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The Role Of Viscoelastic Hemostatic Assays (TEG And ROTEM) In Goal-Directed Hemostatic Resuscitation for Trauma-Induced Coagulopathy: A Laboratory Specialist's Guide to Principles, Analytical Quality, and Clinical Interpretation

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Abstract

Uncontrolled traumatic hemorrhage and the resultant acute coagulopathy remain the leading causes of preventable death in severely injured patients. Conventional coagulation tests (CCTs), such such as Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT), suffer from significant operational and mechanistic limitations in the acute trauma setting, particularly their inability to assess dynamic clot formation, platelet function, and fibrinolysis in real time. Viscoelastic Hemostatic Assays (VHAs), principally Thromboelastography (TEG) and Rotational Thromboelastometry (ROTEM), have emerged as essential Point-of-Care (POCT) diagnostics. These whole-blood tests provide rapid, comprehensive profiles of clot initiation, strength, and stability, allowing for the functional characterization of Trauma-Induced Coagulopathy (TIC). This review provides laboratory specialists and technicians with an in-depth guide to VHA methodology, focusing on analytical quality assurance, detailed parameter interpretation, and the integration of VHAs into goal-directed Massive Transfusion Protocols (MTPs). Despite heterogeneity across next-generation platforms and ongoing clinical debate regarding overall mortality benefit (as demonstrated by trials such as ITACTIC), VHAs consistently accelerate time to diagnosis, facilitate targeted component and concentrate therapy, and demonstrably reduce unnecessary blood product exposure. Successful implementation requires rigorous quality management, strict pre-analytical control, and institutional commitment to device-specific, evidence-based transfusion algorithms.

Keywords Trauma-Induced Coagulopathy; Viscoelastic Hemostatic Assays; Thromboelastography (TEG); Rotational Thromboelastometry (ROTEM); Massive Transfusion Protocol; Point-of-Care Testing; Fibrinolysis; Quality Assurance; Transfusion Medicine.

Introduction

Background

The Clinical Burden and Definition of Trauma-Induced Coagulopathy (TIC)

Traumatic injury remains a major global public health concern, and uncontrolled hemorrhage, often compounded by intrinsic coagulopathy, constitutes the most common cause of preventable death following trauma. The timely diagnosis and correction of hemostatic failure are therefore paramount to improving patient outcomes. This necessity drives the continuous refinement of emergency resuscitation strategies in advanced trauma centers.

While traumatic injury itself may appear anatomically localized, the physiological response is systemic. Trauma-Induced Coagulopathy (TIC) is an acute intrinsic coagulopathy, an emergent property resulting from the combination of severe tissue injury and systemic hypoperfusion, or shock. This condition is distinct from coagulopathy caused solely by dilution following volume resuscitation. Early TIC is frequently associated with profound hypocoagulability, which stems from factors including impaired thrombin generation, platelet dysfunction, and depletion of critical coagulation factors like fibrinogen. This state is dangerously amplified by the presence of the "lethal triad": coagulopathy, hypothermia, and acidosis. In contrast, patients who survive the initial phase may progress into a later state of hypercoagulability, driven by ongoing endothelial injury and inflammation, which significantly increases the risk of venous thromboembolism and subsequent multiple organ failure (MOF). The dual nature of TIC—rapid transition from hypo- to potentially hyper-coagulation—demands a diagnostic tool capable of monitoring the entire clotting lifespan in a dynamic, continuous manner.

The population requiring immediate aggressive intervention, though small, consumes disproportionate resources. Only approximately 3% of civilian trauma patients in the US require a Massive Transfusion (MT), typically defined as the administration of 10 or more units of red blood cells (RBCs) within 24 hours of admission. However, these patients utilize an estimated 70% of all blood products transfused at a trauma center. The development and implementation of Massive Transfusion Protocols (MTPs) have become standardized practice, requiring significant preplanning and coordination across the emergency department, operating room, and blood bank to ensure the rapid availability and delivery of large volumes of blood components.

Limitations of Conventional Coagulation Tests (CCTs) in Acute Trauma Care

Despite the critical need for rapid hemostatic assessment, Conventional Coagulation Tests (CCTs)—such as Prothrombin Time (PT), International Normalized Ratio (INR), and Activated Partial Thromboplastin Time (aPTT)—are fundamentally ill-suited for acute trauma diagnostics due to both mechanistic and operational shortcomings.

The primary mechanistic limitation of CCTs lies in their acellular nature. These tests are performed on plasma, which necessitates separating cellular components (platelets, red blood cells) from the sample prior to testing. This methodology precludes the assessment of the crucial contributions of platelets and red blood cells to physical clot strength, thus yielding an incomplete picture of a patient's functional hemostatic capacity. CCTs are useful for identifying gross deficiencies in circulating coagulation factors but fail entirely to evaluate the functional fibrinogen concentration, platelet function, or the critical process of fibrinolysis.

Operationally, CCTs suffer from unacceptable turnaround time (TAT) in the context of life-threatening hemorrhage. In trauma care, where minutes translate directly to mortality risk, the delay inherent in sample transport, centrifugation, and subsequent analysis means that results frequently arrive too late to inform timely resuscitation decisions. Compounding this issue, CCTs may fail to identify significant functional coagulation deficits. Clinical data reveals that only 31% of patients diagnosed with trauma-induced coagulopathy exhibit abnormalities in both conventional coagulation assays and viscoelastic coagulation assays. This significant diagnostic discrepancy emphasizes that CCTs miss functional deficits in the majority of coagulopathic trauma patients, particularly those deficiencies related to fibrinogen function and platelet aggregation that are crucial for clot stability.

