmatic model for navigating coagulopathy across diverse settings.

### **UNDERSTANDING COMPLEX COAGULOPATHIES**

Severe trauma and tissue damage occur because of the combined effects of haemorrhagic shock, tissue injury, and elapsed time injury.<sup>5</sup> Trauma-induced coagulopathy (TIC) is a fatal clotting disorder in

#### **Mihai Ștefan**

Department of Anaesthesiology and Intensive Care, “Prof. C. C. Iliescu” Emergency Institute for Cardiovascular Diseases, Bucharest, Romania

“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

#### **Afak Nsiri**

Surgical Emergencies Intensive Care and Anaesthesia Department, CHU Ibn Rochd, Casablanca, Morocco

Faculty of Medicine and Pharmacy, University Hassan II, Casablanca, Morocco

#### **Tae Yop Kim**

Department of Anesthesiology and Pain Medicine, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Republic of Korea

Institution for Patient-centered Goal-directed Strategy, Konkuk University, Chungju, Republic of Korea

severe trauma characterised by widespread activation of endothelial cells with glycocalyx release, impaired platelet function, consumption of coagulation factors, dysregulated anticoagulation, and hyperfibrinolysis (Table 1).<sup>6</sup>

Trauma-induced coagulopathy represents a dynamic spectrum rather than a single entity. In the early phase, typically within the first hours after injury, hypoperfusion and tissue damage trigger endothelial dysfunction, activation of protein C pathways, platelet dysfunction, and hyperfibrinolysis, resulting in a hypocoagulable state with impaired clot formation.

As haemorrhage control is achieved and inflammation evolves, this phenotype may shift toward hypercoagulability, characterised by increased clot strength, fibrinolytic shutdown, and heightened thrombotic risk. Recognising this temporal evolution is essential to avoid both under- and overtreatment.<sup>7</sup>

During the early stage of active bleeding after trauma, viscoelastic assays show a hypocoagulable state without or with fibrinolysis.<sup>3</sup> Despite a normal platelet count, platelets are dysfunctional, and despite normal levels of coagulation factors, haemostasis is impaired. Coagulation factors are usually depleted because of systemic consumption, dilution, and degradation by the overproduction of various anticoagulation and fibrinolytic systems, mainly activated protein C and plasmin. In early TIC, the inability to form and sustain clots causes excessive bleeding and worsens shock. High levels of plasmin break down fibrin and fibrinogen, leading to hyperfibrinolysis.<sup>8</sup> Reduced thrombin formation causes the fibrin network to be loose and more susceptible to lysis, which further amplifies bleeding.<sup>6</sup> Intravascular volume resuscitation and blood transfusion dilute coagulation factors and induce iatrogenic resuscitation-induced coagulopathy in severely injured bleeding patients.

After achieving haemostasis, TIC shifts toward a more hypercoagulable state over minutes to hours. Inflammation and dysfunction of the endothelium and platelets may lead to thrombosis and organ dysfunction. Severe trauma triggers sympathoadrenal activation and

endotheliopathy, and extensive tissue and endothelial damage leads to increased loss of the endothelial glycocalyx and expression of tissue factor (TF), resulting in coagulation activation.<sup>9</sup>

As part of the inflammatory response to trauma, damaged tissues and activated immune cells, such as neutrophils, increase the release of damage-associated molecular patterns, potent proinflammatory mediators, and complement levels. These, in turn, trigger the cytokine release and further amplify and prolong the inflammatory response.<sup>10</sup> Platelets interact with circulating leukocytes to activate the immune response and stimulate leukocyte migration to the injury site. Activated neutrophils and macrophages promote platelet aggregation and thrombin formation.<sup>11</sup>

