

The role of viscoelastic tests in trauma: “TEG and ROTEM”

Ayten Saraçoğlu M.D.¹, Ayşen Yarat PhD², Şermin Tetik PhD

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BACKGROUND: Each year, 5.8 million people die as a result of trauma. Uncontrolled bleeding and inappropriate policies applied for patient blood management play a significant role in most of these deaths.

METHOD: Hemostasis may become more problematic in the presence of trauma. Trauma induced coagulopathy (TIC), known as “blood vicious triad”, is characterized with acidosis, hypothermia, increased platelet number and coagulation factors. TIC, which has been related to several mechanisms, originates from platelet dysfunction, hyperfibrinolysis, endothelial dysfunction and hypo-dysfibrinogenemia. So hemorrhage monitoring is crucial for planning patient-specific transfusion and avoiding undesirable effects of excessive volume load. The monitoring procedure starts with anamnesis and continues with laboratory tests.

RESULTS: The laboratory tests routinely applied for the analysis of coagulation do not reveal the risk of hemorrhage, and it is obvious that blood and blood products used as prophylactic agents may have an additive effect especially on bleeding. Moreover, it was indicated that prothrombin time (PT) and partial thromboplastin time (PTT) are badly correlated with acute resuscitation efforts, and patients experience shock deteriorating secondary to consecutive massive transfusion. Classical tests give information about the period until formation of thrombin which constitutes 5% of the whole process. However, they do not give information about the interaction of endothelium, thrombocyte and enzymes with cell phospholipids, clot quality and fibrinolysis.

Each year, 5.8 million people die because of trauma. Uncontrolled bleeds and inappropriate policies applied for patient blood management play a role in most of these deaths. Bleeding has been associated with 80% of deaths in the operating room (1).

Hemostasis, which is a natural defensive mechanism against vascular damage and hemorrhage, is a multi-phase process involving both cellular and humoral elements of coagulation. This process may become even more problematic in the presence of a factor that can trigger coagulopathy, such as liver failure or trauma. Hemorrhage monitoring is crucial for planning patient-specific transfusion and avoiding undesirable effects of excessive volume load. The monitoring procedure starts with anamnesis and continues with laboratory tests. Diagnosis is made through laboratory methods and in the light of clinical findings.

During bleeding, the diagnosis is made using Cascade (standard) model or cellular model (POC) for the management of treatment. The cell-based model, which is commonly used today, composes of 3 important phases. The initiation phase is the step when thrombin forms. At the amplification phase, thrombin burst develops with the IIb-3a receptor on the surface of the platelet. The propagation phase involves the spread of clots by platelet activation. In this model, the most important factor is the tissue factor (TF) as the interaction of TF with Factor VIIa (FVIIa) is a significant step in clot formation.

Trauma induced coagulopathy (TIC), also known as “blood vicious triad”, is characterized with acidosis, hypothermia, increased platelet (PLT) and coagulation factors. In 1968, Kadis et al. (2) indicated the relation of coagulation abnormalities with poor prognosis. Moreover, it was indicated

DISCUSSION: Point of care (POC) tests such as Thromboelastography (TEG) and Rotational thromboelastometry (ROTEM) evaluate all thrombin mediated processes. They have a unique ability to measure the development of blood clots and the strength of the platelet-fibrin bond and allow observation of the internal interactions in blood and the contributions of cellular content. If the coagulation cascade was to be compared with a house construction, conventional tests would represent the time until the first basis of the house is laid while TEG and ROTEM show how fast the house is built and how strong the construction is. ROTEM and TEG, indeed, depend on the same principles and give the same graph, but ROTEM has some differences compared to TEG. Considering that the turnaround time, the timing of bedside tests seems to be more appropriate for perioperative bleeding monitoring.

CONCLUSION: The utilization of POC tests reduces the incidence of unnecessary blood product transfusion; and consequently leads to a reduction in mortality, morbidity, and cost in traumatic patients.