Table 1: Comparison of Conventional Coagulation Tests (CCTs) and Viscoelastic Hemostatic Assays (VHAs) in Trauma

Feature	**CCTs (PT/aPTT/INR)**	**VHAs (TEG/ROTEM)**
Sample Matrix	Plasma (Acellular)	Whole Blood (Cellular)
Hemostasis Components Assessed	Coagulation Factors (Time to Fibrin)	Factors, Platelets, Fibrinogen, Fibrinolysis (Clot Dynamics)
Test Output	Time-based endpoint (seconds/ratio)	Dynamic graphical trace and quantitative metrics (mm/time)
Turnaround Time (TAT) in Trauma	Slow (often >45 minutes to results)	Rapid (5–15 minutes to actionable parameters)
Detection of Functional Deficits	Poor sensitivity to fibrinogen and platelet dysfunction	High sensitivity to fibrinogen and platelet contribution (MA/MCF, FIBTEM)
Fibrinolysis Assessment	Only D-dimer (indirect, delayed)	Direct, real-time measurement (CL/LY, APTEM)

Literature Review: The Evolution of Hemostatic Resuscitation

From Empirical Ratios to Goal-Directed Therapy

The management of massive traumatic hemorrhage has undergone a paradigm shift, moving away from volume expansion with crystalloids toward hemostatic resuscitation, followed by a progression from empirical transfusion ratios to goal-directed therapy (GDT).

Initial Massive Transfusion Protocols (MTPs) popularized empirical, high-ratio administration of blood components (e.g., 1:1:1 ratios of Fresh Frozen Plasma [FFP], platelets, and red blood cells). While observational studies provided weak evidence suggesting improved survival with higher ratios compared to previous practices , these approaches failed to define a specific fixed ratio that was unequivocally superior across all patient populations. This ratio-based approach carries the inherent risk of over-transfusion and unnecessary patient exposure to blood products if the patient's specific deficits do not align with the empirically administered ratio.

The current emphasis in trauma centers is on GDT . GDT recognizes that coagulopathy in trauma is heterogeneous and highly individualized, requiring real-time diagnostic guidance to identify and target specific, measurable deficiencies in the coagulation cascade or clot structure. The goal of this tailored approach is to provide transfusion therapy based upon individual patient deficits, thereby minimizing unnecessary transfusion requirements and associated resource consumption.

Global Consensus and Guideline Recommendations

The limitations of CCTs and the inherent time sensitivity of trauma resuscitation have led major international clinical bodies to incorporate VHA into standard management protocols. The Eastern Association for the Surgery of Trauma (EAST) Practice Management Guidelines Committee evaluated the role of TEG and ROTEM in acutely bleeding patients. They conditionally recommend using TEG/ROTEM-guided transfusions over traditional coagulation parameters to guide blood component transfusions in adult trauma patients with ongoing hemorrhage . This recommendation is based on the recognition that clinical assessment and conventional tests are often inaccurate and time-consuming in this critical patient group.

In Europe, guidelines for the management of trauma-induced major bleeding and coagulopathy strongly endorse the use of Point-of-Care Viscoelastic Methods (VEM, including TEG and ROTEM) to facilitate target-controlled hemostatic treatment. These protocols emphasize that measures to monitor and support coagulation should be initiated as early as possible to guide a goal-directed treatment strategy. Although the evidence does not uniformly demonstrate the superiority of VEM over CCT-guided therapy for all outcomes (as discussed in Section 6.3), the clinical utility lies in the rapidity of diagnosis and the specificity of therapeutic guidance offered.

Adjunctive Pharmacologic Agents Guided by VHA

The development of VHA has been integral to optimizing the administration of powerful pharmacological hemostatic adjuncts, such as fibrinogen concentrate, Prothrombin Complex Concentrate (PCC), and tranexamic acid (TXA).

Tranexamic Acid (TXA), an antifibrinolytic agent, has gained prominence in trauma care and is associated with a survival benefit, particularly when administered immediately or within three hours of injury. However, the use of TXA requires precision medicine guided by diagnostics. VHAs are the only rapid diagnostic tools that can identify hyperfibrinolysis—the specific target for TXA intervention—by observing rapid clot breakdown (lysis) in real-time. In contrast, fibrinogen concentrate and PCCs are used to rapidly replete specific clotting factor deficiencies detected by VHA parameters, often reducing the need for large volumes of FFP and accelerating clot stability.

The ability of VHA to rapidly phenotype the patient's coagulation status is critical for managing these agents. VHA allows clinicians to determine if a patient is experiencing profuse clot lysis (hyperfibrinolysis), necessitating TXA, or if they are in a state of fibrinolytic shutdown (minimal lysis), where TXA may potentially be harmful by aggravating microcirculatory clotting. The VHA thus supports evidence-based decision-making, minimizing the risks associated with empirical pharmacologic administration.

Viscoelastic Hemostatic Assays (VHAs): Principles and Technological Detail

For laboratory specialists, a deep understanding of the analytical principles, device limitations, and platform heterogeneity of VHA is essential for ensuring accurate testing and proper result interpretation in the highly demanding trauma environment.

Core Principles of Viscoelastic Testing

Viscoelastic hemostatic assays measure the entire clotting process in whole blood, providing a dynamic analysis of the physical properties of the forming clot. Unlike CCTs, VHAs involve the dynamic interaction of platelets, red blood cells, coagulation factors, and fibrinogen—the full physiological components of hemostasis.