### SPECIAL CONSIDERATIONS: MAJOR SURGERY

Major surgery is frequently associated with complex disturbances of haemostasis resulting from the combined effects of surgical trauma, haemodilution, inflammation, hypoperfusion, and iatrogenic factors. Extensive tissue injury promotes activation of coagulation pathways through tissue factor exposure, while perioperative bleeding and fluid resuscitation dilute coagulation factors and platelets. At the same time, inflammatory responses, endothelial dysfunction, hypothermia, and metabolic derangements may impair platelet function and enzymatic coagulation reactions. The resulting haemostatic phenotype is often dynamic, evolving from early hypocoagulability with bleeding tendency to a later hypercoagulable state associated with thrombotic complications. These alterations are particularly relevant in major procedures such as cardiac, hepatic, trauma, vascular, and complex oncologic surgery, where large blood loss, prolonged operative time, and extensive tissue manipulation are common<sup>3</sup>. Understanding these mechanisms is essential to guide targeted haemostatic management within a patient blood management framework.

In cardiac surgery, cardiopulmonary bypass (CPB) generates a multifactorial, complex coagulopathy: CPB-induced haemodilution and surgical bleeding reduce coagulation factors and fibrinogen; TF tissue exposed to surgical trauma activates coagulation factors and platelets, increasing fibrinolysis; and contact activation of the

**Table 1** – Mechanisms and Phenotypes of Complex Coagulopathy across Clinical Settings

Clinical Context	Dominant Mechanisms	Typical Haemostatic Phenotype	Key Diagnostic Features	Clinical Implications
Early trauma (TIC)	Endotheliopathy, activated protein C, hyperfibrinolysis, platelet dysfunction	Hypocoagulable ± hyperfibrinolysis	Normal counts with poor clot formation; VET shows reduced clot strength and early lysis	Early TXA, fibrinogen replacement, physiology correction
Late trauma	Inflammation, endothelial activation	Hypercoagulable	Increased clot strength, fibrinolytic shutdown	Thrombosis risk, avoid overtreatment, think about anticoagulant
Cardiopulmonary bypass	Haemodilution, contact activation, platelet dysfunction, fibrinolysis	Mixed hypocoagulable state	Prolonged clotting time, reduced clot firmness	VET-guided fibrinogen, PCC, platelet transfusion, TXA, desmopressin
Iatrogenic/resuscitation-induced	Crystalloids, citrate, hypocalcaemia	Progressive hypocoagulability	Hypocalcaemia, dilutional patterns	Calcium replacement mandatory

Abbreviations: DIC, disseminate intravascular coagulopathy; PCC, prothrombin complex concentrate; TF, tissue factor; TIC, trauma-induced coagulopathy; TXA, tranexamic acid, VET, viscoelastic testing

haemostatic system depletes coagulation factors.<sup>12,13</sup> The volume and characteristics of priming fluid for CPB are also crucial to its impact on fibrinogen and platelet activity and coagulation performance.<sup>14,15</sup> In addition to surgical perioperative bleeding, nonsurgical bleeding, oozing, or diffuse microvascular bleeding at sites remote from the surgical field can be associated with coagulopathy and platelet dysfunction due to various and multiple conditions such as metabolic acidosis, hypocalcaemia, hypothermia, coagulation factor deficiency (inherited or acquired), hyperfibrinolysis, or disseminated intravascular coagulation (DIC).<sup>16</sup>

### THE PBM FRAMEWORK APPLIED TO COAGULOPATHY

PBM moves away from treating bleeding as an isolated event, recognising instead that haemostatic failure results from the interaction of tissue injury, haemodilution, hypoperfusion, inflammation, hypothermia, acidosis, and iatrogenic influences. This systems perspective is strongly emphasised across contemporary guidance, both national and international.<sup>2,17–20</sup>

The first PBM pillar, optimisation of RBC mass, ensures that patients enter surgery with adequate physiological reserve. Preoperative anaemia affects up to 40% of surgical patients and increases transfusion requirements, postoperative complications, and mortality. Recent international recommendations promote routine preoperative anaemia screening with ferritin-based definitions of iron deficiency (ferritin <100 µg/L, or <300 µg/L in chronic anaemia, with transferrin saturation <20%) and timely intravenous iron when surgery is imminent.<sup>21,22</sup> These interventions reduce transfusion and improve tolerance to blood loss. In trauma, although preinjury optimisation is not possible, recognising baseline anaemia or anticoagulation helps anticipate haemostatic vulnerability.

