

Multidisciplinary perspective on the use of viscoelastic tests in clinical practice (part 2)

Perspectiva multidisciplinaria del uso de test viscoelásticos en la práctica clínica (parte 2)

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Abstract

Viscoelastic tests, point-of-care coagulation devices, are key tools in hemorrhage management, especially in surgery, but their use is expanding to other fields such as obstetrics, ECMO patients, and burn victims. While their role in cardiac surgery, polytrauma, and liver transplantation is more established, evidence regarding their impact on mortality remains controversial. One of the main limitations is the lack of result validation, as viscoelastic tests are not comparable to standard coagulation tests, showing significant variability (up to 83% in ROTEM®). Additionally, quality control is not always managed by the laboratory, which may affect reliability. Anesthesiology, laboratory medicine, and hematology are involved in their interpretation. This document, supported by their respective scientific societies, aims to provide a comprehensive perspective of the functionality, scientific evidence, implementation, quality control, and potential economic benefits of viscoelastic tests.

Keywords: Viscoelastic tests. Point of care. Haemostasis. Bleeding. Surgery. ECMO.

Resumen

Los test viscoelásticos, pruebas de coagulación en el punto de atención, son herramientas clave en el manejo de la hemorragia, especialmente en cirugía, pero su uso se expande a otros ámbitos como obstetricia, pacientes en ECMO y quemados. Aunque su papel en cirugía cardíaca, politraumatizados y trasplante hepático está más consolidado, la evidencia sobre su impacto en la mortalidad sigue siendo controvertida. Una de las principales limitaciones es la falta de validación de resultados, ya que los test viscoelásticos no son comparables con los test estándar de coagulación, mostrando una variabilidad significativa (hasta el 83% en ROTEM®). Además, el control de calidad no siempre depende del laboratorio, lo que puede

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Date of reception: 22-02-2025

Date of acceptance: 23-07-2025

DOI: 10.24875/RHT.M25000082

Available online: 11-11-2025

Hemost Trombos (Eng). 2025;2(3):81-100

www.revistahemostasiaytrombosis.com

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afectar su fiabilidad. Anestesiología, laboratorio y hematología participan en su interpretación. Este documento, respaldado por sus respectivas sociedades científicas, busca ofrecer una visión integral sobre el funcionamiento, la evidencia, la implementación, el control de calidad y los posibles beneficios económicos de los test viscoelásticos.

Palabras clave: Test viscoelásticos. Punto de atención al paciente. Hemostasia. Hemorragia. Cirugía. ECMO.

Scientific evidence for the use of viscoelastic tests in various clinical scenarios

Cardiac surgery

Cardiac surgery is probably one of the clinical scenarios in which viscoelastic tests (VET) have been most widely used to guide the transfusion of hemostatic blood components. On one hand, these patients are usually exposed preoperatively to antiplatelet and anticoagulant drugs; on the other, most of them require the use of a perfusion pump to obtain an immobile surgical field, which necessitates a certain degree of hemodilution and the administration of heparin to limit the activation of blood coagulation and the inflammatory cascade produced by the contact of blood cells with the artificial surfaces of the extracorporeal circuit. All of this results in consumption of coagulation factors and platelet activation¹. They, therefore, present a multifactorial coagulopathy that complicates management and requires knowledge of the hemostatic and fibrinolytic capacity in the shortest possible time – information that currently only VET can provide.

Since the publication of the meta-analyses by Li et al.² and Meco et al.³, it has been demonstrated that the use of VET in the management of bleeding or coagulopathy in cardiac surgery is effective in reducing allogeneic blood product transfusion and postoperative bleeding at 12 and 24 hours after surgery. Subsequent studies, such as that of Kuiper et al.⁴, which analyzed the implementation of a transfusion algorithm guided by rotational thromboelastometry (ROTEM®), confirmed these results and further showed cost savings, but found no reductions in re sternotomy or mortality rates, nor improvement in prognosis.

Thromboelastometry has also been studied in this surgical field as a predictor of postoperative blood loss. It was determined to have a negative predictive value of up to 94%, but a very low positive predictive value (0-22%), which should alert us to the existence of false positives⁵.

Studies conducted in patients undergoing cardiac surgery after disconnection from extracorporeal circulation to determine whether VET (ROTEM®) could

detect factor XIII deficiency have not been able to predict this deficiency⁶.

The results of all these investigations have led to the incorporation of VET into current clinical guidelines for transfusion algorithms in cardiac surgery, with the aim of reducing perioperative bleeding and blood transfusion, with a Class I, B recommendation⁷⁻⁹.

Regarding the latest type of VET that uses sonorheometry, expert opinions are controversial as to whether it is interchangeable with the other VET¹⁰. Nevertheless, used on its own within an algorithm, it has demonstrated a reduction in transfusion requirements¹¹. Larger studies in cardiac surgery are needed to prove its equivalence or superiority compared to other VET.

Liver transplantation (patients with liver failure or cirrhosis)

CIRRHOSIS

Cirrhotic patients present a special situation of fragile “rebalancing” between coagulation, anticoagulation, and fibrinolysis. Coagulation factors (II, V, VIII, IX, X, XI, XII, XIII, and fibrinogen), natural anticoagulants (proteins C and S, antithrombin), and the protease ADAMTS13 are decreased. In addition, these patients present thrombocytopenia due to splenic sequestration from portal hypertension and reduced thrombopoietin synthesized in the liver. Conversely, endothelial-derived factors (VIII, von Willebrand factor) are increased, thrombomodulin synthesized in the endothelium is normal, and fibrinolytic components – plasminogen (decreased) and plasminogen activator (increased) – tend toward hypofibrinolysis, which aggravates the risk of thrombosis associated with portal hypertension.

Until now, conventional laboratory tests (prothrombin time [PT], activated partial thromboplastin time [aPTT], and international normalized ratio [INR]) and platelet count have been used to guide the treatment of coagulopathy with blood product transfusions in clinical bleeding scenarios, such as GI bleeding, and prior to invasive or interventional procedures (central venous access, paracentesis, liver biopsy, radiofrequency LOES [Local Ablation with External System], etc.)¹².

The INR only reflects the first 5-10% of fibrin formation and does not provide data on the interaction of the different components, nor on clot firmness or stability. Prolonged INR functions as a marker of liver failure but is not a good indicator of hypocoagulability. The limitations of conventional markers have renewed interest in global hemostasis assays such as thromboelastography (TEG) and ROTEM®, which have been widely used in the context of liver transplantation and perioperative hemorrhage.

In the study by Hum et al.¹³, patients with cirrhosis at different stages presented prolonged INR but VET values within normal range on TEG (r-time, alpha angle, k-time, and maximum amplitude [MA]), although all worsened as disease stage advanced, with MA values in Child stage C slightly below normal. This reaffirms that INR and isolated platelet count do not reflect the hemostatic state of cirrhotic patients.

VET have advantages over conventional laboratory tests because they provide this information; they are whole-blood, dynamic analyses, and they yield information on procoagulant factors, anticoagulants, and platelets.

There is a growing body of evidence demonstrating the superiority of VET for determining bleeding risk prior to interventional procedures in cirrhotic patients, thus avoiding unnecessary transfusions. Although clinical trials using VET, INR, and platelet count to guide transfusions before invasive procedures in cirrhosis have shown a statistically significant reduction in transfusions of fresh frozen plasma (FFP), platelets, and cryoprecipitates with VET, no differences were found in ICU stay, hospital admissions, or mortality¹⁴.

In GI bleeding and coagulopathy – frequent complications in cirrhotic patients, with limited evidence regarding the best transfusion strategy – there are data favoring VET-guided transfusion. VET use is widely accepted in liver transplantation, and extrapolating its use to other clinical situations in cirrhotic patients may optimize blood product use¹⁵.