Key Words: TEG; ROTEM; Trauma

Abbreviations: TF: Tissue Factor; TPA: Tissue Plasminogen Activator; PTT: Partial Thromboplastin Time; PT: Prothrombin Time; ACT: Activated Coagulation Time; 4-PCC: Four-factor Prothrombin Complex Concentrate; PROMMTT: Prospective, Observational, Multicenter, Major Trauma Transfusion; PROPPR: Pragmatic Randomized Optimal Platelet and Plasma Ratios; aPTT: Activated partial thromboplastin time; TEG: Thromboelastography; ROTEM: Rotational Thromboelastometry

that prothrombin time (PT) and partial thromboplastin time (PTT) are badly correlated with acute resuscitation efforts, and patients experience shock deteriorating secondary to consecutive massive transfusion. Hayem et al. reported the viscosity of blood during clotting in 1889. Koffman stated the viscoelastic feature of blood for the first time in 1910. With the use of cell-based coagulation model, which has been now comprehended, and the need for a shorter turnaround time, the demand for such devices has increased. The laboratory tests routinely applied for the analysis of coagulation do not reveal the risk of hemorrhage, and it is obvious that blood and blood products used as prophylactic agents may have an additive effect especially on bleeding. Clinicians now use liquids, blood products, and procoagulant drugs depending on the algorithms generated in line with the results of the laboratory tests. Thus, there is a significant reduction in the use of blood products. Again in 2003, Brohi et al. (3) reported that coagulopathy started within 30 min in the presence of tissue hypoperfusion and poor cellular oxygenation. Additionally, the combination of hypothermia, acidosis and dilution was reported to contribute to the dysfunction of enzymes and platelets.

METHODS

Several mechanisms have been argued to be associated with TIC, and PLT dysfunction, hyperfibrinolysis, endothelial dysfunction and decreased hypo-dysfibrinogenemia lead to reduction in clot stiffness (4). Acidosis, hypothermia, hemodilution, severe bleeding causing the depletion of coagulation factors, and high fluid resuscitation have an active role in here. The main mechanism involves direct tissue damage, shock, and endothelial hypoperfusion caused by systemic anticoagulation and hyperfibrinolysis (5).

¹Department of Anesthesiology, Marmara University Medical School, Istanbul, Turkey, ²Department of Biochemistry, Marmara University School of Dentistry, Istanbul, Turkey, ³Department of Biochemistry, Marmara University Faculty of Pharmacy, Istanbul, Turkey,

Correspondence: Dr. Ayten Saraçoğlu, Marmara University Medical School, Department of Anesthesiology, Istanbul-Turkey, Telephone 0216 414 0545, e-mail anesthiayten@gmail.com

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The presence of hypoperfusion and hypoxia leads to catecholamine discharge and the shedding of the endothelial glycocalyx through up-regulation of endothelial cell (6). This condition results in thrombin generation inducing an increase in thrombomodulin expression, activation of protein C that binds to thrombin released by tissue damage. This complex activity elevates the level of protein C. Plasminogen activator leads to hyperfibrinolysis by inhibiting the inhibitor-1 (PAI-1).

Activated protein C generates a hypocoagulable state by inactivating Factor V (FV) and Factor VIII (FVIII). As a result, the release of tissue plasminogen activator (tPA) strengthens and endogenous heparinization occurs due to impaired endothelial glycocalyx. In this context, it is thought that fresh frozen plasma actually corrects coagulopathy by restoring glycocalyx and replacing coagulation factors. However, this is the case for a four-factor prothrombin complex concentrate (4-PCC) but not for albumin.

Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMTTT) and Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) showed that early transfusion of platelet in trauma patients improve hemostasis (7). The decrease in PLT aggregation after trauma causes poor outcome. However, the mechanism of dysfibrinogenesis and PLT dysfunction is not known. "Acute endogenous coagulopathy" developing in TIC may be resistant to plasma therapy. Due to some mechanical reasons, the pathways can be activated, and transient fibrinolysis can occur (8). As compared to the American model, the more accepted concept in Europe is the Goal-directed Coagulation Therapy (GDCT) based on the results of early point-of-care (POC) viscoelastic tests (9). This approach is called Theranostic Therapy (Table 1).

Intrinsic pathway activation begins following the damage to blood vessels while extrinsic pathway tissue is activated after tissue injury. The extrinsic pathway is initiated by a tissue factor, and the activation of FVII induces the activation of Factor X (FX). In the intrinsic pathway, on the other hand, the contact of the vessel surface with blood activates FXII followed by FXI, FIX, and FX, respectively.

Classical tests give information about the period until formation of thrombin which constitutes 5% of the whole process. However, they do not give information about the interaction of endothelium, thrombocyte and enzymes with cell phospholipids, clot quality and fibrinolysis. Activated partial thromboplastin time (aPTT) and prothrombin time, which are standard laboratory tests, give the results obtained with patient plasma. On the other hand, they do not assess other components of coagulation, such as antithrombin, tissue factor pathway inhibitor, endothelium, platelet and fibrin. Nevertheless, the tests including platelet count, platelet aggregation and Clauss fibrinogen measurements, and fibrin degradation products can assess the components of coagulation separately, but do not take the internal interactions in blood and the contributions of cellular content into consideration. Thromboelastography (TEG) has a unique ability to measure the development of blood clots and the strength of the platelet-fibrin bond. Considering that the turnaround time- time from the drawing of the blood sample until when the results are obtained- takes 30-90 min, the timing of bedside tests seems to be more appropriate for perioperative bleeding monitoring. For instance, PT and PTT are severely affected in acute liver failure, but bleeding does not occur as the thrombin level stays normal or goes up. Therefore, these tests are inadequate for the assessment of hemostatic state. PT and aPTT are sensitive only to severe hypofibrinogenemia (60-70 mg/dL) and insensitive to FXIII deficiency (Table 1).

Protein C and antithrombin must be activated by the thrombin-thrombomodulin complex and glycosaminoglycans, which are found in endothelial cells and in a few plasma cells, to show anticoagulant activities. Conventional tests, therefore, fail to assess the hemostatic status, a direct result of pro-anticoagulant balance. Nevertheless, some trauma centers have a modified test panel called coagulation panel.

TABLE 1
The features of POC tests

Features	Points to consider:
No need for a permanent and special area.	Results can be influence by personal experience and calibration.
Possibility of use at the bedside.	It is an expensive method.
Indication of results with portable devices.	It requires training.
Possibility of viscoelastic measurement in whole blood.	Results must be correlated with clinical condition.
Ability to evaluate all thrombin mediated processes.	

In these devices, clot formation takes place between the development of viscoelastic strength in whole blood and the pin dipped in the sample. Viscoelastic signal depends on endogenous thrombin formation, fibrin polymerization and the interaction between fibrin and glycoprotein 2b3a receptors. These tests evaluate all thrombin mediated processes. Studies have indicated that the cost of POC tests is higher as compared to conventional coagulation tests (10). The cost of combined viscoelastic and aggregometry coagulation tests ranges from € 25 to € 35. On the other hand, the cost of conventional tests is less than € 10 per patient. However, a study indicated that the cost of a red blood cell (RBC) procedure can reach €1400 with the addition of donor and production costs, spending for the transfusion preparations at the hospital, spending for the treatment of adverse effects and transfusion-transmitted infectious diseases, and hemovigilance costs and the expenses for legal proceedings (11).