The second PBM pillar, minimising blood loss and bleeding, lies at the core of trauma and surgical haemostatic management. Preoperatively, congenital and acquired coagulation deficits should be identified and optimised. In trauma, there is a vicious relationship between acidosis, hypothermia, hypocalcaemia, and coagulopathy, which have previously been described as the lethal diamond of death<sup>23</sup> (Figure 1). Even small deviations worsen haemostasis: temperatures <35°C impair platelet function, pH <7.2 reduces enzymatic coagulation, and ionised calcium <1.0 mmol/L impairs thrombin generation and myocardial contractility. In cardiac surgery, coagulopathy evolves more gradually through haemodilution, CPB-related platelet dysfunction, contact activation, fibrinolysis, and extensive tissue injury.<sup>24</sup> Across guidelines, a consistent theme emerges; maintain physiological conditions, administer antifibrinolytics early, avoid unnecessary crystalloids, and treat the specific haemostatic defect rather than applying schematic transfusion.<sup>25,26</sup>

Once bleeding is controlled, optimisation of tolerance to anaemia becomes central. Enhancing oxygen delivery through optimisation of cardiac output, ventilation, analgesia, and microcirculatory flow allows many patients to safely tolerate lower haemoglobin concentrations. In stable patients, restrictive transfusion thresholds (typically 7–8 g/dL) are supported by robust evidence and help minimise unnecessary exposure to allogeneic blood.<sup>27–30</sup>

## Trauma Lethal Diamond

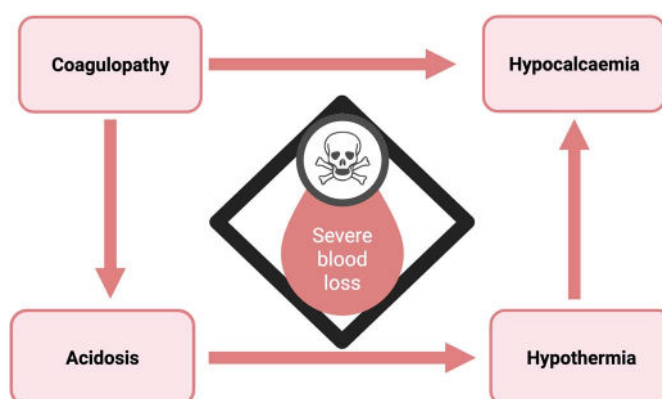


Figure 1 – The lethal diamond of trauma

Together, these pillars convert coagulopathy management from a reactive transfusion-led model into a proactive PBM strategy that anticipates haemostatic failure, individualises treatment, and minimises exposure to allogeneic blood.

### DIAGNOSTIC AND MONITORING STRATEGIES

Managing severe bleeding requires timely and accurate diagnostic input. Conventional assays such as prothrombin time/international normalised ratio, activated partial thromboplastin time, fibrinogen, and platelet count remain important, but they offer delayed, static results that do not fully reflect the rapid changes occurring in haemorrhagic shock. Contemporary trauma and surgical guidelines on bleeding management therefore encourage supplementing them with rapid, physiologically aligned diagnostics.

Viscoelastic testing (VET)—rotational thromboelastometry, thromboelastography, or ClotPro—provides dynamic assessment of clot initiation, propagation, strength, and fibrinolysis under conditions that more closely approximate bleeding physiology.<sup>31</sup> VET enables differentiation between hypofibrinogenemia, platelet dysfunction, impaired thrombin generation, and abnormalities of fibrinolysis, including both hyperfibrinolysis and fibrinolytic shutdown.<sup>32,33</sup> This precision is foundational for targeted therapy.