VET also play an important role in patients who develop portal vein thrombosis, a situation not evaluable with conventional laboratory tests.

About 25% of decompensated cirrhotic patients present portal vein thrombosis. Hypercoagulability varies depending on cirrhosis etiology (5% in non-cholestatic cirrhosis, 28% in biliary cholangitis 1A, 45% in sclerosing cholangitis), as demonstrated by VET, despite prolonged INR¹⁶.

Evidence is clearer in cirrhotic patients who develop hepatocellular carcinoma, with a direct relationship

between increased maximum clot firmness (MCF) amplitude in FIBTEM and portal vein thrombosis development.

Decompensated cirrhotic patients who develop sepsis usually present hypocoagulability values on TEG and ROTEM®¹⁷.

Assessment of bleeding risk and VET-guided transfusions result in reduced use of blood products in cirrhotic patients requiring invasive procedures or presenting hemorrhage. Despite these advantages, studies conducted to date have limited statistical power to validate widespread VET use in these patients¹⁸. Cut-off values in VET must be standardized to ensure more reproducible bleeding risk assessment in cirrhosis. VET may contribute to the development of transfusion guidelines and preventive fibrinolysis protocols for the optimal management of cirrhotic patients with associated coagulopathy.

LIVER TRANSPLANTATION

The coagulopathy already described in cirrhosis adds to alterations produced during the different phases of liver transplantation, with absence of factor synthesis in the anhepatic phase and variable synthesis after reperfusion of the implanted organ. Ischemia and reperfusion release toxins that condition the so-called reperfusion syndrome, mainly causing hemodynamic but also hemostatic instability, increasing bleeding. Hemostatic competence is not restored until the implanted liver recovers its synthesis and metabolic function¹⁹.

The introduction of global coagulation assays, such as thrombin generation or VET, has represented significant progress in the assessment and management of patients with liver disease. In 2019, the Liver Intensive Care Group of Europe (LICAGE) recommended VET as the best reflection of bleeding risk vs standard laboratory tests, albeit with limitations (recommendation 1C)²⁰. Similarly, the following year the Society of Critical Care Medicine also suggested the use of VET over laboratory tests²¹. In 2022, the International Society on Thrombosis and Haemostasis recommended against laboratory tests for bleeding risk assessment but did not issue guidance regarding VET²². Parallel to these recommendations, VET use has become widespread in clinical practice, and evidence has increased in recent years. Hartmann et al.²³ conducted a meta-analysis demonstrating that VET-guided bleeding management in cirrhotic or liver transplant patients resulted in a significant reduction in platelet transfusion (fivefold

lower), combined platelet and plasma transfusion, and overall blood component transfusion, without increased bleeding risk, and with reduced 7-day mortality. A reduction in FFP use was also observed, although it did not reach statistical significance.

Specifically in liver transplantation, evidence for VET-guided transfusion is limited, yet paradoxically they are used in most centers. A 2019 study showed that a thromboelastometry-based algorithm reduced blood component transfusion by four units, with increased fibrinogen use, decreased FFP transfusion, and tranexamic acid administration²⁴. More recently, the Spanish Society of Liver Transplantation and the Spanish Society of Thrombosis and Hemostasis published a consensus document recommending VET use (recommendation 1B)²⁵. They highlight its utility as a tool to assess coagulopathy severity before invasive procedures, to develop protocols, and, intraoperatively, to identify the cause of bleeding and optimize patient hemostasis in an individualized, dynamic, and evolving manner, as well as to evaluate the effect of hemostatic agents.

In conclusion, VET have enabled global and dynamic assessment of coagulopathy in liver patients, offering better evaluation of hemorrhagic risk than standard laboratory tests and optimizing the use of hemostatics and blood products. Nevertheless, further studies are needed to establish reference values to optimize and standardize perioperative management in these patients.

POLYTRAUMA PATIENTS

Polytrauma patients are characterized by a coagulopathy due to exogenous and endogenous mechanisms, known as acute coagulopathy of trauma shock (ACoTS), which is early in onset and dynamic, and determines patient prognosis (these patients will have higher mortality, more multiorgan failure, and longer lengths of stay)²⁶. For this reason, it has been the target of recent resuscitation strategies for these patients, establishing the concept of damage control resuscitation (DCR), with massive transfusion protocols as a cornerstone. The main feature is to implement an early resuscitation that attempts to improve hemostatic capacity, thereby helping to minimize hemorrhage²⁷.

However, these strategies are often applied empirically and with little individualization, which entails the risk of unnecessary overtreatment, associated with specific morbidity and mortality and consumption of resources that are often scarce. All this occurs in a

context of coagulopathy with a wide variety of phenotypes, ranging from hypo- to hypercoagulability²⁸. In this strategic line, monitoring with VET has been introduced; the rapid availability of results, their greater specificity, and the possibility of goal-directed therapy make them especially attractive in a highly dynamic scenario with substantial phenotype variability²⁹. Gradually, specific algorithms have been designed and a new goal-directed treatment strategy based on these techniques has been defined, which in general is linked to the use of factor concentrates³⁰.

What evidence do we have that this strategy is useful in the scenario at hand? To answer this question, we should turn to the most influential document: the European guidelines for the management of the polytrauma patient, sixth edition. In this document, VET are recommended from different perspectives³¹:

- *Recommendation 11*. Early and repeated monitoring of hemostasis is recommended using either conventional laboratory techniques such as PT, INR, Clauss fibrinogen, and platelet count, or point-of-care PT/INR, or VET (Grade 1C).
- *Recommendation 24*. Strategies to monitor and treat coagulation should be initiated immediately upon arrival at the hospital (Grade 1B).
- *Recommendation 26*. Resuscitation measures should be continued using a goal-directed strategy, guided by conventional laboratory techniques or by VET (Grade 1B).
- *Recommendation 27*. If a hemostatic resuscitation strategy based on plasma transfusion is used, subsequent plasma use should be guided by classical laboratory tests (PT or aPTT > 1.5) or by VET evidence of a coagulation factor deficit (Grade 1C).
- *Recommendation 28*. If a strategy based on coagulation factor concentrates is used, treatment with concentrates should be based on classical laboratory tests or on VET evidence of a coagulation factor deficit (Grade 1C).
- *Recommendation 29*. Treatment with fibrinogen concentrate or cryoprecipitate is recommended if major bleeding is accompanied by hypofibrinogenemia (viscoelastic signs of functional deficit or plasma fibrinogen < 1.5 g/L) (Grade 1C). An initial fibrinogen dose of 3-4 g is suggested. This is equivalent to 15-20 units of cryoprecipitate or 3-4 g of fibrinogen concentrate. Repeated doses should be guided by VET and by laboratory-provided fibrinogen levels (Grade 2C).

As we can see, the levels of evidence are only moderate, recommending VET at the same level as

laboratory coagulation times, despite the theoretical advantages of the former, especially from a pathophysiological standpoint. Nor is it considered whether goal-directed therapy might be superior to the application of a fixed ratio. This is largely due to the inherent difficulty of conducting methodologically optimal studies in this setting.

There are indeed studies showing that VET-based resuscitation improves outcomes and minimizes transfusion³², and others demonstrating the diagnostic and prognostic capability of VET³³. There is also a substantial body of literature on the role of hypofibrinogenemia and its management³⁴. Other studies have compared conventional laboratory monitoring with VET^{34,35}. Finally, some studies have compared massive transfusion protocols (MTP) vs goal-directed therapy^{32,36}. Most studies have methodological limitations, but they clearly show a trend favoring the use of VET, although some contradictory results are also found. For this reason, it is worth looking more closely at the most relevant studies.

