REVIEWS AND SPECIAL ARTICLE

A Review of Thromboelastography

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ABSTRACT

This is the first of two articles describing the uses of point of care testing in coagulation management. The first article describes the basis of thromboelastography with its physical principles and uses. The second describes discussions of case studies in clinical scenarios.

Keywords: Point of care tests, Thromboelastography, Coagulation, Haemostasis.

INTRODUCTION

Haemostasis in the process of clot formation is a joint function of platelet activation to form a platelet plug and coagulation cascade leading to clot formation. Traditionally, this function is measured using conventional tests, such as platelet number and function, activated partial thromboplastin time, prothrombin time, thrombin time, fibrinogen levels and fibrin degradation products.

However, these test various parts of the coagulation cascade but in isolation and are static tests, which take time to complete and invariably lead to delay in a timely management. In addition to this, they need to be repeated at intervals and although they assess platelet number, they do not give accurate information on platelet function. Being plasma tests, they might not be accurately reflecting what actually happens to the patient.

Thromboelastography (TEG) is a method of testing the efficiency of coagulation in the blood. It was first developed by Dr Hellmut Hartert at University of Heidelberg, School of Medicine in 1948. TEG overcomes the above-mentioned limitations of conventional coagulation tests.

TEG provides an effective and convenient means of monitoring whole blood coagulation. It evaluates the elastic properties of whole blood and provides a global assessment of haemostatic function.

It is recommended for and commonly used in assessing haemostasis during liver transplantation, obstetric procedures and cardiac surgery. It is useful not only in cases of bleeding patients but also used to predict postoperative thrombosis.[1] In cardiac surgery, where the risk of bleeding is higher, TEG monitoring helps to identify and target those who need transfusion.

METHODOLOGY

The test sample is placed in the oscillating cup at 37° C. A pin is suspended from torsion wire into blood sample (Fig. 1). Development of fibrin strands couple the motion of the cup to the pin. This coupling is directly proportional to the clot strength. Increased tension in the wire is detected by the electromagnetic transducer and electrical signal amplified to create a trace, which is displayed on computer screen. Deflection of the trace is proportional to clot strength.

PARAMETERS OF MEASUREMENT

r-time: Represents period of time of latency from start of test to initial fibrin formation. This represents the standard clotting studies. Normal range: 15 to 23 minutes (native blood); 5 to 7 minutes (kaolin-activated).

k-time: Represents time taken to achieve a certain level of clot strength (where r-time = time zero)—equates to amplitude 20 mm. Normal range: 5 to 10 minutes (native blood); 1 to 3 minutes (kaolin-activated).

α-angle: Measures the speed at which fibrin build-up and cross-linking takes place (clot strengthening), and hence assesses the rate of clot formation. Normal range: 22 to 38 (native blood); 53 to 67 (kaolin-activated).

Maximum amplitude: MA is a direct function of the maximum dynamic properties of fibrin and platelet bonding via GPIIb/IIIa and represents the ultimate strength of the fibrin clot and which correlates to platelet function: 80% platelets; 20% fibrinogen. normal range: 47 to 58 mm (native blood); 59 to 68 mm (kaolin-activated).
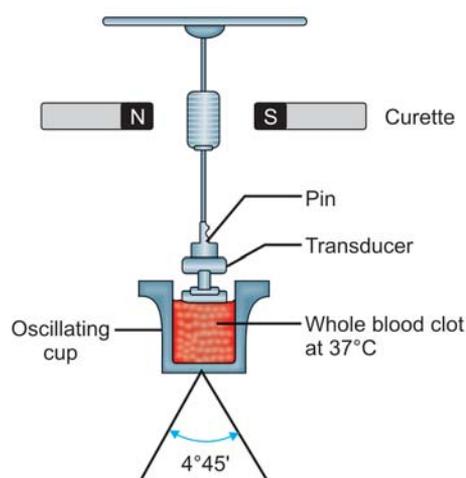

Fig.1: Basis of the thromboelastogram (TEG)

Situations with deficient coagulation factors, such as hypofibrinogenaemia, thrombocytopenia or thrombo-cytopathy show prolonged *r* and *k* times and decreased MA and α angle.