Data from the RETIC trial indicate that viscoelastic-guided use of fibrinogen concentrate (FC) and prothrombin complex concentrate (PCC) can reduce plasma utilisation and accelerate correction of coagulopathy compared with fresh frozen plasma; however, the results are derived from a single-centre study and should be interpreted with caution.<sup>34</sup> Similarly, the VET are valued in CPB-related coagulopathy, where conventional tests are poorly predictive of bleeding.<sup>25</sup>

Importantly, diagnostic tests alone do not improve outcomes. The multicentre iTACTIC trial demonstrated that the availability of VET does not reduce mortality or massive transfusion unless integrated within clear algorithms and training.<sup>35</sup> Structured PBM pathways, as encouraged by World Health Organisation guidance and various national and international guidelines, are critical for translating VET data into improved patient outcomes.

When used appropriately, VET is not a luxury but a strategic tool—particularly valuable in environments with limited blood supply, where targeted therapy avoids unnecessary product consumption and improves safety.<sup>36</sup>

## TARGETED THERAPEUTIC INTERVENTIONS

Effective management of coagulopathy requires a multimodal approach that blends early empiric resuscitation with precise therapy once diagnostic information becomes available (Table 2).

### Fixed-Ratio Strategies and Damage-Control Resuscitation

During uncontrolled haemorrhage, laboratory turnaround times cannot keep pace with the physiological collapse of exsanguination. Fixed-ratio transfusion approximating 1:1:1 (RBCs:plasma:platelets) mitigates dilutional coagulopathy and provides balanced haemostatic support, conceptually trying to reconstitute the unit of whole blood. In trauma patients, the PROPPR trial demonstrated improved haemostasis and fewer deaths from exsanguination in the first 24 h with 1:1:1 compared with 1:1:2, although overall 30-day mortality was unaffected.<sup>37</sup>

### Physiological Stabilisation: Calcium, pH, and Temperature

No haemostatic therapy is effective without correction of key biochemical derangements. Hypocalcaemia—common during massive transfusion due to citrate load—impairs thrombin generation, vascular tone, and cardiac function.<sup>38</sup> Acidosis slows nearly every enzymatic step in coagulation, whereas hypothermia decreases platelet function

and clotting kinetics.<sup>2</sup> Guidelines for both trauma and perioperative severe bleeding uniformly emphasise early physiological optimisation as the foundation upon which all subsequent haemostatic interventions depend.

### Lyophilised Plasma and Field-Deployable Coagulation Support

Freeze-dried (lyophilised) plasma offers rapid reconstitution, room-temperature storage, and reliable delivery of coagulation factors, making it particularly valuable in prehospital, military, remote, and resource-limited environments. One trial showed that prehospital lyophilised plasma improved early coagulation parameters and reduced early transfusion requirements compared with crystalloid-based resuscitation.<sup>39</sup> In contrast, in the RePHILL trial, the administration of a combination of packed RBCs and lyophilised plasma was not superior to saline in patients with trauma-related haemorrhagic shock, reinforcing the challenge of demonstrating mortality benefit in prehospital transfusion studies outside war zones.<sup>40</sup> However, taken together, these data suggest that lyophilised plasma is a practical early haemostatic option when thawed plasma is unavailable.

### Tranexamic Acid

Tranexamic acid (TXA) is one of the few haemostatic interventions with proven mortality benefit, both in traumatic bleeding and in major surgery. In CRASH-2, early administration of tranexamic acid, particularly within the first hour after injury, was associated with reduced mortality and bleeding-related deaths. Administration beyond three hours was associated with worse outcomes, likely reflecting progression toward fibrinolytic shutdown rather than a