The fundamental principle across all VHA platforms involves monitoring the resistance exerted by the clotting whole blood sample against a moving object (a pin or probe) suspended within the sample. This resistance, or viscoelasticity, increases as the clot forms and strengthens, and decreases as the clot lyses. This mechanical output is graphically traced over time, producing a thromboelastogram (TEG) or thromboelastometry (ROTEM) curve.

In the two legacy systems:

- **Thromboelastography (TEG®):** The cup containing the whole blood sample oscillates, and the resulting torque is transmitted via the developing clot to a fixed pin suspended within the cup.
- **Rotational Thromboelastometry (ROTEM®):** The pin rotates slowly within a fixed cup, and the torque or resistance imparted by the clot formation on the pin is measured by a sensitive torsion wire.

The resultant tracing yields specific quantitative parameters that define the chronological steps of coagulation: clot initiation (R/CT), clot kinetics (α/CFT), clot strength (MA/MCF), and clot breakdown (CL/LY).

Comparison of Legacy and Next-Generation VHA Platforms

Viscoelastic testing has progressed significantly since the introduction of TEG in 1948. The legacy devices (TEG 5000 and ROTEM delta) were groundbreaking but presented certain analytical challenges. They required substantial user manipulation, were sensitive to ambient vibration, necessitated relatively large sample volumes, and were prone to user-dependent variability, which could compromise reproducibility .

The last decade has seen the rapid introduction and adoption of next-generation, cartridge-based systems (e.g., TEG 6S, ROTEM sigma, Quantra, and ClotPro). These automated devices represent a major step toward true Point-of-Care Testing (POCT) in the trauma bay. The cartridge design integrates reagents and streamlines the testing process, minimizing pre-analytical and analytical variability that stems from user technique. For instance, the TEG 6S employs resonance technology to measure clot properties , while the ROTEM sigma is a fully automated cartridge system for rotational thromboelastometry. The shift to these cartridge systems has accelerated VHA adoption across critical care settings.

Challenges in Standardization and Device Comparability

Despite the analytical refinement offered by new-generation platforms, the transition has introduced complex challenges regarding standardization and comparability between different devices. Direct comparison between the available VHA technologies is inherently difficult because manufacturers employ different core technologies, measurement principles, and—critically—different reagents for pathway activation.

A key example of this reagent difference lies in the initiation of the extrinsic pathway: ROTEM EXTEM and ClotPro EX-test utilize only tissue factor, whereas the TEG 6s CRT assay employs a dual activation system using both tissue factor and kaolin. Such variations in activators mean that two assays conceptually designed to assess the same pathway may provide substantially different results when analyzing the same patient sample.

Consequently, while researchers frequently find strong to very strong statistical correlations between corresponding parameters across different platforms (e.g., TEG Maximum Amplitude [MA] versus ROTEM Maximum Clot Firmness [MCF]), the absolute numerical values are significantly different for most measurements.

This analytical heterogeneity carries profound operational implications for laboratory management. The lack of direct comparability of absolute values necessitates a stringent approach to internal standardization. Clinically actionable thresholds or target ranges—such as the European recommendation for a FIBTEM MCF of 16 to 20 mm in massively bleeding trauma patients —are device-specific and cannot be blindly transferred between platforms (e.g., from ROTEM to TEG, or vice versa). Therefore, institutions utilizing VHAs must establish and maintain device- and indication-specific transfusion algorithms and reference ranges that are rigorously controlled and validated against local patient populations. This institutional validation is a cornerstone of quality assurance for laboratories operating VHA systems.

Detailed Laboratory Interpretation of VHA Parameters and Assays

The strength of VHA testing lies in its ability to rapidly identify the component deficiency driving the coagulopathy, thus directing specific therapy. This requires a nuanced understanding of the specialized assays and the graphical parameters generated.

Assay Methodology and Activation Pathways

VHAs typically utilize citrated whole blood, which requires the precise completion of the sampling tube to ensure the correct citrate-to-blood ratio and avoid artifactual results due to improper calcium chelation.

Specific ROTEM Assays (with TEG Equivalents):

1. **EXTEM (Extrinsic Activation) / CRT (Complete/Rapid TEG):** Coagulation is activated by a small amount of tissue thromboplastin (tissue factor), reflecting the initiation of the extrinsic pathway. This assay provides the overall dynamics of factor activity and clot strength.
2. **INTEM (Intrinsic Activation) / CK (Kaolin TEG):** Coagulation is initiated via the contact phase, similar to the method used for the aPTT. INTEM is sensitive to deficiencies in factors of the intrinsic pathway (XII, XI, IX, VIII).
3. **FIBTEM (Fibrin Component) / FF (Functional Fibrinogen TEG):** This assay is activated extrinsically, but importantly, a specific platelet inhibitor (such as cytochalasin D) is added to block the contribution of platelets to the clot structure . This technique functionally isolates and quantifies the strength contribution solely derived from fibrinogen polymerization.
4. **APTEM (Aprotinin Test):** Activated extrinsically (like EXTEM), but includes an antifibrinolytic agent (aprotinin or tranexamic acid). Comparing the APTEM tracing to the EXTEM tracing is the laboratory standard for rapid diagnosis of hyperfibrinolysis.
5. **HEPTEM (Heparinase Test):** Activated intrinsically (like INTEM), but includes heparinase, an enzyme that degrades heparin. This test is essential for identifying and confirming circulating heparin contamination or therapeutic heparinization, particularly relevant in patients whose medication history may be unknown.

