

# Viscoelastic-Guided Hemostatic Resuscitation in Trauma: From Endothelial Endotype to System-Level Precision

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**Abstract:** Trauma-induced coagulopathy (TIC) is a biologically heterogeneous and rapidly evolving response to severe injury characterized by endothelial dysfunction, dysregulated thrombin generation, platelet impairment, and divergent fibrinolytic phenotypes. While balanced transfusion strategies have improved early hemorrhage control, they do not fully account for the phenotypic variability observed in TIC. Viscoelastic hemostatic assays (VHA), including thromboelastography and rotational thromboelastometry, provide real-time assessment of clot formation, strength, and fibrinolysis, enabling targeted hemostatic resuscitation. However, randomized trials have demonstrated improvements in transfusion targeting without consistent reductions in overall mortality. This structured narrative review synthesizes contemporary evidence on the biological mechanisms of TIC, fibrinolytic endotypes, and the role of viscoelastic testing in trauma resuscitation. A systematic search of PubMed/MEDLINE, Scopus, and Web of Science from January 2000 to February 2026 was performed, prioritizing landmark randomized trials, mechanistic studies, and international guidelines. The literature suggests that the effectiveness of VHA-guided resuscitation is influenced not only by diagnostic capability but also by the interaction between biological phenotype, timing of intervention, and trauma system performance. A hybrid model integrating early empiric balanced transfusion with subsequent phenotype-guided calibration may represent the most physiologically coherent strategy. Ultimately, viscoelastic testing should be understood as a decision-support modality embedded within mature trauma systems rather than a standalone determinant of survival. Future research should focus on phenotype-stratified clinical trials and system-integrated approaches capable of translating hemostatic precision into consistent outcome improvement.

**Keywords:** Trauma-Induced Coagulopathy; Viscoelastic Hemostatic Assays; Fibrinolysis; Hemostatic Resuscitation.

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## 1. Introduction

Trauma-induced coagulopathy (TIC) is a biologically heterogeneous and temporally dynamic response to severe injury that integrates endothelial dysfunction, dysregulated thrombin generation, platelet impairment, and divergent fibrinolytic phenotypes [1-3]. While balanced transfusion strategies have reduced early death from exsanguination [4], uniform ratio-based approaches do not account for phenotypic variability within TIC. Viscoelastic hemostatic assays (VHA) provide real-time whole-blood characterization of

clot formation, strength, and lysis, enabling early identification of hypofibrinogenemia, amplitude impairment, and hyperfibrinolysis. Despite consistent improvements in transfusion targeting and process-of-care metrics, randomized trials have not demonstrated uniform mortality benefit [5].

This apparent paradox suggests that the impact of viscoelastic-guided resuscitation depends not solely on assay performance, but on the interaction between biologic phenotype, timing of intervention, and trauma system maturity. We critically examine the mechanistic foundations of TIC, fibrinolytic phenotyping, including shutdown, the interpretation of major randomized trials, and the systems-level determinants that modulate outcome impact. We propose a phenotype-driven, system-integrated framework in which viscoelastic testing functions as a decision-support modality whose benefit is contingent upon context rather than as a universal determinant of survival.

## 2. The Evolving Biology of Trauma-Induced Coagulopathy

Hemorrhage is not lethal purely because of blood loss; it becomes lethal when mechanical disruption is compounded by systemic hemostatic dysregulation [6]. TIC emerges within minutes of injury and reflects a coordinated but often maladaptive host response to tissue trauma and hypoperfusion [1, 2]. The contemporary model of TIC centers on endothelial activation and glycocalyx degradation [3]. Hypoperfusion-driven protein C activation attenuates factors Va and VIIIa [2]. Simultaneously, thrombin generation becomes spatially and temporally dysregulated, platelet function deteriorates independent of count, and fibrinogen levels decline rapidly [7, 8]. Importantly, TIC is not monolithic. It is better conceptualized as a spectrum of endotypes defined by distinct hemostatic perturbations. Within this spectrum, fibrinolysis represents one of the most clinically consequential axes of divergence [9].

## 3. Methodology

This manuscript was developed as a structured narrative review incorporating systematic search principles to enhance transparency, reproducibility, and analytical rigor. A comprehensive literature search was conducted in PubMed/MEDLINE, Scopus, and Web of Science, covering publications from January 2000 through February 2026. In addition, the reference lists of key clinical trials, international guidelines, and seminal mechanistic studies were manually screened to identify additional relevant publications.