In 2014, Da Luz et al.³⁷ conducted a systematic review including 55 studies, all of moderate methodological quality, without any randomized clinical trials. They concluded that VET can diagnose the different abnormalities characteristic of coagulopathy in polytrauma patients, but their effect on transfusion requirements and mortality is unclear³⁷.

In 2016, González et al.³⁴ conducted the first randomized clinical trial to compare activation of an MTP guided by VET vs laboratory coagulation times. They concluded that the use of VET in resuscitation of severely polytraumatized patients improves survival compared with the use of laboratory coagulation times, with less transfusion of plasma and platelets³⁴.

In 2017, results of the RETIC study³⁶ were published, aiming to compare management of coagulopathy (diagnosed early by VET with ROTEM®) using FFP vs factor concentrates (initially fibrinogen). The study was terminated early for safety and futility reasons, as many patients in the FFP group had to be rescued with concentrates and had a clearly higher need for massive transfusion. The authors particularly highlight the importance of early fibrinogen administration in patients with severe trauma. The relevance of this study lies in underscoring the importance of early diagnosis and appropriate treatment.

Later, in 2020, another systematic review and meta-analysis sought to determine the level of evidence regarding VET-guided transfusion management in different settings, with the aim of generating

recommendations³⁸. Using the PICO methodology (Population, Intervention, Comparison, Outcomes), the following question was posed: In the bleeding adult polytrauma patient with suspected coagulopathy, should a VET-guided transfusion strategy be used instead of a non-guided strategy to reduce mortality, transfusion, and the need for other hemostatic interventions? The authors conditionally recommend the guided strategy over the non-guided one. The effect on mortality and transfusion is inconsistent, but the potential benefit of minimizing transfusion seen in some patients and the safety of the strategy lead the authors to make this conditional recommendation.

Lastly, we must mention the ITACTIC study (Implementing Treatment Algorithms for the Correction of Trauma-Induced Coagulopathy)³⁵. This study also sought to compare whether outcomes were better when guiding the MTP with VET or with laboratory coagulation times. The results were that, although the VET-guided group received various treatments earlier, no differences were found. However, these results were later questioned for several reasons: there were few patients with coagulopathy at admission or with high transfusion requirements, suggesting that inclusion criteria may need to be better specified; all patients initially received the MTP bundle, which may have masked the potential benefit of VET-guided therapy; and the study aimed to detect very ambitious differences in mortality and transfusion, which likely limited the ability to demonstrate them.

In conclusion, monitoring with VET in polytrauma patients is a technique supported by evidence and included in guideline recommendations, albeit with only moderate grades of recommendation. VET appear to be a safe strategy that, in general, will help minimize transfusion and improve outcomes, but randomized prospective clinical trials are still needed to provide stronger evidence and to determine whether goal-directed therapy is better than a fixed-ratio approach, or whether a hybrid strategy is preferable to a guided strategy from the outset. Therefore, when designing our treatment protocols or drafting consensus documents, we should keep in mind the pathophysiology of the scenario together with the specific literature, prioritizing the importance of administering the most appropriate treatment as early as possible.

POSTPARTUM HEMORRHAGE

Postpartum hemorrhage remains the leading cause of mortality in pregnant women. Most deaths occur in

developing countries, but in developed countries deaths still occur for this reason and it is also a major cause of morbidity. It is crucial to establish, early on, obstetric measures to stop the bleeding, as well as intensive resuscitation and appropriate management of coagulopathy when it appears. Early recognition is essential.

The coagulopathy of postpartum hemorrhage is due to a dilutional mechanism, consumption coagulopathy, and hyperfibrinolysis, worsening as bleeding, hypothermia, and acidosis worsen. This coagulopathy will present earlier and more aggressively depending on the etiology and duration of the postpartum hemorrhage. In most cases it is not of immediate onset, being identified in only 3% (though it may appear later if hemorrhage is not diagnosed or treated early), except in cases due to amniotic fluid embolism or placental abruption, in which it will be rapid and characterized by hyperfibrinolysis and disseminated intravascular coagulopathy³⁹.

In any case, when coagulopathy appears, it is essential to recognize and treat it as soon as possible; of note that one of the repeatedly described problems in this scenario is precisely the lack of an adequate early diagnosis of postpartum hemorrhage, which will obviously translate into delayed management of said coagulopathy. Regarding its specific treatment, most guidelines recommend management based on the administration of FFP and red blood cell concentrates at a fixed ratio (MTP); however, this approach has been extrapolated from polytrauma patients and it is controversial whether its application in this scenario is indicated. Moreover, it has been described that such empirical transfusion will lead in many cases to overtransfusion of plasma and platelets, since, as noted, most patients will not present coagulopathy at the outset. For all these reasons, VET – thanks to their rapid turnaround and specificity that enables goal-directed treatment – have gained prominence in this context.

Regarding the scientific evidence, the European guidelines for the management of postpartum hemorrhage⁴⁰ recommend the use of VET:

- *Recommendation 35.* It is recommended to monitor hemostatic competence and the risk of coagulopathy in severe postpartum hemorrhage using laboratory tests (platelet count, PT, aPTT, fibrinogen value) or VET, in order to appropriately, goal-directedly guide the indication of blood components and hemostatic agents (Grade 1B).

Secondly, with the use of VET in postpartum hemorrhage, various authors have observed a reduction in transfusions as well as improved outcomes.

In 2015, Mallaiah et al.⁴¹ published the results of a 12-month prospective observational study following the introduction at their institution of a VET-based algorithm instead of the traditional empirical massive transfusion approach. They observed a statistically significant reduction in total blood components transfused, in FFP, in cryoprecipitates, and in fibrinogen concentrate. There were no differences in the need for red cell concentrates, but there were more patients requiring > 6 units in the group that followed an empirical MTP.

In 2017, results of the observational OBS2 study⁴² conducted by Collins et al.⁴² were reported, comparing empirical FFP administration vs VET-guided FFP administration. It was observed that VET use led to a substantial reduction in FFP administration, without any impairment of hemostatic competence.

In 2018, Snegovskikh et al.⁴³ compared 2 historical cohorts: one in which patients were resuscitated using an MTP and another in which a VET-based algorithm was applied. They analyzed clinical and economic variables. With VET use, there was a statistically significant reduction in transfusions of red cells, FFP, and platelets, as well as lower estimated blood loss, less need for hysterectomy and ICU admission, and fewer hospital days. Similarly, hospitalization costs were lower in the VET-guided resuscitation group.

In 2019, McNamara et al.⁴⁴ presented the results of another retrospective analysis, comparing certain outcomes after 4 years of implementing a VET-based algorithm instead of the previous empirical MTP. Again, there was a statistically significant reduction in blood component transfusions, as well as morbidity (especially transfusion-associated circulatory overload). There was also a reduction in ICU admissions and in the need for hysterectomies and transfusion of more than five units of red cells, although in this case the differences were not statistically significant.

Finally, also in 2019, Collins et al.⁴⁵ published a literature review highlighting the role of VET in postpartum hemorrhage with the aim of reducing blood loss and transfusion⁴⁵. Particular importance is placed on the early correction of hypofibrinogenemia when indicated by VET – often the first and, many times, the only correction needed.

In conclusion, within multidisciplinary protocols for managing postpartum hemorrhage, the evidence indicates that we should include VET-based algorithms for the management of coagulopathy. It is true that this

evidence comes from methodologically suboptimal studies and that there are no randomized clinical trials comparing the classical strategy with VET; however, their results are fully aligned with pathophysiology, enabling individualized and therefore more precise treatment, with a clear impact on outcomes.