Interpretation of Coagulation Initiation (R time / CT)

The first measurable parameter is the time until initial clot formation begins, marked by a 2 mm amplitude on the tracing . This is termed the Reaction Time (R) in TEG and Clotting Time (CT) in ROTEM.

The R/CT primarily reflects the functional concentration and activity of circulating coagulation factors required for thrombin generation . A significantly prolonged R or CT indicates delayed initiation of the coagulation web, most commonly due to factor deficiency (which may be corrected by FFP or PCC) or the presence of circulating anticoagulants. The analytical window for VHA parameter acquisition, including the initial CT/R, is sensitive to pre-analytical variables, such as the time the blood sample was taken relative to the trauma event, as coagulation status evolves rapidly post-injury.

Interpretation of Clot Strength (MA / MCF)

The definitive parameter reflecting the mechanical stability and strength of the final clot is the Maximum Amplitude (MA) in TEG and Maximum Clot Firmness (MCF) in ROTEM. MA/MCF integrates the contributions of fibrin polymerization, platelet count, and platelet function.

MA/MCF provides critical prognostic information; depressed values are strongly associated with the need for blood transfusion and increased mortality in trauma patients. This functional parameter is superior to a simple platelet count because it accounts for both the quantity and the functional quality of platelets, as well as the fibrinogen contribution.

Functional Fibrinogen Assessment

The distinction between platelet dysfunction and fibrinogen deficiency, which both contribute to a low MA/MCF, is achieved by interpreting the FIBTEM/FF tracing .

Fibrinogen is often the first factor to become critically deficient in TIC, particularly given its role in the final common pathway of clotting. A low MCF in the EXTEM/CRT tracing mandates rapid interpretation of the corresponding FIBTEM/FF result. If the FIBTEM MCF is low, for example, an A5 value (amplitude at 5 minutes) below 7 mm, or below 12 mm in the setting of ongoing bleeding, this deficit strongly indicates the need for fibrinogen replacement therapy, such as cryoprecipitate or fibrinogen concentrate. Expert recommendations for massively bleeding trauma patients often target high fibrinogen functional levels, such as an EXTEM MCF of 55 to 60 mm and a FIBTEM MCF of 16 to 20 mm.

If the FIBTEM result is adequate but the overall MA/MCF remains low, platelet dysfunction or severe thrombocytopenia is indicated, triggering the need for platelet transfusion. The ability of VHA to provide this rapid differential diagnosis allows for the highly targeted administration of specific components (fibrinogen concentrate versus platelet concentrate), preventing delays and unnecessary exposure to non-indicated products.

Table 2: Core Viscoelastic Hemostatic Assay Parameters and Targeted Therapy

VHA Parameter (TEG / ROTEM)	Phase of Hemostasis	Primary Physiological Component	Abnormal VHA Pattern	Targeted Therapeutic Intervention
R / CT (Reaction / Clotting Time)	Initiation	Coagulation Factors (Intrinsic/Extrinsic)	Prolonged R/CT	FFP or Prothrombin Complex Concentrate (PCC)
α Angle / CFT (Clot Formation Time)	Amplification/Propagation	Fibrinogen/Fibrin Kinetics, Initial Platelet function	Shallow α/Prolonged CFT	Fibrinogen Concentrate/Cryoprecipitate
MA / MCF	Maximum	Fibrinogen &	Low MA/MCF	Platelets,

(Maximum Amplitude / Clot Firmness)	Strength	Platelets		Cryoprecipitate, or Fibrinogen Concentrate
CL / LY (Clot Lysis / Maximum Lysis)	Fibrinolysis	Fibrinolytic System (Plasmin)	Elevated CL/LY (Hyperfibrinolysis)	Tranexamic Acid (TXA)
FIBTEM MCF / FF MA	Fibrin-specific Strength	Fibrinogen Contribution Only	Very Low FIBTEM MCF (<16 mm)	Fibrinogen Concentrate/Cryoprecipitate

Interpretation of Fibrinolysis (CL / LY and APTEM)

The clot lysis phase, measured by **Clot Lysis (CL)** in TEG and **Maximum Lysis (LY)** in ROTEM, is perhaps the most unique and clinically critical element assessed by VHAs, as it provides real-time functional information on the patient's capacity to break down the clot.

Trauma patients exhibit two distinct, high-mortality fibrinolytic phenotypes that CCTs cannot differentiate:

1. **Hyperfibrinolysis:** Characterized by excessive and rapid clot breakdown (high CL or LY, often $>15\%$ at 30 minutes). Although the least common phenotype in trauma patients (18% of one study cohort), it is associated with the highest mortality rate (37%) primarily due to massive hemorrhage . The immediate confirmation of hyperfibrinolysis requires comparison of the EXTEM tracing with the APTEM tracing: if clot lysis is normalized in the APTEM assay (which contains a fibrinolytic inhibitor), hyperfibrinolysis is confirmed . This finding mandates immediate administration of antifibrinolytic agents (TXA).
2. **Fibrinolytic Shutdown:** This is the most prevalent phenotype (46% of patients) and is characterized by minimal or zero clot lysis, indicating a suppressed fibrinolytic system. Although hemorrhage is still a risk, deaths in this group are often attributed to later complications, such as multi-organ failure (MOF), linked to microcirculatory fibrin deposits .

The ability to rapidly and functionally differentiate between hyperfibrinolysis and fibrinolytic shutdown is paramount. Since the risks and benefits of TXA are dependent on the underlying fibrinolytic state , VHA analysis moves the management of fibrinolysis from an empirical, time-based decision to a precise, diagnostic-driven intervention.