In hypercoagulable states, *k* and *r* times are decreased with an increase in MA and α angle.

Coagulation index (CI)

A mathematical formula determined by the manufacturer, which takes into account the relative contribution of each of these four values into one equation. CI (normal range – 3 to 3 mm) is an overall indicator of coagulation and indicates normal, hypo- or hypercoagulable state.

LY30: This is percentage decrease in amplitude 30 minutes post-MA and gives measure of degree of fibrinolysis (Fig. 2). Normal range < 7.5% (native blood); < 7.5% (celite-activated) and similarly, LY60 is the percentage decrease in amplitude 60 minutes post-MA.

A30 (A60)

Amplitude at 30 (60) minutes post-MA.

EPL

Represents 'computer prediction' of 30 minutes lysis based on interrogation of actual rate of diminution of trace amplitude commencing 30 seconds post-MA and is the earliest indicator of abnormal lysis.

Early EPL > LY30 (30 mins EPL = LY30)
Normal EPL < 15%

Fibrinolysis leads to ↑ LY30/↑ LY60 ↑ EPL and ↓ A30/↓ A60.

CLINICAL INTERPRETATION OF DIFFERENT STAGES OF COAGULATION BY TEG

- Clot formation
  - Clotting factors—*r, k times*
- Clot kinetics
  - Clotting factors—*r, k times*
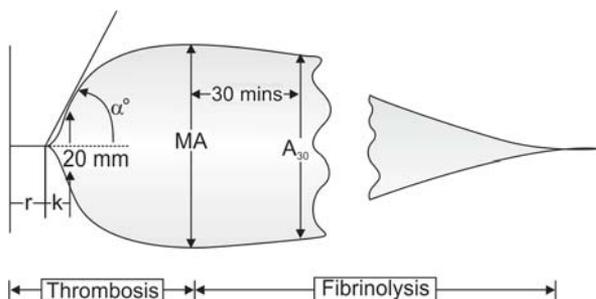 - Platelets—*MA*

Fig. 2: A typical TEG trace

- Clot strength/stability
  - Platelets—*MA*
  - Fibrinogen—Reopro-mod *MA*
- Clot resolution
  - Fibrinolysis—LY30/60; EPL A30/60.

Useful Modifications

Each thromboelastograph has two sets of curette-pin-transducer. Up to eight channels may be connected to the computer. So, each evaluation may be simultaneously performed in different channels with the addition of activators, plasma, platelet concentrate, heparinase, antifibrinolytics, and titrated protamine, aiming not only at coagulopathy diagnosis but also at testing the treatment *in vitro*.

Thromboelastographic evaluation of clot formation during heparinisation (i.e. cardiopulmonary bypass) is now available. Heparinase (an enzyme breaking heparin) has been introduced to the TEG(r) technology, assisting in identification of abnormal coagulation in 'heparinised' patients, prior to heparin reversal with protamine. This is useful during long pump runs, deep hypothermia and use of ventricular assist devices or complicated major vascular cases such as thoracoabdominal aneurysm. The test will also help us to decide, if more protamine is needed to fully reverse heparin (Fig. 3).

Other antifibrinolytic agents, such as Epsilon-aminocaproic acid, tranexamic acid and aprotinin (still has a role in liver transplant, though use in cardiac surgery in question due to postoperative renal failure) can be added to test their effectiveness in treatment of fibrinolyis.

Adding c7E3 Fab (Reopro), which binds to the platelet GPIIb/IIIa receptors, will eliminate platelet function from the thromboelastogram. The MA will become a function of fibrinogen activity (MAR). Platelet function can then be calculated by subtracting MAR from the whole blood MA.