Algorithms for correction of hemostasis

Bedside coagulation monitors based on VET provide results in 10-15 minutes – three times faster than conventional laboratory tests – allowing clinicians to avoid empirical administration of blood components and to tailor bleeding treatment to the real-time needs. This is known as “goal-directed therapy,” and algorithms have been designed to apply it in different bleeding scenarios.

The implementation of these algorithms has proven effective in reducing transfusion requirements, costs, and complication rates⁴⁶⁻⁴⁹.

Currently, this VET-guided bleeding management is considered an essential part of Patient Blood Management programs⁵⁰, and the most recent perioperative bleeding management guidelines recommend the use of interventional algorithms that incorporate predefined thresholds and treatment targets, based on VET coagulation monitoring to individually guide hemostatic treatment⁵¹.

Basic concepts in algorithm development

Algorithms to guide VET-based bleeding management all follow a similar structure and the same purpose: to administer the right treatment (blood components or prohemostatic drugs), at the right time (which implies clearly defining the threshold), at the right dose (which requires defining a target), and in the right order – treating first what is most relevant, whether due to its impact on mortality (hyperfibrinolysis), the existence of a specific treatment (anticoagulant antidotes), or its importance in bleeding (fibrinogen deficit). The sequence of steps is as follows:

1. Confirm the presence of bleeding.
2. Rule out hyperfibrinolysis.
3. Rule out the presence of anticoagulant treatment.
4. Ensure clot firmness.
5. Promote thrombin formation.

The number of therapeutic interventions that coincide after each analysis depends on the severity of the bleeding and the coagulopathy observed. In an initial analysis with major defects in firmness and markedly

prolonged coagulation times, up to three simultaneous treatments may be necessary; as the severity of bleeding and coagulopathy decreases, each defect can be treated individually, repeating the test to assess the effect before initiating a new treatment.

The low positive predictive value of VET (< 30%) implies that a parameter abnormality should never be treated in the absence of bleeding, as this may result in overtreatment. Conversely, their high negative predictive value (> 90%) indicates, with high probability, that bleeding – if present – is not due to coagulation abnormalities; in such cases, one should suspect, for example, a surgical source of bleeding.

Thresholds and treatment targets

Currently, numerous ROTEM®- and TEG-guided algorithms with thresholds and treatment targets have now been proposed. A list of references where they are published and some example algorithms are presented later.

Although most are based on expert opinion and retrospective data, in some settings and for certain VET (fundamentally ROTEM®) thresholds have been determined in observational studies using ROC curves or multivariable regression analyses⁵²⁻⁵⁴, and the targets have been validated in interventional studies that have evaluated whether treatment succeeds in correcting hemostasis, reducing transfusions, or improving outcomes.

Treatment thresholds

Table 1 illustrates VET-guided treatment thresholds as defined by different guidelines, comparing them with those published by Görlinger et al.³⁰ for ROTEM®³⁰ and by Baksaas-Aasen et al.³⁵ (used in the ITACTIC study)³⁵ for ROTEM® and TEG⁵⁵ in different scenarios.

Evidence on fibrinogen treatment thresholds

Clinical practice guidelines⁵⁵⁻⁵⁸ recommend considering treatment with fibrinogen concentrate or cryoprecipitate when the fibrinogen level in a bleeding patient is < 1.5 g/L. This cutoff is based on the high negative predictive value (> 95%) of fibrinogen values > 1.5 g/L⁵⁹.

FIBTEM is the viscoelastic parameter for assessing fibrinogen that has been most studied and has shown the best correlation with Clauss fibrinogen: a FIBTEM

Table 1. Treatment thresholds for bleeding patients established by different scientific societies, compared with those published by Görlinger et al. and by Baksaas-Aasen et al. (ITACTIC study)

Treatment thresholds	Obstetrics		Trauma			Cardiac surgery and extracorporeal circulation		
	Curry et al. ¹²	Görlinger et al. ¹⁰	European Guideline, Spahn et al. ¹³	ITACTIC study, Baksaas-Aasen et al. ¹¹	Görlinger et al. ¹⁰	JCTVA, Raphael et al. ¹⁴	EACTA, Erdoes et al. ¹⁵	Görlinger et al. ¹⁰
FIBTEM (ROTEM®)	A5 < 12	A5 < 12	MCF < 8-10	A5 < 10	A5 < 9	A10 < 10	MCF 4-6	A5 < 9
FF (TEG)	?	-	MA < 12	MA < 20	-	MA < 8	?	-
Platelets (ROTEM®)	?	A5 _{EX} < 35 and A5 _{FIB} ≥ 12	?	A5 _{EX} - A5 _{FIB} < 30	A5 _{EX} < 35 and A5 _{FIB} ≥ 9	A10 _{EX} < 40 and A10 _{FIB} > 10	-	A5 _{EX} < 30 and A5 _{FIB} ≥ 9
Platelets (TEG)	?	-	?	rMA - FFMA < 45	-	TEG MA < 40 and FF > 8	?	-
Plasma or PCC (ROTEM®)	?	A5 _{FIB} ≥ 12 and CT _{EX} > 80	FIB TEM ≥ 10 and CT _{EX} > 80	A5 _{EX} ≥ 40 and CT _{EX} > 80	A5 _{FIB} ≥ 9 and CT _{EX} > 80	CT _{EX} > 100	?	A5 _{FIB} ≥ 9 and CT _{EX} > 80
Plasma or PCC (TEG)	?	-	?	rMA ≥ 65 and rACT > 120	-	hTEG R > 12	?	-
TXA (ROTEM®)	Do not wait for VET result ML _{FIB} ≥ 10%		Do not wait for VET result ML _{FIB} ≥ 5%			Prophylactic tranexamic acid or ML _{FIB} ≥ 15%		
TXA (TEG)	?		Do not wait for VET result rTEG LY30 > 10%			Prophylactic tranexamic acid or rTEG LY30 > 3%		

Firmness values (A5, MA, MCF) are expressed in millimeters.

Clotting times (CT, rACT) are expressed in seconds.

hTEG (R) is expressed in minutes.

ACT: activated clotting time; PCC: prothrombin complex concentrate; CT: clotting time; MA: maximum amplitude; MCF: maximum clot firmness; rACT: rapid TEG ACT; rMA: Rapid TEG MA; hTEG: TEG with heparinase.

of 8 mm is a good predictor of a Clauss fibrinogen of 1.5 g/L.

There are no studies establishing the predictive capacity of Quantra®s FCS (fibrinogen contribution) parameter for different Clauss fibrinogen cutoffs. The trauma guideline is the only one that justifies a VET-guided treatment threshold based on an equivalent value. In bleeding patients, a Clauss fibrinogen < 1.5 g/L correlates well with a FIBTEM (ROTEM®) maximum clot firmness < 10 mm⁶⁰, while for functional fibrinogen (TEG) it sets a value < 12 mm⁶¹.

Other authors base their fibrinogen administration cutoffs on values that have shown a high capacity to predict the need for massive transfusion. An amplitude at 5 minutes in the EXTEM test (A5EX) ≤ 35 mm predicts the need for massive transfusion in 71%¹⁹, and an amplitude at 5 minutes in the FIBTEM test (A5FIB) ≤ 9 mm predicts massive transfusion in 77.5% of patients⁵².

For TEG, a threshold of < 20 mm for the MA of functional fibrinogen is set for fibrinogen administration⁵³.

During pregnancy, specific reference ranges for fibrinogen and FIBTEM – higher than in the general population – are defined⁶². To establish obstetric thresholds, the predictive capacity for bleeding and transfusion is considered. Thus, patients receiving more than four units of red cells have an A5FIB of 13 mm (interquartile range [IQR], 12-17), while those receiving fewer have A5FIB values of 19 mm (IQR, 16-24)^{41,60-65}. Some studies have shown adequate hemostasis with values > 12 mm⁴¹. With these criteria, the British Society for Haematology guideline⁵⁵ sets an A5FIB threshold < 12 mm for fibrinogen administration during postpartum hemorrhage.