Analytical and Logistical Quality Management for the VHA Laboratory

Given that VHAs often operate as Point-of-Care (POCT) tests outside the controlled central laboratory environment, meticulous adherence to Quality Assurance (QA) and Quality Control (QC) protocols is essential. Reliable, accurate, and precise results are mandatory to guide life-saving clinical decisions.

Pre-analytical Variables: The Critical First Steps

Pre-analytical variables represent the largest potential source of error in VHA testing, particularly in the high-stress environment of the trauma bay. Laboratory expertise is crucial for managing these steps.

Sample Integrity: Because VHAs measure functional coagulation in whole blood, the integrity of the sample must be maintained.

- **Anticoagulant Ratio:** VHAs typically require citrated blood. A strict ratio of citrate to blood is essential for accurate results; incomplete filling of the collection tube results in an excess of citrate, artificially chelating too much calcium and leading to spuriously prolonged CT/R times.
- **Contamination:** Sampling must avoid contamination, particularly with heparin, which is often used in intravenous lines or catheters. Heparin contamination will drastically inhibit coagulation, rendering the EXTEM/INTEM results unusable unless the effect can be neutralized or confirmed using the HEPTEM assay .
- **Time Sensitivity:** The coagulation status of a trauma patient changes rapidly. The time the blood sample is drawn relative to the injury, and the delay between collection and analysis, are critical parameters that must be logged and monitored. Any delay compromises the value of the result, as the VHA is intended for real-time decision-making (results within 15 minutes).

Quality Assurance (QA) and Quality Control (QC) Protocols

To ensure reliability, the hemostasis laboratory must maintain rigorous quality processes encompassing internal and external mechanisms.

Internal Quality Control (IQC): Modern viscoelastic devices are designed with extensive internal electronic and software checks to monitor the integrity and performance of key subsystems (e.g., thermal regulation, mechanical sensors). These IQC checks are automated and typically run at startup, during pre-test validation, and on a periodic basis (e.g., every eight hours) to verify system performance within established limits. These comprehensive internal controls check the integrity of the entire testing process across analytical and post-analytical phases, and even partially into the pre-analytical phase.

External Quality Assessment (EQA): Given the inherent technological differences and the lack of standardization in absolute values across platforms , participation in EQA programs is essential. These programs allow laboratories to benchmark their performance against others, which is vital for verifying the validity of institution-specific reference ranges and algorithms. Furthermore, the complexity introduced by device-specific reagents and proprietary technologies means that reference ranges must be internally validated following strict guidelines, such as those published by the Clinical and Laboratory Standards Institute (CLSI EP23-A).

Point-of-Care (POCT) vs. Centralized VHA Deployment

The implementation of VHA in trauma care inherently involves a decision regarding its location of use. The primary advantage of deploying VHA as a POCT device (i.e., in the trauma bay or operating room) is speed—the ability to obtain real-time results that impact immediate clinical decisions, bypassing the delays associated with sample transport to a central lab.

However, this decentralized model introduces logistical and economic challenges. POCT devices typically incur a higher cost per test due to the expense of cartridges, and they demand more frequent calibration, quality control testing, and diligent inventory management compared to high-throughput centralized platforms.

Crucially, the deployment of POCT necessitates rigorous governance. To maintain analytical quality and prevent adverse events resulting from operator error or failure to diagnose, the management of POCT devices must remain under the stringent oversight of the central laboratory. Laboratory professionals are tasked with managing the technical validation, operator training, and ongoing outcome-based assessment to ensure that the rapid results generated by POCT systems are consistently accurate and lead to appropriate timed treatment.

Integration of VHAs into Massive Transfusion Protocols (MTPs): Evidence and Outcomes

VHA-Guided Treatment Algorithms in Practice

The central utility of VHA in trauma care is its ability to rapidly generate actionable data—often within 5 to 15 minutes—that allows clinicians to transition from empirical resuscitation to a targeted, goal-directed strategy.

VHA tracings provide efficient identification of specific coagulation abnormalities. For example, a prolonged CT/R indicates a factor deficiency requiring plasma or PCC, while a low FIBTEM MCF points specifically to a need for fibrinogen concentrate . This targeted approach ensures that transfusion decisions are based on the individual patient's deficits, rather than fixed ratios. Observational studies have consistently demonstrated the utility of VHA parameters in predicting transfusion requirements better than CCTs; for instance, MA/MCF is superior to platelet count for predicting the need for platelet transfusion.

By identifying specific component deficiencies, VHA-guided algorithms facilitate the appropriate administration of plasma, cryoprecipitate, and platelets. Studies comparing VHA-guided protocols to empirical or CCT-guided strategies have repeatedly shown that VHA guidance results in non-inferior patient outcomes while significantly reducing the overall consumption of blood products.

Impact on Blood Product Utilization and Resource Management

The resource-sparing effect of VHA-guided transfusion protocols is well-documented and represents a significant operational benefit for trauma centers. A VHA-based strategy has been associated with a demonstrable reduction in overall blood product use and associated costs. Furthermore, one strategy was linked to an increase in the number of patients who were alive and free of massive transfusion at 24 hours.

The ability of VHA to provide rapid, functional data allows treatment to be precisely tailored, avoiding the unnecessary administration of components that are not deficient. This reduction in unnecessary transfusion limits patient exposure to allogeneic blood products, which minimizes associated morbidity and resource utilization.

Analysis of Major Randomized Controlled Trials (RCTs) and Controversies

While VHA has been widely adopted and recommended in clinical guidelines , its superiority over CCT-guided therapy in terms of overall mortality remains a subject of intense debate, primarily centered around the results of the Implementing Treatment Algorithms for the Correction of Trauma Induced Coagulopathy (ITACTIC) trial .