ROTEM

Rotational thromboelastometry uses a modification of TEG, signal of the pin is transmitted using an optical detector instead of a torsion wire. Movement orginates from pin and not the cup. The ROTEM uses an electronic pipette, which improves reproducibility and performance. In ROTEM, the sensor shaft rotates rather than the cup. The ROTEM technology avoids several limitations of traditional instruments for thromboelastography, especially the susceptibility to mechanical shocks and vibrations. However, TEG is rated as the best compromise between usability, usefulness and cost as compared to ROTEM[2] (Fig. 4).

PLATELET FUNCTION ANALYSIS

Personalised antiplatelet therapy is possible with TEG. TEG analysis provides the measure of maximum platelet function, and hence the degree of hypercoagulability and extent of inhibition needed. The platelet mapping assay reports the percent inhibition and net platelet function. So, you can identify

- Whether patients are resistant to antiplatelet therapy
- The effect of the therapy
- Whether they are at their therapeutic level
- Their risk for ischaemic or bleeding event.

Platelet aggregometry is also an alternative test but it is more laboratory based rather than point of care.

CLINICAL USES OF THROMBOELASTOGRAPHY

Thromboelastography is mainly used in the following:
- Cardiac surgery
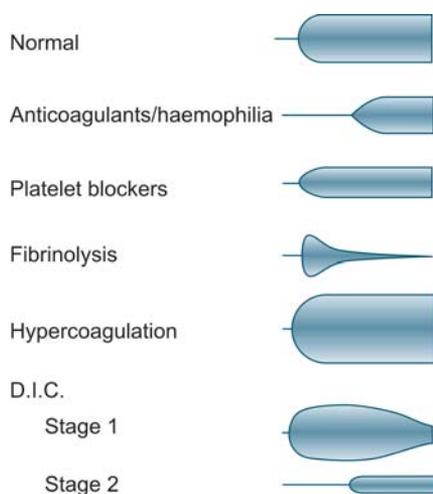- Liver transplantation
- Major obstetric haemorrhage.

Fig. 3: Examples of qualitative TEG traces for interpretation
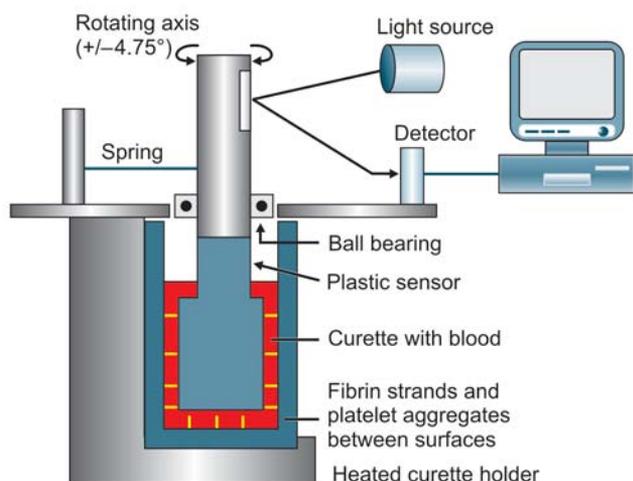

Fig. 4: Basis of ROTEM (Rotational thromboelastometry)

Cardiac Surgery and TEG

The main reasons for bleeding in cardiac surgery patients can be classified under four broad headings of preoperative factors, cardiopulmonary bypass (CPB) factors, post-CPB factors and surgical bleeding. Preoperative factors include antiplatelet medications, such as aspirin/clopidogrel, patients on warfarin/heparin and pre-existing clotting or platelet abnormalities. Intraoperative factors might be decreased platelet count or heparin effect. Postoperatively factors could be reversal of heparin nonfunctional platelets or fibrinolysis. TEG helps in pinpointing the specific problem and also predicting how treatment would work, thereby reducing blood transfusion in cardiac surgery[3-5] (Fig. 5).

Liver Transplantation and TEG

The TEG is a unique gross test of clot strength perfectly suited to the changes during liver transplantation.[6] The use of TEG in liver transplantation is focused on monitoring coagulation and management of blood products transfused rather than identification of patients at risk.