The search strategy was adapted to each database. In PubMed/MEDLINE, the following combination of terms was used: (trauma-induced coagulopathy OR acute traumatic coagulopathy OR endotheliopathy) AND (viscoelastic OR thromboelastography OR TEG OR thromboelastometry OR ROTEM) AND (massive transfusion OR hemorrhage OR resuscitation). In Scopus, the strategy was: TITLE-ABS-KEY((trauma-induced coagulopathy OR endotheliopathy) AND (viscoelastic OR TEG OR ROTEM) AND (massive transfusion OR damage control resuscitation OR fibrinolysis)). In Web of Science, the search was performed using: TS=((trauma-induced coagulopathy OR acute traumatic coagulopathy OR endotheliopathy) AND (viscoelastic OR thromboelastography OR thromboelastometry OR TEG OR ROTEM) AND (hemorrhage OR transfusion OR resuscitation)).

Eligibility criteria were defined according to PICO-aligned principles. Studies were included if they involved adult trauma patients with suspected or confirmed major hemorrhage, evaluated viscoelastic hemostatic assays (VHA), including thromboelastography (TEG) or rotational thromboelastometry (ROTEM), for diagnostic purposes or guidance of hemostatic resuscitation, and/or addressed transfusion strategies relevant to early hemostatic resuscitation, such as balanced transfusion ratios, VHA-guided transfusion algorithms, or fibrinolysis-directed therapy. Eligible study designs included randomized controlled trials, large prospective cohorts or registry-based studies, systematic reviews or meta-analyses, and international clinical guidelines. Studies restricted to pediatric populations, those focusing exclusively on non-trauma surgical bleeding, or re-

ports lacking clinically interpretable outcomes were excluded. All retrieved records were exported to reference management software and duplicates were removed prior to screening. Titles and abstracts were independently screened by two reviewers, with disagreements resolved through consensus discussion. When eligibility could not be determined based solely on the abstract, the full text was retrieved and assessed.

Evidence synthesis prioritized landmark randomized trials, including the PROPPR trial [4] and the ITACTIC trial [5], as well as mechanistic studies that defined endothelial dysfunction and fibrinolytic phenotypes in trauma [2, 8, 9]. Contemporary European guidelines on trauma-induced bleeding and coagulopathy [10, 11] were also incorporated. Conflicting or neutral findings were intentionally included to maintain interpretative balance. Given the methodological heterogeneity across studies, evidence was synthesized using a structured narrative approach rather than pooled quantitative estimates, organizing the literature across major domains including biological mechanisms and endotypes, diagnostic strategies and VHA thresholds, randomized trial evidence, clinical implementation and human factors, and health system or resource constraints.

## 4. Discussion

### 4.1 Fibrinolytic Endotypes and Therapeutic Implications

Recognition of fibrinolytic phenotypes, hyperfibrinolysis, physiologic fibrinolysis, and fibrinolysis shutdown, has reframed trauma hemostasis from a binary model to a spectrum with distinct outcome trajectories [9]. Hyperfibrinolysis is tightly coupled to early exsanguination, whereas shutdown has been associated with later thrombotic complications and organ dysfunction, suggesting that indiscriminate antifibrinolysis may be biologically misaligned in a subset of patients [9].

Viscoelastic platforms provide real-time access to lysis dynamics through parameters such as LY30 (TEG) and maximum lysis (ROTEM), enabling early identification of pathologic lysis states that conventional plasma-based tests cannot resolve [7]. Yet phenotype recognition is only clinically valuable insofar as it changes decisions within a timeframe that still permits physiologic rescue; therefore, phenotyping must be coupled to rapid logistics, algorithm discipline, and definitive hemorrhage control [6].

### 4.2 Ratio-Based Resuscitation: Operational Strengths and Biological Limitations

Balanced component therapy remains foundational because it addresses the time-critical reality of early hemorrhagic shock. The PROPPR trial reinforced that early balanced transfusion improves hemorrhage control and may reduce death from exsanguination, even when longer-term mortality differences are attenuated [4]. The operational success of ratio-based strategies lies in simplicity: they reduce cognitive load during peak chaos and provide a reliable bridge when physiological data are incomplete. However, ratio-based resuscitation is intrinsically non-phenotypic. It assumes a degree of biological homogeneity within TIC that is increasingly inconsistent with evidence of distinct endotypes [8]. In practice, uniform plasma and platelet exposure risks over-treatment in patients whose primary deficit is fibrinogen depletion, platelet dysfunction without quantitative thrombocytopenia, or absent fibrinolysis. These limitations provide the physiologic rationale, though not proof, for viscoelastic-guided calibration.