The ITACTIC trial was a pragmatic, multicenter, randomized controlled trial designed to compare outcomes in severely injured patients receiving Massive Hemorrhage Protocols (MHPs) supplemented by goal-directed interventions guided by either CCTs or VHAs.

The Itactic Trial Findings:

The primary outcome of the ITACTIC trial—28-day mortality—did not show a statistically significant difference between the VHA group (25% mortality) and the CCT group (28% mortality) . Similarly, there was no difference in the proportion of patients alive and free of massive transfusion at 24 hours .
Operational Analysis and Interpretation:
A deeper analysis of the ITACTIC trial data highlighted critical issues regarding the translation of rapid diagnostic capability into effective patient care . The study demonstrated that VHA-guided patients were significantly more likely to receive goal-directed treatment (GDT) than the standard CCT group (76% versus 47%) and received that treatment significantly faster (median time to first GDT was 68 minutes

for VHA versus 110 minutes for CCT) .
However, despite receiving quicker treatment, the analysis revealed that only 54% of patients overall received an indicated GDT, and of those, only 20% succeeded in correcting their coagulopathy by the end of the initial resuscitation period . The lack of a uniform overall mortality benefit was hypothesized to be a result of systemic failure: despite providing a faster diagnosis, the necessary blood products or factor concentrates were delivered too late or in insufficient quantity to effectively reverse the coagulopathic state in time to save the patient . The median time to GDT of 68 minutes, while faster than CCT, is considered excessively delayed for rapidly exsanguinating trauma patients.

This controversy reinforces a crucial logistical point for laboratory specialists and hospital administration: the clinical utility of VHA is inextricably linked to the operational efficiency of the MTP. VHA provides the analytical answer quickly, but if the logistical chain (blood bank processing, delivery, and administration) cannot keep pace, the diagnostic advantage is lost.

Subgroup Outcomes:
Importantly, not all studies corroborate the general lack of mortality benefit. Some randomized controlled trials and systematic reviews have demonstrated that VHA-guided strategies were either superior or equal to CCT-guided strategies in reducing mortality . Subgroup analyses, particularly in patients with severe traumatic brain injury (TBI), suggested that VHA guidance improved 28-day mortality outcomes .

Table 3: Key Findings from Clinical Trials Evaluating VHA-Guided Resuscitation in Trauma

Trial/Review Focus	Design/Reference	Primary Outcome Finding	Secondary Outcome/Subgroup Finding
ITACTIC Trial	RCT (NCT02593877)	No difference in overall 28-day mortality (VHA: 25% vs CCT: 28%) .	VHA reduced blood product usage and accelerated time to goal-directed therapy (68 min vs 110 min) .
Systematic Reviews	Meta-analysis/Reviews	Most studies found no significant difference in mortality.	VHA was superior or equal to CCT in reducing mortality in certain subgroups (e.g., TBI patients) .
VHA Utility vs CCT	Observational/Validation Studies	VHA parameters (rapid TEG, α-angle, MA) better predicted need for transfusion (RBC, plasma, platelets) than PT or PTT.	VHA provides a functional diagnosis that guides immediate specific component therapy, reducing unnecessary exposure to blood products.

VHA Utility in Specific Trauma Subpopulations

Traumatic Brain Injury (TBI) and Platelet Dysfunction

Traumatic Brain Injury (TBI) presents a unique and particularly challenging coagulopathy that frequently exacerbates primary neurological injury . Coagulopathy is highly prevalent in TBI and is strongly associated with poor outcomes, including increased mortality and progression of intracranial hemorrhage (tICH) .

The hemostatic disorder associated with TBI often manifests as a primary disorder of hemostasis, specifically platelet dysfunction . This dysfunction involves the inhibition of key platelet receptors, particularly those mediated by adenosine diphosphate (ADP) and arachidonic acid (AA), and occurs independent of the total circulating platelet count . Elevated soluble platelet ligands have been observed in severely injured patients, further supporting the role of functional platelet deficits.

In this specific population, the advantages of VHA over CCTs are magnified. Since CCTs are insensitive to functional platelet deficiencies , the VHA’s ability to functionally assess clot strength (MA/MCF) becomes the critical, real-time measure of primary hemostasis . Admission TEG parameters, such as abnormal R time and MA, have been correlated with predicting the need for neurosurgical intervention and the progression of intracranial bleeding, which CCTs generally fail to achieve . This functional diagnosis allows for immediate guidance on crucial interventions in neurotrauma, such as rapid platelet transfusion or, if appropriate, pharmacological reversal of antiplatelet medications.

Furthermore, a significant proportion of patients with severe TBI exhibit fibrinolytic shutdown (suppressed clot lysis), which is independently associated with worse clinical outcomes . VHA's capacity to identify this specific phenotype guides the appropriate administration or avoidance of TXA, contributing to more precise patient management.

Detection of Hypercoagulability and Thrombotic Risk

Beyond guiding acute resuscitation, VHAs offer a valuable tool for serial monitoring throughout the trauma patient's hospital course. As discussed, the trajectory of TIC often evolves from an acute hypocoagulable state to a subacute or late hypercoagulable state.

VHA parameters can reliably detect evolving hypercoagulability, manifested as shortened R/CT times or hypernormal MA/MCF values. Longitudinal VHA monitoring can identify patients at increased risk of venous thromboembolism (VTE) due to this prothrombotic phenotype. This capability supports the transition from aggressive hemostatic resuscitation to appropriate thromboprophylactic strategies in the critical care setting. Future research may explore the use of VHA profiles to guide individualized, timing-based initiation of thromboprophylaxis, further advancing precision medicine in trauma care.