**Table 2.** – PBM-aligned, Goal-directed Haemostatic Interventions in Major Bleeding

Intervention	Targeted Deficit	Diagnostic Trigger	Evidence Level	Suggested dose	Key Cautions
Tranexamic acid	Hyperfibrinolysis	Early trauma/major surgery	High	Trauma: 1 g IV over 10 min, followed by 1 g over 8 h (CRASH-2 regimen). Surgery: 10–20 mg/kg IV or 1 g IV, with or without infusion depending on procedure	Harm if delayed (>3 h in trauma)
Fibrinogen concentrate/cryoprecipitate	Low fibrinogen/weak clot	FIBTEM A5 ↓ or fibrinogen concentration <1.5–2.0 g/L	Moderate–high	Fibrinogen concentrate: 3–4 g initial dose in trauma, 25–50 mg/kg in surgery (adjust according to tests). Cryoprecipitate: 10 pooled units.	Avoid empiric overcorrection
Platelet transfusion	Quantitative/qualitative platelet deficit	Low count or reduced clot strength	Low	1 apheresis unit or 1 random donor unit per 10 kg body weight	Dysfunction may precede thrombocytopenia
PCC (4-factor)	Impaired thrombin generation	Prolonged clotting time on VET, or INR↑	Moderate	25–50 IU/kg IV depending on severity and indication	Thrombosis risk if empiric
Plasma (FFP/lyophilised)	Global factor deficiency	Early uncontrolled haemorrhage	Moderate	1:1 with PRBCs early in resuscitation	Volume load, delayed effect
Physiological correction	pH, Ca <sup>2+</sup> , temperature	Universal	High	Maintain ionised Ca <sup>2+</sup> >1.0 mmol/L, temperature >35–36°C, pH >7.2	No therapy works without this

PCC, prothrombin complex concentrate; FFP, fresh frozen plasma; VET, viscoelastic test

direct harmful effect of the drug itself.<sup>41</sup> CRASH-3 similarly demonstrated reduced head-injury mortality in patients with traumatic brain injury, as long as TXA was administered early.<sup>42</sup>

Across major surgical fields—including orthopaedic, obstetric, hepatic, and cardiac surgery—TXA has been proved to reduce blood loss and transfusion, whereas the risk of thrombotic complications at standard doses remains low to negligible.<sup>43–45</sup> Very high doses, historically used in cardiac surgery, may increase postoperative seizures, reinforcing the need for guideline-based regimens.<sup>46</sup> Current European, U.K., and French guidelines consistently endorse early TXA in trauma and routine use in major surgery with high risk of bleeding.<sup>2,17,24,25</sup>

### **Fibrinogen Replacement (Concentrate and Cryoprecipitate)**

Fibrinogen is typically the first coagulation factor to fall below critical levels (<1.5–2.0 g/L) during major haemorrhage. Low fibrinogen levels impair fibrin polymerisation and weaken clot structure. Viscoelastic parameters such as FIBTEM A5 provide rapid assessment of fibrin-based clot stability.<sup>32</sup> Correcting fibrinogen deficiency is a cornerstone of haemostatic therapy, underpinning both clot strength and platelet interaction.

FC offers rapid, standardised replacement with predictable dosing and minimal volume. The FIBRES trial showed 4 g of FC to be noninferior to 10 u cryoprecipitate for fibrinogen correction in cardiac surgery, with similar clinical outcomes.<sup>47</sup> Trauma data—including RETIC—suggest that VET-guided FC reduces plasma use and accelerates coagulation correction.<sup>34</sup> Expert guidance supports FC in CPB-related coagulopathy.<sup>13,25</sup>

Cryoprecipitate remains widely used as an alternative to FC or if FC is unavailable. Each unit of cryoprecipitate typically contains approximately 150–250 mg of fibrinogen in a volume of 10–20 mL, together with factor VIII, von Willebrand factor, factor XIII, and fibronectin. Its fibrinogen content is variable, depending on the concentration of the donor, and thawing adds delay, but it remains effective and is recommended across U.K. and French guidelines when fibrinogen levels fall below 1.5–2.0 g/L.<sup>25,26</sup>

### **Prothrombin Complex Concentrates**

PCCs rapidly restore thrombin generation through concentrated vitamin K–dependent factors (II, VII, IX, and X). They are effective for dilutional coagulopathy, vitamin K antagonist reversal, and persistent bleeding after CPB.<sup>17</sup>