In cardiac surgery, the European Association of Cardiothoracic Anaesthesiology (EACTA) recommends, in patients with significant non-surgical bleeding, replacing fibrinogen if FIBTEM MCF is ≤ 6 mm, and

considering administration under the same circumstances if FIBTEM is 6-8 mm; after treatment, maintain FIBTEM levels > 9 mm without exceeding 14 mm⁵⁸. In the algorithms of Görlinger et al.³⁰ the transfusion threshold for fibrinogen is justified by the association established by Karkouti et al.⁶⁴ between a post – cardiopulmonary bypass fibrinogen level < 2 g/L – which corresponds to an A5FIB < 9 mm (A10FIB < 10 mm) – and a high probability of transfusing ≥ 5 units of red cells.

Patients with cirrhosis present thrombocytopenia and decreased synthesis of both procoagulant and anticoagulant factors, maintaining a fragile balance. For this reason, reference ranges are lower than in the general population, translating into lower thresholds for administering fibrinogen and platelets. ROTEM® thresholds have been set as follows: for fibrinogen, < 25 mm; for A5EX, 35 mm; for A10EX, 45 mm; for MCFEX, 45 mm; and for A5FIB < 8 mm (9 mm for A10FIB and 10 mm for MCFIB)⁵⁴.

EVIDENCE ON TREATMENT THRESHOLDS WITH PLATELETS

Classically, the threshold for platelet administration in bleeding was based on maximum firmness (after extrinsic pathway activation, ROTEM® EXTEM MCF; or intrinsic, TEG® MA) below the reference value, with firmness determined by a normal fibrinogen value. Thus, the Society of Cardiovascular Anesthesiologists (SCA) guidelines (Table 1) establish platelet transfusion thresholds for ROTEM® at EXTEM MCF ≤ 40 mm + FIBTEM > 10 mm, and for TEG at MA < 40 mm + MCF > 8 mm⁷. Similarly, bleeding-management algorithms in trauma recommend platelet transfusion if EXTEM A10 < 40 mm and FIBTEM A10 > 12 mm^{33,65}.

In liver transplantation, Görlinger et al. set A5EX < 25 mm and A5FIB ≥ 8 mm for platelet administration³⁰. When fibrinogen is low (FIBTEM < 10 mm or functional fibrinogen < 8 mm), the simultaneous need for platelets will be determined by very low maximum firmness values. An A5EX < 15-20 mm mandates administration of both fibrinogen and platelets⁶⁶.

Another way to assess the platelet contribution to clot firmness is to measure the difference between EXTEM and FIBTEM MCF, yielding a parameter known as PLTEM. This parameter has shown good correlation with platelet count, such that PLTEM (EXTEM MCF – FIBTEM MCF) < 44 mm or (A10 EXTEM – A10 FIBTEM) < 33 mm corresponds to a platelet count < 100,000²⁴.

With these criteria, the algorithms of Baksaas-Aasen et al.⁵³ for ROTEM® and TEG also indicate platelet transfusion if (A5EX - A5FIB) < 30 mm and (rTEG MA – FF TEG MA) < 45 mm.

Evidence on treatment thresholds with coagulation factors

Clotting time (CT) in ROTEM® and reaction time (R) in TEG reflect the status of the plasma coagulation system by measuring the time to formation of the first fibrin mesh. TEG measures it using kaolin (intrinsic pathway activator), although Rapid TEG combines kaolin and tissue factor, and ROTEM® uses tissue factor (extrinsic pathway activator, EXTEM test).

A correlation has been established between ROTEM® EXTEM CT (reference range: 38-79 s) and INR values: an INR between 1.2 and 2.0 corresponds to a CT of 80 s; between 2 and 3 to a CT of 100 s; and > 3 to a CT of around 140 s⁶⁷.

In the SCA clinical practice guidelines (Table 1), plasma transfusion (10-15 mL/kg) in cardiac surgery is indicated when ROTEM® CT is >100 s or TEG heparinase R is > 12 min⁷.

There is an association between clot-firmness parameters (FIBTEM, ROTEM® MCF; FF, TEG MA; FCS; Quantra® Clot Stiffness) and coagulation times (ROTEM® CT and TEG R). After administering fibrinogen or platelets, coagulation times decrease significantly. The European trauma guidelines take this fibrinogen influence on coagulation time into account and recommend administering prothrombin complex concentrate only when fibrinogen levels have been corrected (Clauss ≥ 1.5 g/L or FIBTEM ≥ 10 mm) and CT remains prolonged⁵⁶. Likewise, the ITACTIC study algorithm⁸ also accounts for this, indicating plasma administration if, in ROTEM®, A5EX ≥ 40 mm and CTEX > 80 s, or in TEG if rTEG MA ≥ 65 mm and rTEG ACT < 120 s. That is, with firmness corrected, persistence of prolonged coagulation times indicates administration of plasma or prothrombin complex concentrate.

Coagulation times measured with VET should better distinguish between moderate factor defects that could be treated with plasma and severe defects in which factor concentrates may be indicated. In this regard, it has been suggested that an INR of 3 or an EXTEM CT > 140 s may indicate treatment with prothrombin complex concentrate (in trauma at 25 IU/kg, and in cardiac surgery at 12.5 IU/kg due to thrombotic potential)⁶⁸. However, more studies are needed to confirm this.

In patients with cirrhosis, coagulation time thresholds are lower than in the general population. Görlinger et al.³⁰ establish CTEX > 75 s (with normal FIBTEM > 8 mm) for administration of plasma or prothrombin complex concentrate.

Evidence on thresholds for tranexamic acid administration

Hyperfibrinolysis is defined in ROTEM® as a reduction of more than 15% in MCF measured up to 60 minutes after the start of clot formation following tissue factor activation. In Rapid TEG it is defined as a decrease in maximum clot amplitude of more than 3% at 30 minutes after the start of clot formation following kaolin plus tissue factor activation. The ITACTIC study⁶⁹ sets the Rapid TEG threshold at LY30 > 10%.

VET are not very sensitive for detecting hyperfibrinolysis when compared with measurement of plasmin – antiplasmin complexes (the reference method). FIBTEM appears to be the most sensitive parameter for detecting fibrinolysis⁷⁰.

Clinical practice guidelines recommend administering tranexamic acid whenever hyperfibrinolysis is detected on VET. Thus, the algorithms of Görlinger et al.³⁰ indicate tranexamic acid if A5EX < 35 mm or FIBTEM CT > 600 s, or if maximal lysis (ML) on EXTEM or FIBTEM is ≥ 15% (5% in trauma), and the algorithms of Baksaas-Aasen et al.⁵³ indicate it if, in ROTEM®, LI30EX < 85% and, in TEG, if rTEG Lysis 30 > 10%⁵³. However, following the CRASH-2⁷¹ and WOMAN⁷² trials in trauma and obstetrics, tranexamic acid should be administered within the first 3 hours of bleeding, and one should not wait for VET results.

In cardiac surgery, prophylactic administration of tranexamic acid is recommended (evidence 1A)⁸, so it is uncommon to detect hyperfibrinolysis on VET. In liver transplantation, after reperfusion, 80% of patients present fibrinolysis, generally self-limited and not requiring treatment.

Treatment targets

There is little evidence on the target level for each parameter after administering blood components in bleeding situations.