EVIDENCE TO SUPPORT

TEG correlates well with ACT and coagulation profiles and the TEG is the most accurate predictor of bleeding.[7] TEG had the best positive predictive factor values (PPV) for increased postoperative bleeding, with PPV of 62.5%. Negative predictive value (NPV) for increased postoperative bleeding was distributed as follows: Platelet count below 130×10^9/L (100%); TEG (92.3%); bleeding time above 9 minutes (91.7%); fibrinogen below 175 mg/dL (90%); APTT (85.7%); PA (75%). Although, the bleeding time and platelet count had sensitivities similar to the TEG, TEG specificity was greater. In addition, they suggested that patients with an abnormal TEG were at increased risk of bleeding but that excessive bleeding in the face of a normal TEG implied surgical bleeding and FFP, and platelets should not simply be used empirically.[8]

Shore-Lesserson compared 'TEG-based' and 'conventional' protocols to manage postoperative bleeding. While there was no significant difference in mediastinal tube drainage between the groups, blood and blood component therapy was significantly less in the 'TEG' than in the 'conventional' group[4] (Fig. 6).

ADVANTAGES OF TEG

While other conventional tests evaluate the coagulation pathway until the formation of the first fibrin strands, the TEG continuously evaluates clot formation, its strength, platelet function until eventual clot lysis or retraction. Hence, it is dynamic and gives information on the entire coagulation process and not just an isolated part.
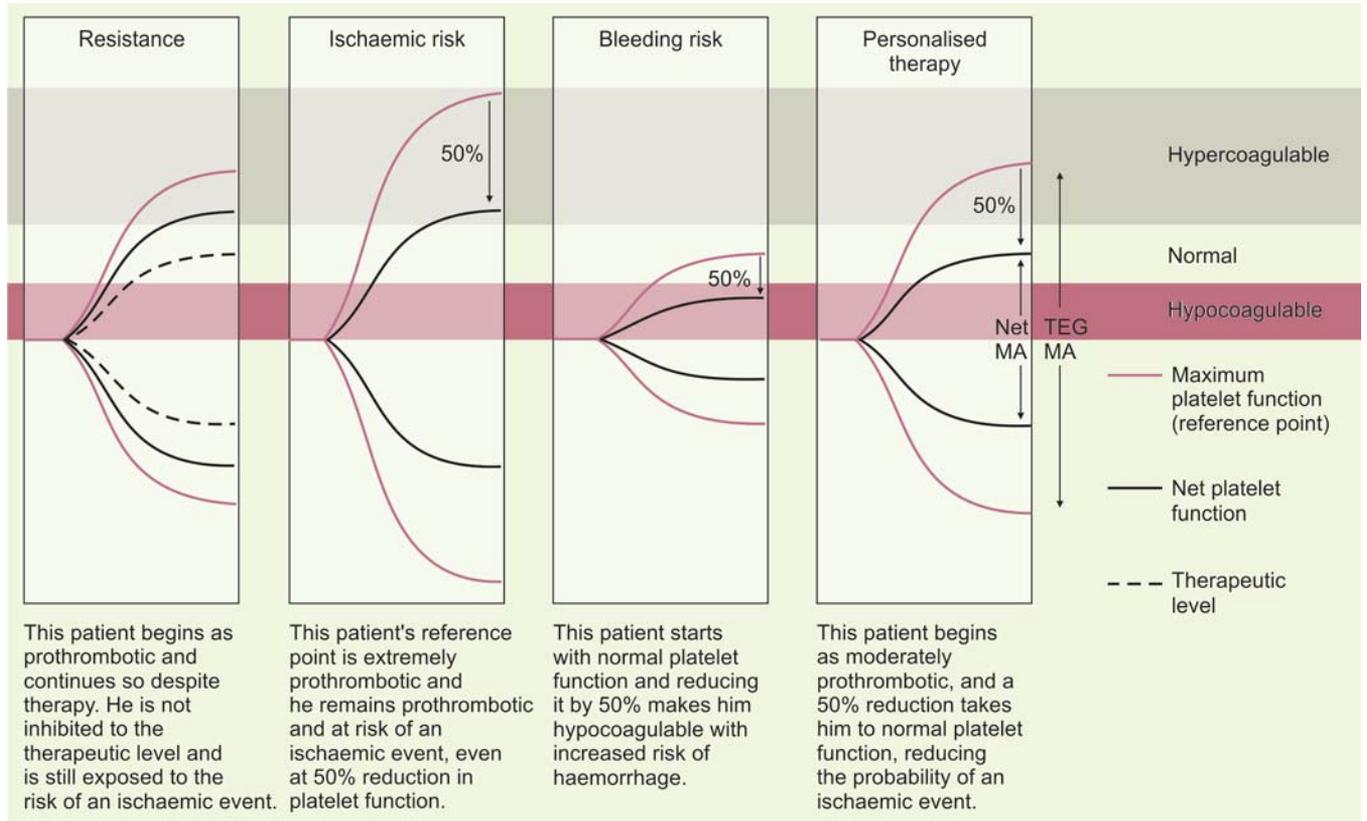
Fig. 5: Interpretation of TEG and platelet function analysis traces (*Source:* Haemonetics UK)
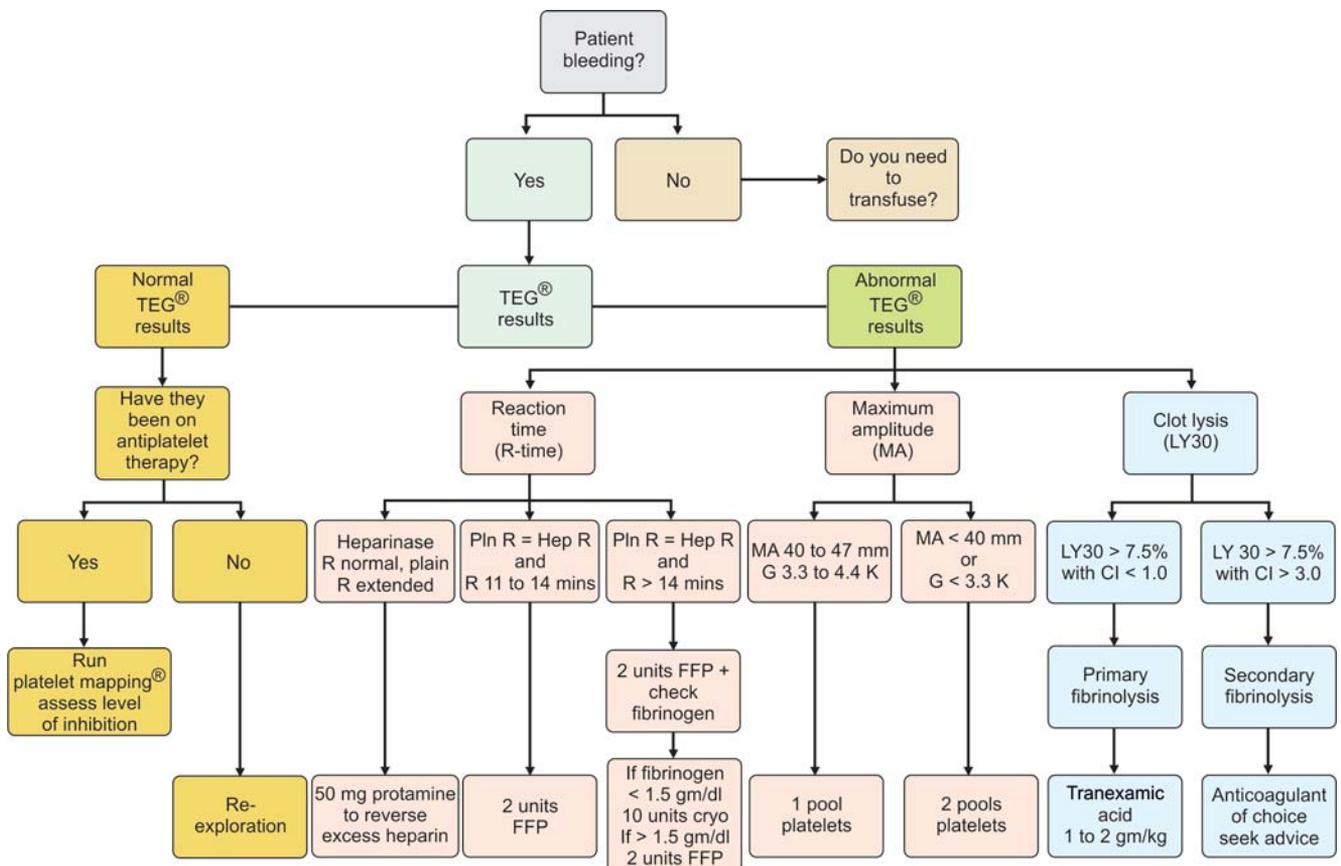