### 4.3 Viscoelastic-Guided Trials and the Mortality Paradox

Randomized data demonstrate that VHA-guided strategies can alter transfusion patterns and accelerate targeted hemostatic interventions, yet mortality signals remain heterogeneous across pragmatic trial designs [5, 11]. In PROPPR, patients with severe trauma at risk for massive transfusion were randomized to 1:1:1 versus 1:1:2 plasma:platelet:RBC strategies; the co-primary endpoints were 24-hour and 30-day all-cause mortality [4]. The trial was designed for rapid early delivery of balanced components within damage-control resuscitation workflows and demonstrated improved early

hemorrhage control, including reduced death from exsanguination, despite the absence of a statistically significant difference in 30-day mortality.

In ITACTIC, the primary endpoint was the proportion of patients alive and free of massive transfusion at 24 hours, with 28-day mortality as a key secondary endpoint [5]. Viscoelastic guidance improved targeting but did not reduce overall 28-day mortality, highlighting that assay availability alone may be insufficient when definitive hemorrhage control is delayed, physiology is already beyond rescue, or protocol execution is incomplete. These considerations support systems interpretation: VHA may maximize benefit when paired with rapid hemostasis, reliable component access, and algorithm discipline rather than when deployed as an isolated diagnostic upgrade [6].

#### **4.4 The Early Resuscitation “Dead Zone” and the Hybrid Paradigm**

The first 30–60 minutes of trauma resuscitation represent a period in which coagulopathy evolves rapidly while diagnostic certainty remains limited. During this “dead zone,” empiric balanced transfusion is rational for patients with high-risk hemorrhage physiology, because the penalty for under-resuscitation is immediate death [4, 6]. A hybrid model operationalizes two truths: early empiric balance is often necessary, but prolonged non-phenotypic transfusion is neither efficient nor necessarily aligned with biology. Viscoelastic assays can provide actionable early amplitudes within minutes, allowing recalibration toward targeted fibrinogen therapy, platelet-directed strategies, or anti-fibrinolytic refinement when indicated [11]. The clinical challenge is not whether to “switch” from empiric to guided therapy, but how to execute a disciplined transition that prevents both early under-treatment and late over-exposure.

#### **4.5 Platform Variability, Thresholds, and Standardization Risk**

A persistent barrier to generalizability is cross-platform variability between TEG and ROTEM, as well as between device generations, reagents, and analytic settings. Thresholds for fibrinogen replacement, clot strength impairment, and pathologic lysis are not interchangeable and are often guideline- and system-dependent [10, 11]. To reduce the risk of clinically unsafe extrapolation, protocols should specify device and parameter nomenclature. Examples commonly used in trauma algorithms include ROTEM-based triggers such as low FIBTEM amplitude at 5–10 minutes (A5/A10) to support early fibrinogen replacement and EXTEM/INTEM amplitudes to contextualize global clot firmness, whereas in TEG platforms low maximum amplitude (MA) and elevated LY30 are commonly used to support platelet-directed therapy and recognition of hyperfibrinolysis, respectively [7, 9].

Absolute cutoffs vary by platform and local calibration; therefore, institutions should validate device-specific triggers against local outcomes and blood product pathways before clinical deployment. Standardization efforts should move toward phenotype-based definitions that preserve biologic meaning across platforms while retaining device-specific operational parameters. Without this, the precision that VHA promises can become a source of misclassification and overtreatment in high-stakes hemorrhage care.

#### **4.6 TXA, Viscoelastic Phenotyping, and Practical Decision-Making**

Tranexamic acid (TXA) has robust evidence for early administration in bleeding trauma and traumatic brain injury when delivered within established therapeutic windows [12, 13]. The practical dilemma is not the initial dose in patients with suspected major hemorrhage, where early administration is strongly supported, but how (and whether) viscoelastic phenotyping should refine continuation or escalation, particularly when lysis is absent or shutdown is present [9].