In postpartum hemorrhage, the British Society of Haematology⁵⁵ sets the fibrinogen administration target at FIBTEM > 12 mm. However, Görlinger et al.³⁰, based on FIBTEM values at which obstetric bleeding is not

associated with massive transfusion (median A5FIB: 19; IQR, 16-24)^{60-64,73}, set it at 16 mm.

In cardiac surgery, EACTA sets a FIBTEM target > 9 mm but not exceeding 14 mm⁵⁸. Görlinger et al.⁷⁴, for their part, indicate a target A5FIB ≥ 12 mm (fibrinogen concentration ≥ 2.5 g/L), and a second target – if the patient continues to bleed after complex cardiovascular surgery – of A5FIB ≥ 15 mm (fibrinogen concentration ≥ 3 g/L). Both algorithms justify these targets based on studies by Ranucci et al.⁵⁹, which established 14 mm FIBTEM or Clauss fibrinogen 2.8 g/L as the values with the best negative predictive value for bleeding (98%); above these, no additional benefit is observed.

Considerations for correct interpretation of parameters

Proper interpretation of VET results requires considering factors related to the reagents used in each test (e.g., platelet inhibitors) and also contributions to the result from factors that cannot be measured by VET (e.g., factor XIII).

Factors influencing the measurement of the fibrinogen contribution to clot firmness

PLATELET INHIBITORS

Incomplete platelet inhibition – especially in TEG functional fibrinogen and Quantra® FCS, which use abciximab (a glycoprotein IIb/IIIa receptor inhibitor), and to a lesser degree in FIBTEM, which uses cytochalasin D as a platelet inhibitor – will overestimate fibrinogen's contribution to clot firmness. Cytochalasin D is more effective at platelet inhibition, and FIBTEM is more accurate in determining fibrinogen's contribution to firmness⁷⁵, although in both cases a high platelet count can overestimate fibrinogen's contribution to firmness. The best platelet inhibition in these tests is achieved by combining abciximab and cytochalasin D, as in ClotPro® functional fibrinogen.

ADMINISTRATION OF FIBRINOGEN CONCENTRATE

After administering fibrinogen concentrate, the fibrinogen level measured with VET may not correlate as well with Clauss fibrinogen, since endogenous and exogenous fibrinogen structures are not the same. Generally, after fibrinogen administration, higher

firmness corresponds to a lower Clauss fibrinogen (the linear curve is steeper).

PRESENCE OF HEPARIN

The presence of heparin affects the reliability of fibrinogen measurement depending on the VET used. The TEG 5000 (but not the TEG 6S) can measure in a cup with heparinase, which neutralizes heparin concentrations above 4 IU/mL (commonly detected during cardiopulmonary bypass)^{75,76}. Quantra® and ROTEM® Sigma use reagents for FCS and FIBTEM that contain hexadimethrine bromide, which neutralizes heparin up to 4-5 IU/mL⁷⁷. Above 6-8 IU/mL, fibrinogen concentration will be underestimated. Using heparin-neutralizing substances in ROTEM® Sigma and Quantra® tests that assess fibrinogen (but not in TEG 6S) allows, in complex surgeries, analysis – before coming off bypass (when unclamping the aorta) – of blood samples still in the presence of high heparin concentrations. This helps anticipate treatment needs if diffuse bleeding is detected on coming off bypass.

CONTRIBUTION OF FACTOR XIII

Factor XIII's contribution to clot firmness via stabilization of the fibrin clot must be considered, and its deficiency suspected when a low fibrinogen contribution to firmness (FIBTEM < 8 mm) is associated with normal plasma fibrinogen levels (Clauss > 2 g/L). This is not infrequent in complex cardiac surgery with cardiopulmonary bypass. In such cases, cryoprecipitate used to replenish fibrinogen is a source of factor XIII, and the effect of this supplementation is better assessed by VET than by Clauss, as it will improve FIBTEM firmness but not the Clauss fibrinogen value.

Factors influencing the measurement of the platelet contribution to clot firmness

ELASTICITY VS FIRMNESS

It has been shown that the platelet contribution to clot firmness – by both number and function – is better discriminated by measuring maximum clot elasticity (MCE) than MCF. The formula for elasticity is: $MCE = (100 \times MCF) / (100 - MCF)$. The formula for the platelet contribution to elasticity is: $MCE_{platelets} = MCE_{EXTM} - MCE_{FIBTEM}$. This parameter is measured automatically on the Quantra® device ($PCS = CS - FCS$), whereas in other VET systems it must be

calculated manually. The relationship between the two measures is non-linear. Unlike MCF, MCE reflects the force (viscosity and elasticity) with which the clot resists rotation within the device. However, even though it is better, the association of MCE with platelet function remains poor. Within a platelet count range of 10,000 to 100,000/ μ L, MCF variation remains constant, while MCE variation increases as the platelet count rises⁷⁸.

The best cutoff for the platelet contribution to clot firmness measured by elasticity (representing the combination of platelet count and platelet function) is 142, which has a very high negative predictive value (93%), indicating that above this figure the bleeding should not be due to platelets. Unfortunately, the positive predictive value is low (45%); therefore, a lower figure would also not by itself indicate platelet transfusion unless there is significant bleeding not attributable to any other cause⁷⁹.

Quantra® System⁷⁹ uses ultrasound technology to measure viscoelastic properties in whole blood. Elasticity is expressed in hectopascals. The CS parameter measures clot stiffness from the combined contribution of fibrinogen and platelets. The FCS parameter (obtained after adding abciximab to inhibit platelets) detects the fibrinogen contribution; the platelet contribution is provided by the PCS parameter obtained from the difference $CS - FCS$.

Changes in PCS can be attributed to the interaction of platelet count and function by about 40% (25% depends on count and 15% on function determined by ADP activation measured with Multiplate®); the remaining 60% is unclear to what it can be attributed⁸⁰. Currently, there is no point-of-care viscoelastic device considered standard for measuring platelet function, and further studies are needed to establish the relationship of parameters derived from both amplitude and elasticity with bleeding and the need for platelet transfusion.

PRESENCE OF ANTIPLATELET INHIBITORS

Platelet aggregation occurs via the GPIIb/IIIa receptor, which links platelets together through fibrinogen bridges. Drugs acting on this receptor (e.g., tirofiban) have a very potent platelet-inhibiting effect, and VET are sensitive to this inhibition, showing a significant reduction in clot firmness.

By contrast, VET are not sensitive to the effect of drugs that inhibit the thromboxane pathway (acetylsalicylic acid) or the ADP P2Y₁₂ receptor (thienopyridines and ticagrelor), because the reagents used (kaolin,

tissue factor) to activate and accelerate coagulation favor thrombin synthesis – a potent activator of the pro-tease-activated receptor on the platelet surface – resulting in robust platelet activation that masks drug effects. The only VET sensitive to these is platelet mapping, which uses heparin to inhibit thrombin and then, via agonists (arachidonic acid or ADP), can unmask the presence of platelet inhibitors.

Factors influencing the measurement of coagulation times

PRESENCE OF HEPARIN

The use of full-dose heparin during cardiopulmonary bypass requires ruling out persistent circulating heparin as a cause of bleeding after protamine administration. In ROTEM®, a CT_IN/CT_HEP ratio < 1.25 correlates with anti-Xa activity below 0.2 U/mL and rules out heparin presence³⁷. Therefore, a CT_IN/CT_HEP ratio ≥ 1.25 indicates protamine administration, whereas in TEG, protamine is indicated with a CKH-R/CK-R < 0.5.

EXCESS PROTAMINE

Another aspect to consider is protamine overdose, suspected when CT_IN/CT_HEP is ≤ 1^{81,82}. It is associated with increased bleeding, transfusions, and reoperations for bleeding due to inhibition of both factor V and platelet function³⁰.