Conclusion and Future Directions

Viscoelastic Hemostatic Assays (TEG and ROTEM) represent a critical advancement in the laboratory assessment and management of trauma-induced coagulopathy. These whole-blood, Point-of-Care tests overcome the fundamental limitations of CCTs by providing rapid, dynamic, and comprehensive functional profiles of clot formation, strength, and dissolution, information indispensable for guiding goal-directed hemostatic resuscitation . The clinical significance is evident in the VHA's ability to differentially diagnose coagulation factor deficiency, functional fibrinogen deficits, and distinct fibrinolytic phenotypes (hyperfibrinolysis versus shutdown) .

For the laboratory specialist, the successful integration of VHA technology requires a deep commitment to analytical rigor. The operational benefits—reduced blood product utilization and accelerated time to targeted therapy —are only realized when stringent quality management protocols are upheld, especially concerning pre-analytical variables and device-specific calibration . The lack of direct comparability between absolute values across different VHA platforms necessitates institutional validation of local, device-specific transfusion algorithms.

While large-scale randomized trials like ITACTIC have indicated that VHA guidance, in isolation, does not uniformly improve overall mortality compared to CCT guidance, the detailed analyses confirm that VHA provides a significantly faster and more targeted diagnosis . The failure to observe widespread mortality reduction is attributed not to the diagnostic tool itself, but to operational bottlenecks—the persistent time delay in translating the rapid VHA result into the actual delivery of corrective therapy .

Future efforts in trauma care must focus on bridging this diagnostic-therapeutic gap. This involves optimizing logistics, improving Massive Transfusion Protocol training, and refining MTP processes to ensure that VHA's analytical speed leads to therapeutic delivery within clinically relevant timeframes. Furthermore, ongoing research will refine the utility of next-generation VHA devices and explore their expanded role in managing specific trauma coagulopathies, particularly functional platelet dysfunction in TBI, thereby securing VHA's role as a cornerstone of precision medicine in hemostatic resuscitation .

References

1. Uncontrolled hemorrhage and trauma-induced coagulopathy (TIC) are the two predominant causes of preventable death after trauma.
2. In acutely injured trauma patients, only 3% of US civilian patients and 7% of military patients require MT, consuming approximately 70% of all blood transfused at a trauma center.
3. The development and implementation of massive transfusion protocols (MTPs) have been associated with a reduction in mortality and overall blood product use in trauma centers.
4. Acute intrinsic coagulopathy arising in severely injured trauma patients is now termed trauma-induced coagulopathy (TIC) and is an emergent property of tissue injury combined with hypoperfusion.
5. Early TIC is often associated with hypocoagulability due to factors such as fibrinogen depletion, impaired thrombin generation, and platelet dysfunction, and is exacerbated by the “lethal triad” of coagulopathy, hypothermia, and acidosis. In contrast, late TIC can present as a hypercoagulable state, linked to venous thromboembolism and multiple organ failure.
6. Hypocoagulability is a multifaceted component of trauma pathophysiology that involves coagulation factor inhibition, platelet dysfunction, fibrinogen consumption, and hyperfibrinolysis. These changes occur more often in those trauma victims having both severe anatomical injury and tissue hypoperfusion from major blood loss.
7. Conventional coagulation tests (CCTs) have been incorporated into algorithms but suffer from slow turn-around times and may lack the ability to guiding individual therapies.
8. Only 31% of patients with trauma-induced coagulopathy present with abnormalities in both conventional and viscoelastic coagulation assays.
9. A plethora of observational studies provided weak evidence of improved survival with higher blood product:RBC ratios than was with usual care at that time, though no specific ratio (eg, 1:1 or 1:2 of FFP:RBC or platelet:RBC, respectively) was unequivocally superior.
10. Subsequent studies have confirmed the value of VETs in targeting BCT for trauma patients who require blood component resuscitation as well as adjunct hemostatic agent resuscitation with Prothrombin Complex Concentrate (PCC), fibrinogen concentrate, activated recombinant Factor VIIa (rFVIIa), and the antifibrinolytic tranexamic acid (TXA).
11. r-TEG can be used to guide resuscitation strategy by permitting transfusion based upon individual patient deficits.
12. Clinical assessment and commonly used coagulation tests are inaccurate and time-consuming.
13. In patients with ongoing hemorrhage and concern for coagulopathy, we conditionally recommend using TEG/ROTEM-guided transfusions, compared with traditional coagulation parameters, to guide

blood component transfusions in each of the following three groups: adult trauma patients, adult surgical patients, and adult patients with critical illness.