Spalding et al. (12) demonstrated in the study involving 1422 patients scheduled for elective cardiac surgery that the cost of blood products and hemotherapeutic drugs decreased by 50% with the use of POC tests. This study, in which patients with 200 ml/st hemorrhage were enrolled in the study for a period of 6 months, demonstrated a 25% decrease in the use of erythrocyte suspension, a 50% decrease in thrombocyte suspension usage and 100% reduction in the use of FVIIa. The total reduction in the cost was stated to be 40%.

Görlinger et al. (13) noted that POC tests provided a 34.3% decrease in the cost linked to the use of blood products. However, Görlinger et al. mentioned an increase in the cost resulting from 104.6% factor usage although there was a 6.5% net reduction in the costs associated with the use of hemotherapeutic agents. It was emphasized that it may be possible to avoid unnecessary transfusion of plasma and platelets through tromboelastometry-based restrictive transfusion management. In this way, transfusion-related side effects and increased hospital costs can be prevented.

If the coagulation cascade was to be compared with a house construction, conventional tests would represent the time until the first basis of the house is laid while TEG and rotational thromboelastometry (ROTEM) show how fast the house is built and how strong the construction is. TEG and ROTEM analyze the clot formation at the pre-coagulation phase, the time to first clotting, and the strength of the clot at the coagulation phase, and the stability of the clot at the fibrinolysis phase. The lysis rate of the clot is also analyzed. Viscoelastic coagulation tests assess the coagulation status in a cuvette under static conditions without flow. For this reason, clinical state must not be ignored while evaluating the in vitro outcomes of viscoelastic tests.

Clot formation starts when thrombin level sufficiently increases which is reflected in the graph with the elevation of amplitude. Besides the time to the formation of fibrin polymers, it is also possible to monitor the status after clot formation.

The stiffer the clot is, the higher force is generated against the rotation or vibration movements of the measuring device. An extension in the reaction time @ or clotting time (CT) is the indicator of a reduction in factors or inhibition. When thrombus formation starts, the clot gets stronger through the interaction between platelet and fibrin which attracts attention to amplitude A. This value is measured at the 5th, 10th, and 15th minutes. The maximum amplitude (MA) in TEG and maximum clot firmness (MCF) in ROTEM refer to a complete association between fibrin and platelet. Decreased MA in TEG refers to PLT tx requirement. However, in ROTEM, there is a need for an advanced analysis such as FIBTEM.

In a typical ROTEM, the CT/R ratio indicates the beginning of clot formation, thrombus formation and clot polymerization. A prolonged R shows hemodilution, endogenous heparin release due to tissue embrittlement, and lack of coagulation factors. Conversely, the R-time shortens in cases of hypercoagulation.

The normal range of global clot strength (G) is 5.3-12.4 dyn/cm², and if it goes above 10, it should be considered a tendency to thrombosis. G (dyn/cm²) determines clot thickness and the contribution of thrombocyte and enzymes to the strength of the clot. Whereas, an extended R-time and decreased G indicate factor defect, normal G range reflects hemodilution.

The ratio of clot formation time (CFT) to kinetics (K) relates to the formation of both thrombin and fibrin. The clot formation time expresses the time from the formation of the clot until the clot reaches 20 mm. Kinetic time (K-time) represents the time taken to achieve stable fibrin formation in TEG. For this reason, fibrinogen is administered in the treatment of extended K-time. A short K suggests that clot formation is rapid with a rapid consumption of

hypercoagulation or coagulation factors. Alpha angle (α angle) is related to fibrinogen level and reflects the velocity to reach the maximum clot. The normal range of α angle, which shows the rate of fibrin formation, is 66° to 82°. It shows the average fibrin formation rate. In other words, higher α angle is a predictor of higher clot formation. As α angle is a reflection of fibrinogen activity, it can be applied to analyze the rate of formation of fibrin covalent bonds and the rate of clot formation. Alpha angle decreases significantly when the platelet count is below 50000.