ENDOGENOUS HEPARINIZATION

Endogenous heparinization has been detected in 5% of patients with severe trauma and in 50% of liver transplants after reperfusion. It can be detected with VET. A CT_IN/CT_HEP ratio ≥ 1.25 appears related to endothelial glycocalyx degradation, and hemodynamic stabilization is the main treatment, although protamine may also help⁸³.

Examples of published algorithms

ROTEM®

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ROTEM® AND TEG

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Viscoelastic tests vs conventional coagulation tests

Perioperative coagulation monitoring is critical to understand the causes of bleeding, to guide hemostatic treatment, and to predict bleeding risk during anesthetic and surgical procedures. Point-of-care devices that provide information on the viscoelastic properties of blood have proven particularly useful in situations of massive transfusion and in cardiac and hepatic surgery. The advantage of these techniques, compared with conventional coagulation tests, is that they have the potential to measure virtually the entire coagulation process, from fibrin formation, continuing through clot formation, and, finally, fibrinolysis. In addition, by using whole blood, the interaction of coagulation proteins with other cellular elements (red cells, leukocytes, and platelets) involved in coagulation can be evaluated.

Characteristics of conventional laboratory tests and VET

The most widely used laboratory parameters to assess coagulation are the aPTT, PT, fibrinogen, and platelet count. Compared with VET, these are standardized tests performed by trained personnel and are low-cost. However, their usefulness in the perioperative context is debated⁸⁴, since results are not immediate (assays are run on plasma and the sample must first be centrifuged), and they do not assess the effect of other contributors to coagulation (red cells, platelets, and leukocytes).

VET such as TEG, ROTEM®, and Sonoclot® overcome some disadvantages of conventional tests in this setting: they are easy to use, results are available within minutes, and they are performed at the bedside. Nevertheless, there are limitations, such as differences from conventional test results, potential operator error, higher cost, and device-specific option limits – typically without the possibility of adding new ones⁸⁵.

In both conventional tests and VET, coagulation is assessed under static conditions (no flow) and in a cup (not on an endothelial surface), so neither can account for the endothelium's contribution to coagulation. This

is important to consider in certain clinical situations (e.g., bleeding from the surgical bed).

Of note, whole-blood analyses differ slightly from plasma-based ones. TEG shows that the maximum rate of clot formation is higher in whole blood than in plasma; the reason is the presence of platelets, which accelerate the coagulation process⁸⁶.

Clinical evidence

CARDIAC, HEPATIC, AND TRAUMA SURGERY

TEG has demonstrated utility in improving outcomes in cardiac and hepatic surgery⁸⁶; however, its role is debated in trauma patients. A Cochrane systematic review⁸⁷ found insufficient evidence to prove that ROTEM® or TEG are superior for diagnosing trauma-associated coagulopathy compared with PT or INR. The authors refrain from firm conclusions, as it is questionable whether PT or INR alone are good standards, since they assess only the extrinsic pathway. Current evidence is largely cohort-based, and systematic prospective studies are needed to validate these findings.

Monitoring anticoagulant therapy

There is growing evidence for VET use in other scenarios, such as monitoring anticoagulant therapy. A small randomized clinical trial showed that TEG can better guide heparin anticoagulation during extracorporeal membrane oxygenation (ECMO) vs aPTT, reducing the amount of heparin used⁸⁸.

Sonoclot® ACT and VET modified with heparinase have been used to guide unfractionated heparin therapy. However, their role is less clear for monitoring low-molecular-weight heparin and other heparinoids; when needed, plasma measurements such as anti-Xa are recommended⁸⁹.

A systematic review assessed monitoring of direct oral anticoagulants (DOACs) with VET. No correlation was found between VET parameters and different drug concentrations, as VET are extremely sensitive to the presence of these agents. Rivaroxaban, dabigatran, and apixaban were observed to alter CT and R, whereas edoxaban only prolonged EXTEM CT. Test sensitivity increases when VET modified for monitoring direct factor Xa and thrombin inhibitors are used⁸⁹. Currently, plasma drug levels are recommended for DOAC monitoring, but urgent availability is limited in many laboratories and these tests are complex and time-consuming. Therefore, in urgent

situations – trauma, thrombosis, urgent surgery, etc. – having VET available as a screening tool may be useful. The ClotPro® system includes two tests, RVV (detects direct factor Xa inhibitors) and ECA (detects direct factor II inhibitors), which allow detection of clinically significant drug levels.

Antiplatelet therapy

Conventional VET are not sensitive to platelet-function inhibitors, so specific assays have been developed to evaluate platelet function in the presence of these drugs⁹⁰.

VET designed to assess platelet function (TEG platelet mapping and ROTEM® Platelet) can detect inhibition by clopidogrel and acetylsalicylic acid in surgical patients. The results show good correlation between the degree of drug inhibition and the coagulability detected⁹¹. Sonoclot® has also shown good sensitivity for detecting platelet inhibition mediated by glycoprotein IIb/IIIa antagonists⁹¹. However, there are no definitive thresholds defining inhibitory vs non-inhibitory ranges for proceeding with a procedure. Thus, while these results provide a snapshot of the patient's coagulation status, there is no consensus on decision-making using these devices.

Other scenarios

Beyond coagulopathies associated with surgical procedures and other interventions, congenital coagulopathies merit mention. In specific factor deficiencies, VET have proven useful for monitoring some treatments not based on factor replacement and for assessing the patient's coagulative capacity. By contrast, they have not shown utility for monitoring factor replacement therapy; in this case, plasma assays are superior⁹².

Economic impact of viscoelastic tests: blood-component savings and shorter lengths of stay

The use of VET is not an isolated element in the therapy of bleeding or potentially bleeding patients; rather, it must be framed within the broader and current context of Patient Blood Management (PBM).

In 2021, the World Health Organization published a brief but forceful document on the urgency of implementing PBM programs after periods of severe shortages of blood resources during the COVID-19 pandemic, which led to drastic reductions in donation volumes.

PBM is often identified with anemia correction and optimization of hemoglobin values via iron and hematinics (PBM pillar 1); however, anemia can also be a comorbidity associated with medical and surgical processes, linked to increased morbidity and mortality, prolonged stays in hospital or ICU, and reduced quality of life⁹³.

VET play a role precisely in bleeding associated with surgical trauma or childbirth, or in coagulopathic states, allowing clinicians to address PBM's second pillar: minimizing blood loss and correcting coagulation.

PBM program results in Western Australia between 2008 and 2014 showed a 15% reduction in hospital stay and cost savings of 18.5 million dollars in blood products.

Managing bleeding and efficiently, early correcting coagulation disorders are important – above all for patient safety, but also regarding health care cost savings and system sustainability.

It is useful to know the official (average) prices of blood components, VET, and standard laboratory tests to gauge potential savings with VET use. In Spain, regional bulletins report fairly similar final prices for transfusion-ready blood components: €600 per platelet concentrate, €300 per red-cell concentrate, and approximately €60 per unit of fresh frozen plasma. A global hemostasis VET using a cartridge system (ROTEM® Sigma, TEG6®, Quantra®) costs about €100, whereas with ROTEM® Delta each individual determination costs about €25. Platelet-function testing with TEG6® cartridges costs €120. With ROTEM® Delta, each platelet receptor studied (arachidonic acid, ADP, thrombin) costs €16.

Standard coagulation tests are cheaper than VET (prices vary by hospital), but they do not provide immediate or rapid results, delaying decision-making.

Transfusion of blood components is, *per se*, associated with increased morbidity and mortality and longer lengths of stay⁹⁴, with a proportional relationship between transfused volume and complications⁹⁵. Saving blood components already justifies VET use; additionally, reduced length of stay lowers care costs. Unfortunately, exact calculations are difficult, but as a guide, a day in a critical-care bed in Spain costs €800 – €1,500 (depending on the region), excluding staff and drug costs.