14. Based on the available evidence, the Eastern Association for the Surgery of Trauma conditionally recommends using TEG/ROTEM to guide blood transfusion for patients with ongoing hemorrhage and concern for coagulopathy.[13]
15. Point-of-care viscoelastic methods (VEM) assist target-controlled haemostatic treatment.[14]
16. Measures to monitor and support coagulation should be initiated as early as possible and used to guide a goal-directed treatment strategy.
17. The use of tranexamic acid (TXA) and fibrinogen, guided by these visco-elastic tests, has shown promise in trauma patients. TXA has been associated with survival benefit when administered immediately or within 3 hours of injury.
18. Reflex testing with APTEM is performed when maximum lysis in EXTEM is $>15\%$. APTEM should be compared to EXTEM to identify hyperfibrinolysis.
19. Most importantly, the figures of clot activation, kinetics, and strength are available within 15 min using rapid testing.
20. Viscoelastic hemostatic assay (VHAs) are whole blood point-of-care tests that have become an essential method for assaying hemostatic competence in liver transplantation, cardiac surgery, and most recently, trauma surgery involving hemorrhagic shock.
21. The Thromboelastogram (TEG) provides an active, comprehensive view of clotting formation and lysis. The test works by measuring stickiness, or resistance, of a clot forming around an immersed pin.
22. TEG® parameters: R – reaction time; k – kinetics; α - alpha angle; MA – maximum amplitude; CL – clot lysis. ROTEM® parameters: CT – clotting time; CFT – clot formation time; α - alpha angle; MCF – maximum clot firmness; LY – clot lysis.
23. Within the last decade, the cup and pin legacy devices, such as thromboelastography (TEG® 5000) and rotational thromboelastometry (ROTEM® delta), have been supplanted not only by cartridge systems (TEG® 6S and ROTEM® sigma), but also by more portable point-of-care bedside testing iterations of these legacy devices.
24. Shortcomings of current systems include substantial laboratory intensity, user-dependent reproducibility, relatively large sample volumes, sensitivity to ambient vibration and limited comparability between techniques and devices.
25. Although ROTEM EXTEM and ClotPro EX-test assays activate only via tissue factor, TEG6s CRT uses dual activation via tissue factor and kaolin.
26. Strong to very strong correlations were observed between corresponding TEG 6s and ROTEM Sigma parameters. However, absolute values showed significant differences for most of the measurements.
27. Device- and indication-specific transfusion algorithms are essential for the accurate interpretation of measurements and adequate hemostatic therapy.
28. “Correct sampling“ means: Complete filling of the sampling tube (in order to ensure the correct citrate-blood ratio); the assurance, during sampling from catheters, that no contamination with heparin or other.
29. In EXTEM, coagulation is activated by a small amount of tissue thromboplastin (tissue factor). In FIBTEM, coagulation is activated as in EXTEM, but platelets are blocked. In APTEM, a fibrinolysis inhibitor is added. HEPTEM adds heparinase to degrade heparin.
30. TEG® Functional Fibrinogen uses extrinsic pathway activation with a platelet inhibitor to restrict platelet function. This allows for quantification of fibrinogen contribution to clot strength.
31. Time blood sample taken relative to trauma (< 1 h/ > 1 h). Clotting time (period to 2 mm amplitude) is measured by ROTEM CT or TEG R (reaction time).
32. Prolonged reaction time (R) in TEG and clotting time (CT) in ROTEM indicates delayed initiation of the coagulation web.
33. TEG® MA and ROTEM® MCF are associated with both the need for blood transfusion and mortality.
34. If FIBTEM A5 <7 mm or less than 12 mm with ongoing bleeding, fibrinogen replacement may

improve clinical hemostasis.

35. European ROTEM users recommend EXTEM MCF of $55-60$ mm and FIBTEM MCF of $16-20$ mm as target values in massively bleeding trauma patients.
36. Hyperfibrinolysis was the least common phenotype (18% of study population) but was associated with the highest mortality (34%), whereas fibrinolytic shutdown was the most common phenotype (46%) and was associated with increased mortality (22%).
37. Platelet dysfunction has also been associated with TBI by several studies.
38. Quality assurance in a clinical laboratory is essential to ensure reliable, accurate and precise laboratory test results all the time.
39. The internal QC checks verify the integrity of the testing process across the analytical, post-analytical, and part of the preanalytical phases. These electronic/software checks are performed on 3 timing cycles: (a) during Power On, (b) during pre-test validation, and (c) on a periodic basis (every 8 h).
40. The biggest advantage of POCT is the ability to obtain real-time results that impact immediate clinical decisions. POCT devices require frequent calibration, quality control testing, and reagent replenishment, all of which increase operating costs.
41. POCT test introduction in clinical practice should be assessed by an outcome-based policy to avoid adverse events, failure to diagnose providing appropriate timed treatment.
42. In the setting of trauma, studies have shown that both ROTEM- and TEG-guided treatment algorithms result in non-inferior patient outcomes and result in decreased overall usage of blood products compared to empiric massive transfusion protocols.
43. A VHA-based strategy was associated with an increase of the number of patients alive and free of MT at 24 h together with an important reduction of blood product use and associated costs. However, that did not translate into an improvement in mortality.
44. 28-day mortality was not different overall (VHA: 25%, CCT: 28%).
45. Median time to first goal-directed treatment was 68 (53 to 88) min for viscoelastic and 110 (77 to 123) min for standard ($P = 0.005$). Interventions arrived late during resuscitation.
46. 71% were coagulopathic on admission, and 16% developed a coagulopathy during resuscitation. However, only 54% of patients received goal-directed treatment, and only 20% corrected their coagulopathy.
47. Notable, two RCTs showed that the VHA-guided strategy was superior or equal to the conventional coagulation test-guided strategy in reducing mortality, respectively. In the ITACTIC study, a reduction in 28-day mortality was observed in trauma patients who also had a severe traumatic brain injury (TBI) when guided by VHA.
48. Given the heterogenous nature of the available evidence including methodology and study outcomes, the comparative difference between VHA and CCA in predicting rates of neurosurgical intervention, tICH progression, or mortality in patients with TBI remains inconclusive.
49. Prognosis and progression of intracranial bleeding are dependent on coagulopathy identified by admission TEG® parameters but not CCAs.

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