MCF refers to the maximum amplitude of clot firmness. It is a reflection of the contribution of thrombocyte function and count and FXIII level to clot stability. The clot formation time in ROTEM shows the time to the formation of 20 mm amplitude. Clot firmness correlates with the thrombocyte- fibrin clot strength, and thus, is affected by the changes in the count and function of fibrinogen and thrombocyte. The decrease in the maximum amplitude indicates hypofibrinogenesis or a decrease or deterioration in platelet function. Alpha angle and the maximum amplitude are correlated with the level of coagulation factors, fibrinogen concentration and platelet count. CI refers to the coagulation index. The coagulation index is found by calculating the linear indexes of R, K, MA and α angle. A LY30 higher than 20% means hyperfibrinolysis. The activated coagulation time (ACT), R-time and K-time correlate with PT, INR (international normalized ratio) and aPTT, while α angle correlates with platelet count.

In fact, the traces of TEG and ROTEM are similar, but their terms and reference intervals are different. Such difference results from the use of different cups and pins. However, the contact activation is higher in the ROTEM with the plastic container with a larger surface. Moreover, TEG and ROTEM also differs in the coagulation activators used and their compounds and concentrations. For example, the intrinsic coagulation activator is kaolin in TEG, but partial thromboplastin phospholipids in ROTEM.

TEG

TEG is a measure of the physical properties of a clot with both qualitative and quantitative outcomes. TEG, which was developed by Hartert in 1948, was used in a liver transplantation surgery in 1980. TEG can be performed using either citrated or uncitrated whole blood, and a blood sample of 1-5 ml is sufficient for measurement. TEG requires calibration 2-3 times daily. Although it can be performed after a simple laboratory training, TEG should be performed by trained personnel.

The thromboelastogram system basically consists of an electromagnetic transducer, a cylindrical cuvette for blood, and a fixed part for the needle. Calcium chloride, kaolin and phospholipids are placed in the cuvette along with citrated whole blood. In this way, as the fibrin-platelet bonding starts, the needle binds to the blood sample and the rotation movements in the cuvette are transferred onto the needle. The needle is suspended in blood and its movements are converted into electrical signals by an electromagnetic transducer with the beginning of blood clotting. The rate and strength of fibrin-platelet formation affect the magnitude of needle movement and signal amplitude. TEG is a system that measures the physiological features of a blood clot at 37°C in citrated or uncitrated whole blood sample placed in a still cylindrical container (cup). This cup rotates backward and forward through a total angle of 4.45 degrees 6 times per minute. The stationary pin in the cup is sopped in the sample and attached to a torsion wire, which allows the monitorization of the movements. The tension of the clot affects pin vibration, and these dynamic changes are converted into electrical signals through the mechanical transducer and a typical TEG curve showing different phases of coagulation is obtained. Thus, each step can be evaluated qualitatively. When fibrin clots are lysed, the fibrin-platelet interconnections are broken and the movement of the cup decreases. TEG can function in 4 different ways: Standard TEG, accelerated version of the standard test (rTEG), heparinase TEG and platelet mapping method. rTEG is a rapid test, in which intrinsic and extrinsic pathways can be examined. Heparinase TEG is efficient in proving the effect of residual heparin in coagulation.

In the TEG platelet mapping method, blood samples are supplemented with arachidonic acid for aspirin and ADP for clopidogrel. The TEG platelet mapping allows the identification of the pharmacologically inhibited platelet count (14). Rapid-TEG performs the measurements in a blood sample with 8% kaolin and recombinant tissue factor. The aim of using tissue factor instead of kaolin in rTEG is to reduce the time taken to clot formation. Also, abciximab is added to the sample inhibit PLT aggregation. While the R-time results in standard TEG expressed in minutes, the rTEG results are expressed in seconds (15). Standard TEG can be used for only in kaolin-added or citrated blood samples. In rTEG, the platelet component can be calculated as elasticity (E), which can be considered as equivalent to the CE (clot elasticity) parameter in ROTEM (16).