In trauma, the evidence is mixed. RETIC suggested that VET-guided PCC may reduce plasma use and expedite haemostatic correction.<sup>34</sup> However, the multicentre PROCOAG trial showed that empiric early PCC does not reduce transfusion and is associated with increased thromboembolic events.<sup>48</sup> Therefore, across European and national guidelines, PCC is recommended only for diagnostics-guided correction of impaired thrombin generation, not as empiric therapy.<sup>2,17</sup>

In cardiac surgery, PCC has emerged as an important component of targeted haemostatic therapy for post-CPB coagulopathy, where haemodilution, heparin–protamine imbalance, and consumption of

vitamin K–dependent factors can impair thrombin generation. PCC offers several advantages over plasma, such as faster onset, more predictable correction of clotting times, and avoidance of the large infusion volumes (this leads to potentially less transfusion related complications such as transfusion-related acute lung injury or transfusion-associated circulatory overload). Current guidelines supports its use within viscoelastic-driven algorithms when prolonged clotting time reflects true factor deficiency.<sup>25,49</sup> Inappropriate or high-dose administration may increase thrombin potential and should be avoided. Thus, PCC functions best as a selective, diagnostics-guided therapy rather than an empiric replacement for plasma.<sup>50</sup>

### **Platelet Therapy**

Platelets play a key role in clot strength, and both quantitative and qualitative abnormalities are fundamental to coagulopathy in trauma and surgery. In trauma, platelet dysfunction may occur early despite preserved counts, whereas CPB impairs platelet number and function more progressively.<sup>11,13,51</sup> Viscoelastic testing or platelet function assays help distinguish whether diminished clot strength rises from platelet insufficiency or fibrinogen deficiency. Maintaining platelet performance also requires correction of hypothermia, acidosis, and hypocalcaemia, which otherwise blunt platelet activity.

Although the PROPPR trial did not demonstrate a difference in overall mortality, early inclusion of platelets as part of a 1:1:1 resuscitation strategy significantly reduced deaths from exsanguination at 24 h compared with a 1:1:2 strategy.<sup>42</sup>

In major surgery, platelet transfusion is recommended for active bleeding when platelet counts fall below  $50 \times 10^9/L$ , or  $100 \times 10^9/L$  in neurosurgery or traumatic brain injury.<sup>2,17</sup> Platelet dysfunction may benefit from desmopressin, particularly in patients receiving antiplatelet agents, in uraemic patients, or in those with CPB-related dysfunction.<sup>17,52,53</sup>

### **TRANSITION TO GOAL-DIRECTED THERAPY**

As soon as haemorrhage control is achieved and diagnostic information becomes available, resuscitation should transition from empiric, fixed-ratio transfusion strategies to goal-directed therapy.<sup>36</sup> VET plays a pivotal role in identifying the dominant mechanism—such as fibrinogen depletion, platelet dysfunction, impaired thrombin generation, or abnormal fibrinolysis—and guiding precise replacement of the missing component.

Targeted therapy limits unnecessary exposure to plasma and platelets, reduces dilutional coagulopathy, and restores physiological coherence by stabilising early clot formation through fibrinogen replacement, accelerating clot propagation via correction of thrombin generation, and preventing premature clot breakdown by modulating fibrinolysis.

### **GLOBAL PERSPECTIVES AND IMPLEMENTATION CHALLENGES**

The management of complex coagulopathy in trauma and major surgery varies widely across the world, reflecting differences in resources, infrastructure, and workforce capacity. Although the principles of PBM are universally applicable, their implementation is profoundly shaped by local realities. High-income health systems