The best-studied VET clinical setting is cardiac surgery, with numerous publications demonstrating reduced transfusion volume and reoperation rates for bleeding. Cost issues in managing coagulopathy in cardiac surgery were addressed as early as 2007 by

Spalding et al.⁹⁶, who reported reductions of 25% in red cells, 50% in platelets, and 80% in prothrombin complex concentrate and factor XIII, with cessation of recombinant activated factor VII use and, conversely, doubled fibrinogen use. Spalding et al.⁹⁶ estimated monthly savings of €21,000 in blood-product costs, with an average of €1,580 in ROTEM® reagents and consumables, and a reduction in re-sternotomy rates for bleeding from 6.6% to 5.5%.

Of note, these benefits are amplified when VET use is paired with algorithm-driven transfusion strategies. In 2016, Karkouti et al.⁹⁷ found substantial reductions in bleeding rates and in red-cell and platelet transfusions, and a 26% decrease in reoperations – despite increasing surgical complexity.

The IMOTEC study⁹⁸, pending publication of results, aims to evaluate the cost-effectiveness of an algorithm-based VET and its impact on quality of life 1 year after surgery, with special emphasis on per-patient hospital costs.

Whiting et al.⁴⁷, in a cost-effectiveness analysis of VET across several scenarios, concluded that in cardiac surgery there is reduced consumption of red cells, platelets, and plasma with these tests, quantifying per-patient savings of £43 with ROTEM®, £79 with TEG, and £132 with Sonoclot®. In polytrauma patients, calculated savings were higher: £688 with ROTEM®, £721 with TEG, and £818 with Sonoclot®.

González et al.³⁴ also reported meaningful reductions in 28-day mortality when VET guided transfusion therapy in polytrauma patients compared with standard laboratory guidance.

A 2020 systematic review and meta-analysis by Santos⁹⁹ directly associated VET use with a significant reduction in mortality, acute kidney injury, red-cell volume transfused, and risk of platelet and plasma transfusion in surgical settings overall.

It is not easy, but it is sensible to extrapolate considerable savings if renal replacement therapy is avoided through appropriate use of hemostatic and transfusion resources.

A 2014 review¹⁰⁰ described in detail many economic aspects of health care, including direct costs derived from or not derived from healthcare (e.g., blood products and drugs are direct healthcare costs, whereas transport, social services, or legal fees are non-healthcare but still direct costs) and indirect costs (productivity losses due to absenteeism or due to disability or morbidity/mortality). Clearly, the calculation is much more complex than it may seem a priori.

Clinical scenarios such as liver transplantation show contradictory evidence in the scientific literature regarding VET utility, although their use is widespread and they constitute a fundamental diagnostic and therapeutic tool in complex conditions with a tendency to hemorrhage or thrombosis. Randomized clinical trials by Bonnet et al.²⁴ and Zamper et al.¹⁰¹ show reductions in red-cell and plasma transfusions with thromboelastometry, although they do not conclude advantages in mortality, reoperation rates, or length of stay.

Finally, in puerperal hemorrhage¹⁰², reduced plasma consumption and a slight trend toward reduced bleeding have been demonstrated when ROTEM® is used to guide hemostasis¹⁰¹.

Many other care situations may benefit from VET and platelet-function mapping – such as interventional radiology procedures with vascular stent placement, or extensive burns requiring repeated fasciotomies and debridements with a marked tendency to bleed – but evidence in these scenarios is scarce.

In conclusion, VET use is cost-efficient not only from the standpoint of saving expensive and scarce blood components, but above all from the perspective of patient safety and optimization of clinical outcomes. Nonetheless, strict cost calculation is complex and multifactorial.

Limitations of viscoelastic tests

Throughout this text we have sought to demonstrate the advantages of VET as tools to assess coagulation at the point of care and to guide hemostatic decision-making toward concrete targets, aiming to illustrate the benefit in those clinical scenarios where the scientific literature provides the strongest evidence. However, these devices have limitations and areas for improvement that we also wish to set out in this review.

The main current limitations – without prejudice to future software and reagent developments that may overcome them – are:

- They do not evaluate the endothelial contribution to hemostasis.
- They are not useful for assessing hemostatic disorders due to von Willebrand factor deficiency or platelet adhesion to the endothelium.
- They do not assess platelet aggregation in patients on antiplatelet therapy such as cyclooxygenase-1 inhibitors (acetylsalicylic acid) or P2Y₁₂ receptor inhibitors (clopidogrel, prasugrel, ticagrelor).

- Some platforms on the market do not allow assessment of direct anticoagulants such as dabigatran, apixaban, rivaroxaban, etc.
- The blood sample used is citrated and re-calcified, so they do not analyze in-vivo hemostatic alterations due to hypocalcemia or acidosis.
- They do not diagnose coagulation disorders caused by hypothermia, nor do they assess the microcirculation, since although the clot can be formed at the patient's temperature (between 30 and 40 °C), it is usually formed at 37 °C.

Final argument in favor of using VET in hospitals

VET have filled a diagnostic gap in the immediate management of massive transfusion and are becoming a standard of care in various clinical scenarios. Barriers to external quality assessment and their global nature have led to slow adoption outside massive hemorrhage management, despite their versatility¹.

Introducing a point-of-care test in a hospital, from a management standpoint, is justified for several reasons, discussed below.

Improved efficiency and shorter wait times

Point-of-care testing enables faster results, which can reduce wait times, avoid consumption coagulopathy, and ultimately improve service efficiency⁴⁷.

Greater diagnostic accuracy and safety

VET provide a view of coagulation closer to reality than isolated routine laboratory tests, improving safety and diagnostic quality in emergency settings.

Improved patient care

As reviewed in the different sections, high-risk clinical situations for bleeding and coagulopathy – such as cardiovascular surgery, liver transplantation, trauma, and obstetric hemorrhage – have been the main indications for VET since their introduction¹⁰³. However, the use of VET-guided interventional algorithms is also recommended in any scenario of perioperative bleeding, since it shortens decision time for transfusion in bleeding patients and allows individualized transfusion guidance⁵¹.

Beyond use in the emergency area (trauma or emergency bays) and the operating room, VET have proven useful in critical care (especially in sepsis) and on inpatient wards (notably in hematology and cancer patients)^{104,105}. In patients with coagulation disorders, VET can help tailor anticoagulant therapy more precisely and rapidly, improving treatment efficacy and reducing the risk of complications^{47,106}.

Reduced costs and length of stay

Appropriate bleeding management with VET can optimize hemorrhage control, reducing costs associated with certain laboratory tests and with uncontrolled transfusion of different blood components, thereby lowering transfusion-related costs. Moreover, VET enable more precise and faster decision-making, helping decrease blood transfusions and, consequently, shorten hospital stays and improve patients' quality of life.

Reduced mortality

Coagulation disorder-related mortality in surgical patients can be high. Implementing ROTEM® technology in hospitals can reduce mortality and improve clinical outcomes. Indeed, the use of ROTEM® in bleeding management has been shown to reduce mortality in patients with coagulopathy. In this regard, implementing ROTEM® in hospitals can enhance patient care and reduce mortality associated with coagulation disorders.

Greater access to services

Introducing point-of-care tools in areas far from central laboratories can improve professionals' access to diagnostic services.

Conclusions

In summary, implementing VET in hospitals can improve bleeding management, reduce costs and prolonged hospital stays, and decrease mortality associated with coagulation disorders. VET allow more precise and faster decision-making, which can improve clinical outcomes and patients' quality of life.

Funding

None declared.

Conflicts of interest

None declared.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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