In the cases when EPL >15% or LY30 >7.5%, the CI value must be checked. If CI <1.0 and the primer >3.0, secondary fibrinolysis should be considered.

Both LY30 and the maximum rate of lysis (MRL) are found to be significantly associated with 24-hour and 30-day mortality. It has been demonstrated that a MRL >0.5 mm/min makes a 10-fold increase in the incidence of 24-hour mortality. Furthermore, when LY30 >3%, the incidence of mortality increases three times. MRL has been found to be a significantly stronger predictor of 30-day mortality as compared to LY30 (24.4% vs. 18.0%; $p < 0.001$) (17).

MRL, TMRL (time to maximum rate of lysis) and TL (total lysis) are some of the parameters that play a role in fibrinolysis. The normal range is 0.18-0.31 mm/min for MRL; 28.2-37.1 min for TMRL and 22-45 mm for TL (18). There is showed that routine thromboelastography (TEG)-based algorithm is very important on bleeding and transfusions in patients undergoing elective coronary artery bypass grafting (CABG). If kTEG-guided algorithm is use as routine reduces the consumption of blood products in patients undergoing elective CABG (19).

ROTEM

ROTEM and TEG, indeed, depend on the same principles and give the same graph, but ROTEM has some differences compared to TEG. These differences include the optical detection system, stationary cup and the direction in which needle/ wire system oscillates. ROTEM was developed with the same logic applied in TEG, but the movement in ROTEM is started using the pin instead of the cup. It does not include a torsion wire, and the cup is stationary and the pin is rotational. The whole blood sample is put in a cuvette, and the pin is dipped into the sample. There is a 1 mm space between the cuvette and the pin which is bridged by blood. The pin is rotated by a spring towards right and left with a 4.75 degree angle for 6 seconds. As long as the blood sample remains fluid, this movement remains unimpeded. However, as blood starts clotting and the strength of the clot increases, the rotation of the clot pin is restricted. This kinetic is determined mechanically. An integrated computer calculates typical curves (TEMogram) and numerical parameters. Only citrated blood sample can be used for measurements. While TEG employs kaolin, EXTEM uses tissue factors, and INTEM utilizes contact activators such as ellagic acid activator.

CT corresponds to R in the TEG and shows the formation of the first clot and also sheds light on the formation of thrombin. CT is more affected by the enzymatic aspects of coagulation including anticoagulants and the tissue factors released from circulating cells.

CFT is the time from the initiation of clot formation at 2 mm until a clot of 20 mm amplitude is formed. CFT is equal to the k-time in TEG. CFT is influenced by thrombin formation, platelet count and function, fibrinogen concentration and fibrin polymerization. Alpha angle represents the time until a clot of 2 mm forms. Maximum clot firmness indicates the maximum firmness and the maximum stiffness of the clot. MCF is affected by platelet count, platelet function and fibrinogen level. The 5th and 10th min of clot formation are referred as A5 and A10, respectively. If EXTEM is lower than 35 mm, there is a high risk for the development of TIC. In INTEM, a MCF <50 mm is considered a risk factor for massive transfusion in the cases where hemoglobin level <10 g/dL (18).

Whereas EXTEM, INTEM A10 and MCF give information on platelet count, FIBTEM A10 and MCF show the fibrinogen level. INTEM (Intrinsic Activation/PTT) utilizes activators including kaolin and ellagic acid. EXTEM (Extrinsic Activation/PT) indicates fibrin formation and stabilization. Coagulation is activated by adding recombinant tissue factor. A low EXTEM despite a normal FIBTEM may suggest the deficiency or dysfunction of platelets as well as the deficiency of the factors including FXIII.