**Table 3** – A summary of interventions depending on resource level (adapted from 24)

Resource setting	Diagnostic capability	Key bleeding control strategies	Coagulopathy management tools	Examples of haemostatic therapies
Low-resource settings (LICs)	Clinical assessment, basic laboratory tests when available, simple clotting tests (e.g., 20-min whole blood clotting test)	Early surgical haemostasis, mechanical compression, packing, appropriate positioning, restrictive fluid administration, prevention of hypothermia	Recognition of coagulopathy based mainly on clinical assessment	Tranexamic acid, vitamin K, desmopressin (if available), cryoprecipitate where accessible
Intermediate resource settings (LMICs / UMICs)	Standard laboratory coagulation testing (PT/INR, aPTT, fibrinogen, platelet count), point-of-care haemoglobin	Structured bleeding protocols, improved surgical haemostasis, autologous blood salvage, restrictive transfusion strategies	Identification of specific haemostatic defects using laboratory testing	TXA, cryoprecipitate or fibrinogen replacement, prothrombin complex concentrate, vitamin K, desmopressin
High-resource settings (HICs)	Full laboratory diagnostics plus point-of-care haemostasis testing (viscoelastic testing, platelet function testing, DOAC assays)	Goal-directed bleeding management algorithms, minimally invasive surgery, interventional radiology, intra- and postoperative cell salvage	Algorithm-driven correction of haemostatic defects	TXA or antifibrinolytics, fibrinogen concentrate, PCC, specific factor concentrates, desmopressin, platelet-stimulating agents

increasingly depend on rapid diagnostics, coagulation factor concentrates, and well-established transfusion services, whereas many low- and middle-income countries face constraints, including limited laboratory capacity, blood shortages, delayed transport, and restricted critical care resources. These differences affect both the timely recognition of coagulopathy and the therapeutic options available during life-threatening bleeding.

Despite these barriers, PBM offers a unifying framework that can be implemented incrementally across diverse settings. Standardised early use of tranexamic acid, minimisation of iatrogenic blood loss, correction of hypothermia and hypocalcaemia, and simple escalation pathways for major haemorrhage represent achievable, high-impact interventions, even where advanced diagnostics or factor concentrates are unavailable.

A major challenge is the uneven availability of blood components. Many countries struggle with unreliable supply, making traditional transfusion-heavy approaches unsustainable. Here, PBM becomes not only a clinical strategy but a health-system intervention: Reducing the demand for allogeneic blood allows scarce units to be reserved for patients who truly need them.<sup>19</sup>

Implementation also depends on culture change. PBM requires multidisciplinary engagement: surgeons, anaesthesiologists, emergency physicians, haematologists, transfusion specialists, and nursing teams must share a common understanding of goals and workflows. Importantly, PBM is not an all-or-nothing model. Countries can begin with foundational steps—standardising TXA use, reducing iatrogenic blood loss, establishing simple escalation pathways for major haemorrhage—and progressively incorporate more advanced diagnostics and therapies as resources expand (Table 3). The overarching aim is the same in every setting: to recognise coagulopathy early, intervene precisely, conserve scarce blood resources, and improve patient outcomes. When adapted thoughtfully, PBM becomes a powerful equaliser, enabling safer care even where resources are limited.

## SUMMARY

Complex coagulopathies in trauma and major surgery are still a significant contributor to preventable morbidity and mortality worldwide. Across the continuum of care, three principles consistently shape better outcomes: anticipate and mitigate the drivers of coagulopathy, intervene early with measures that stabilise physiology and limit blood loss, and individualise therapy as soon as diagnostic information allows. Early ratio-based resuscitation, particularly in trauma, provides a bridge through the most unstable phase, whereas targeted therapy—guided by viscoelastic or laboratory data—enables precise correction of the specific deficits that perpetuate bleeding. This transition from empiric to personalised care reduces unnecessary exposure to allogeneic blood products, avoids secondary iatrogenic harm, and supports organ recovery.

Implementation challenges remain substantial, especially where resource constraints, delayed diagnostics, or limited training hinder the adoption of contemporary strategies. Yet, scalable PBM principles, pragmatic algorithms, and growing international experience show that meaningful improvement is achievable across diverse health-care settings.

**Conflicts of interest** – MS - honoraria for lecturing (CSL Vifor, AstraZeneca, Takeda Pharmaceuticals), consulting (Livanova, Takeda Pharmaceuticals); AN - honoraria for lecturing (Hikma Pharmaceuticals), TYK – consulting (CSL Behring Korea), grants (Korea Health Industry Development Institute).

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