Fig. 6: Suggested guidance for haemostasis management using a TEG-based protocol
(*Source:* Modified Leicester protocol and Haemonetics UK)

TEG is a bedside procedure and rapid results facilitate timely intervention. Also, being computerised process, it is easy to use and results can be recorded and stored.

It not only helps to pinpoint the cause of bleeding but also helps to predict, how specific correction would work and minimises the need for blood transfusion. Due to high negative predictive value of this test, it helps to identify patients, who are at lower risk of bleeding. It also helps to identify those requiring surgical intervention. Hence, it is cost-effective.[4,7,8]

LIMITATIONS

The main limitation of this technique is that it has never been formally validated or standardised by the haematologists in comparison to the conventional tests.

Delay in processing can alter the test result.[9] Review by Samana et al suggests that postoperative hypercoagulability exploration requires the use of specific haemostasis tools as platelet aggregation variables, platelet activation measurements (flowcytometry variables), thrombin-antithrombin complexes, prothrombin fragment 12, type 1 plasminogen activator inhibitor, or plasmin-antiplasmin complexes. Even a modified thromboelastography should not be used alone to express a hypercoagulable state.[10]

REFERENCES

1. Kashuk, Jeffry L, Moore, Ernest E, Sabel, Allison, et al. Rapid thromboelastography (r-TEG) identifies hypercoagulability and predicts thromboembolic events in surgical patients. Surgery. October 2009;146(4):764-74.
2. Jackson GN, Ashpole K, Yentis SM. The TEG vs the ROTEM thromboelastography/thromboelastometry systems. Anaesthesia 2009;64(2):212-15.
3. Von Kier S, Royston D. Reduced hemostatic factor transfusion using heparinase modified TEG during cardiopulmonary bypass. Br J Anaesthesia 2001;86:575-78.
4. Shore-Lesserson L, Manspeizer HE, Deperio M, et al. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. Anesth Analg 1999;88:312-19.
5. Westbrook AJ, Olsen J, Bailey M, Bates J, Scully M, Salamonsen RF. Protocol based on thromboelastograph (TEG) out-performs physician preference using laboratory coagulation tests to guide blood replacement during and after cardiac surgery: A pilot study. Heart lung and circulation 2009;18(4): 277-88. Date of Publication 2009.
6. Gillies BS. Thromboelastography and liver transplantation. Seminars in thrombosis and hemostasis. 21 Suppl 1995;4: 45-49.
7. Spiess BD, Gillies BSA, Chandler W, Verrier E. Changes in transfusion therapy and re-exploration rate after institution of a blood management program in cardiac surgical patients. J Cardiothorac Vasc Anesth 1995;9:168 -73.
8. Essell JH, Martin TJ, Salinas J, et al. Comparison of thromboelastography to bleeding time and standard coagulation tests in patients after cardiopulmonary bypass. J Cardiothorac Vasc Anesth 1993;7:410-16.
9. White H, Zollinger C, Jones M, et al. Can thromboelastography performed on kaolin-activated citrated samples from critically ill patients provide stable and consistent parameters? International journal of laboratory hematology. 2010;32(2): 167-73.
10. Charles Marc Samama. Thromboelastography: The Next Step, Anesth Analg 2001;92:563-64.

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