FIBTEM is informative on fibrinogen and thrombocyte defect. Normal FIBTEM MCF range is 8-10 mm. Additionally, MCF being 10 mm equals to 200 mg/dL fibrinogen. FIBTEM A10 indicates clot amplitude at the 10th minute after clot formation. FIBTEM measurement shows fibrin polymerization in ROTEM. In other words, it is correlated with fibrinogen level. When combined with EXTEM, FIBTEM distinguishes thrombocytopenia from hypofibrinogenemia. APTEM, on the other side, is the combination of EXTEM and aprotinin. It is performed by adding antifibrinolytic to EXTEM and shows hyperfibrinolysis. The normal range is 42-74 mm/ sec for EXTEM; 137-246 sec for INTEM CT; 52-72 mm for INTEM MCF and 9-25 mm for FIBTEM MCF. HEPTTEM can be defined as the heparinase-added INTEM assay.

HEPTEM is used to confirm the effect of residual heparin on coagulation. Treatment is required if EXTEM A10 <35 mm or FIBTEM A10 > 10 mm (1).

ECATEM uses ecarin, snake venom, as the factor activator (20). Ecarin converts prothrombin to meizothrombin which has a low thrombin activity. Meiothrombin is inhibited by hirudin and other direct thrombin inhibitors including argatroban, bivalirudin, and dabigatran. CT in ECATEM is not affected by direct inhibitors of factor Xa, such as warfarin, rivaroxaban, apixaban, and edoxaban, and phospholipid-dependent anticoagulants such as lupus anticoagulants.

NATEM, which can demonstrate fibrinolysis, is activated by recalcifications (star-tem® reagent). In other words, it is susceptible to all endogenous activators including infection from circulating monocytes, sepsis, and cirrhosis and tissue factor released in ECMO. Therefore, it can be a predictor of DIC development in TIC (21).

For a normal clot formation process, INTEM CT should be 122-208 sec; INTEM A10 should be 40-60 mm; INTEM MCF should range from 51-72 mm, and HEPTEM CT should be equal to INTEM CT. In the presence of low dose heparin, INTEM CT >HEPTEM CT, Delta CT >HEPTEM CT. In the presence of high dose heparin, however, INTEM Flat line CT >1200 sec and HEPTEM CT <280 sec. In the presence of high dose protamine, HEPTEM CT >>INTEM CT. In the case of k-dependent factor deficiency, EXTEM CT exceeds 80 sec as in warfarin therapy. In hyperfibrinolysis, EXTEM ML goes above 15% within 60 min. Fibrinogen deficiency leads to an order as EXTEM A10 <40 mm and FIBTEM A10 <10 mm. In thrombocytopenia, EXTEM A10 <40 mm, but FIBTEM A10 >10 mm. In the case of hypercoagulopathy with a thrombotic risk, EXTEM CT <40 sec, EXTEM CFT <50 sec, EXTEM MCF > 68 mm, FIBTEM MCF >24 mm and LI 60 <3% (22).

In a trauma patient, FVIIa activity decreases by 90% and factor VIIa/ TF complex activity decreases by 55% when pH level falls 7.0 from 7.4 (23). The prolongation of EXTEM CT may suggest vitamin K-dependent factor deficiency whereas the reduction of EXTEM, INTEM A10, and MCF or the extension of CFT may suggest fibrinogen deficiency or decreased platelet function. EXTEM or INTEM CLI levels are the indicators of fibrinolysis. An EXTEM A10 lower than 40 mm and a FIBTEM A10 higher than 10 mm can refer to poor platelet function. APTEM CLI infers platelet-dependent clot retraction or decreased fibrin monomer bond associated with FXIII deficiency. In the case of long HEPTEM and INTEM CT, it is not possible to mention factor deficiency. Nonetheless, if HEPTEM CT is normal and INTEM CT is extended, heparin effect should be considered. Fibrinogen of 1 g elevates blood level by 0.2-0.3 g/L in a 80 kg patient which leads to a 2 mm increase in FIBTEM A10 MCF. Modified TEG/ROTEM parameters include maximum velocity of clot formation (maximum rate of thrombus generation, MaxVel), time to reach MaxVel (time to maximum thrombus generation, tMaxVel) and total thrombus generation. These parameters have been found to be more specific to FVII. This new test is called ROTEM tif-TEM (Table 2).