A defensible, implementation-focused approach is to treat TXA as front-loaded therapy for patients at high risk of exsanguination, while using viscoelastic tracings to

avoid reflexive escalation beyond the initial regimen in the absence of hyperfibrinolysis. Where protocols include additional TXA dosing, escalation should be explicitly tied to evidence of clinically relevant lysis on the institution's platform and to patient phenotype rather than used automatically. Because associations between shutdown and thrombotic/organ dysfunction outcomes are primarily observational, VHA refinement should be framed as risk-balancing rather than as definitive prevention of thrombosis, an area that remains an important research priority [8, 9].

#### **4.7 Human Factors, Interpretation Error, and Implementation Discipline**

Viscoelastic testing does not eliminate uncertainty; it redistributes it. Interpretation errors, pre-analytic variability, and technical failures occur most commonly under the same conditions in which decisions carry maximal consequence: a chaotic resuscitation room with competing tasks and limited cognitive bandwidth. The value of VHA therefore depends on simplified algorithms, simulation-based training, quality control, and audit-feedback loops, features of system maturity rather than assay design alone. In practice, a commonly reported failure mode is cognitive: interpreting low clot amplitude as platelet deficit without accounting for fibrinogen contribution or treating minimal lysis patterns as pathologic. Protocol design must minimize cognitive load by making algorithmic, trigger-based, and integrated into massive transfusion workflows [11].

#### **4.8 Damage Control Surgery and Dynamic Hemostatic Assessment**

Sequential viscoelastic monitoring can inform operative strategy by providing dynamic evidence of hemostatic stabilization or persistent coagulopathy. Restoration of clot strength and controlled lysis patterns may support earlier transition from damage control surgery to definitive repair, whereas ongoing coagulopathy may justify abbreviated procedures and continued resuscitation. However, laboratory optimization cannot substitute for hemostatic source control; definitive hemorrhage control remains the dominant determinant of survival [6]. The translational opportunity is to define how viscoelastic trends can serve as time-sensitive physiologic endpoints that guide operative timing, not merely transfusion composition. This requires integration of VHA with surgical decision pathways and measurable timing targets across trauma systems.

#### **4.9 Adaptive vs Maladaptive Coagulopathy: The Next Research Frontier**

An emerging hypothesis is that elements of TIC may initially represent adaptive responses aimed at preserving microvascular perfusion and limiting uncontrolled thrombosis. If so, aggressive laboratory normalization could, in some contexts, oppose compensatory physiology. Distinguishing maladaptive coagulopathy from protective hemostatic modulation is therefore critical [8]. Future research should move beyond aggregate mortality endpoints toward phenotype-stratified designs that incorporate mechanistic biomarkers, viscoelastic signatures, timing to hemorrhage control, and downstream thrombotic risk. Only then can precision resuscitation evolve from improved process metrics to consistent outcome modification.

### **5. Conclusion**

Viscoelastic-guided hemostatic resuscitation represents a conceptual inflection point in modern trauma care, marking the transition from empiric component ratios toward phenotype-aware physiologic calibration. However, the absence of uniform mortality reduction across randomized trials such as PROPPR [4] and ITACTIC [5] underscores a critical insight: laboratory precision does not operate independently of biologic heterogeneity and system-level constraints. Trauma-induced coagulopathy is increasingly understood as a spectrum of endothelial and fibrinolytic endotypes rather than a singular entity [2, 8]. Within this framework, viscoelastic testing provides mechanistic clarity by distinguishing hypofibrinogenemia, amplitude impairment, hyperfibrinolysis, and fi-

brinolysis shutdown [9]. Yet phenotype identification alone cannot overcome irreversible injury burden or delayed hemorrhage control [6].

The clinical value of viscoelastic guidance therefore resides not in universal normalization of laboratory parameters, but in dynamic recalibration of resuscitation aligned with early biologic phenotype and rapid source control. In mature trauma systems with immediate surgical and transfusion capability, VHA may refine already optimized care pathways. In resource-constrained environments, foundational interventions, early tranexamic acid administration [12, 13], temperature control, and calcium repletion, may exert greater marginal survival impact.

The future of trauma hemostasis lies in biologically stratified, system-integrated models of care that couple early phenotype recognition with disciplined implementation and definitive hemorrhage control. Only through phenotype-stratified trial design and context-aware deployment can viscoelastic precision translate into consistent survival advantage rather than procedural refinement alone.

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