TABLE 2
The limitations of ROTEM

Limitations
1. It has decreased sensitivity to GPIIb/IIIa antagonists.
2. It is not sensitive to aspirin and clopidogrel.
3. It is insufficient for the detection of von Willebrand factor (vWF) and thrombocyte function.
4. Its sensitivity to low-molecular-weight heparin is low.
5. The lack of standardization; age, gender and alcohol influence its usage.
6. It must be regularly checked.

As the measurements in ROTEM are performed at 37°C, the coagulation changes in hypothermic patients are ignored. It takes 60 min to fully complete the test, but the MCF values can be obtained within 10 min. However, this time can extend to 30-40 min in anti-coagulated patients. In such cases, using TEG is the solution. The effect of hematocrit on effective plasma volume is not considered either in standard or bedside tests. For this reason, these tests are inadequate for the prediction of coagulation disorders. TEG/ ROTEM cannot manifest the disorders associated with aspirin and clopidogrel or trauma (Table 2).

There is no hand-contact with the sample in ROTEM Sigma and TEG 6s. Both tests function fully automatically. There is a portable microfluidic cartridge without vibration sensitivity which allows automated bloodletting of ~0.4 ml blood sample through four separate channels. Nearly 20 µl

sample is transferred to each cell. As clot develops, the resonance in the system increases forming a trace as a part of mapping.

ROTEM platelets

There are ARATEM (arachidonic acid), ADPTEM (adenosine diphosphate) and TRAPTEM (thrombin activating peptide) components tests in ROTEM for definitive differential diagnosis. Impaired thrombocyte aggregation correlates with a reduction in the curve. The impedance between the two electrodes placed in the cuvette is measured. With the addition of activators, thrombocytes are activated and start to aggregate around the electrodes which turns into a kinetic curve subsequently. The measurement finalizes with 3 different parameters. A6 describes the amplitude after 6 minutes and the aggregation level of platelets after 6 minutes. Maximum Slope (Ohm/min) gives the rate of the aggregation. Area under the curve (AUC) reveals the overall platelet aggregation from the onset of the curve aggregation to the 6th min. Modern TEG devices utilize kaolin instead of adenosine diphosphate and arachidonic acid. In this way, the contribution of platelets to clotting can be more precisely indicated.

EXTEM and FIBTEM MCF correlates with clot strength. Direct tissue trauma, organ hypoperfusion, endothelial injury, and protein C activation leads to an increase in plasma and fibrin degradation. Severe hyperfibrinolysis is the presence of lysis >15% in TEG 30 minutes after the achievement of the maximum clot amplitude, and is seen in 5% of the patients developing trauma-mediated hyperfibrinolysis. It is a fatal condition with a mortality rate of 80%. When if hyperfibrinolysis is mild, more than 3% lysis within 30 min has been linked to the need for blood transfusion and mortality (24).

CONCLUSION

TIC, which has been related to several mechanisms, originates from platelet dysfunction, hyperfibrinolysis, endothelial dysfunction and hypodysfibrinogenemia. As the viscoelastic coagulation tests analyze coagulation in a cuvette, not in blood vessels, and in static conditions, the clinical status must be considered for treatment. Even though TEG CL and ROTEM ML have limited comparability in the detection of numerous parameters, they have equal sensitivity for excessive fibrinolysis. Moreover, TEG MA and ROTEM MCF have been found to be equally effective in predicting the need for blood transfusion and mortality (25). EXTEM A5 and FIBTEM A5 are useful in determining the need for massive transfusion and diagnosing acute endogenous coagulopathy. The utilization of POC tests reduces the incidence of unnecessary blood product transfusion, and consequently, leads to a reduction in cost.

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