Thrombelastography

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Citation

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Abstract

INTRODUCTION

Hazardous risks accompanying the transfusion of heterogenous blood products and increasing shortage of blood products led to further search for better techniques of coagulation monitoring. Because of the limitations of standard coagulation tests, other techniques such as thrombelastography (TEG(r)) have been re-examined. TEG(r) was originally described by Hartert in 1948 ($_1$). Continuous improvements of this technique over the decades made this test a valuable tool for the medical personnel interested in coagulation. The TEG(r) monitors hemostasis as a whole dynamic process instead of revealing information of isolated conventional coagulation screens ($_2$). The TEG(r) measures the viscoelastic properties of blood as it is induced to clot under a low shear environment resembling sluggish venous flow. The patterns of changes in shear-elasticity enable the determination of the kinetics of clot formation and growth as well as the strength and stability of the formed clot. The strength and stability of the clot provides information about the ability of the clot to perform the work of hemostasis, while the kinetics determine the adequacy of quantitative factors available to clot formation.

PRINCIPLES OF THROMBELASTOGRAPHY

The Computerized Thrombelastograph(r) Coagulation Analyzer (Haemoscope Corp. Skokie IL.) is a small instrument capable of running two samples simultaneously, easy to set up. It is connected to a computer (running the TEG(r) Analytical Software) through an A/D interface box . The coagulation profile is displayed on the screen as an outline of the Thrombelastograph(r) Coagulation Analyzer with the range of normal values displayed as dotted lines. The thromboelastogram is one of two clinically available viscoelastic tests that characterize formation and strength of the blood clot over time. The TEG(r) can measure in vitro the life of a clot, the time to initial clot formation, then evaluate a developing clot it's acceleration phase, strengthening and retraction. TEG(r) can also detect clot lysis. A sample of celite activated whole blood (0.36 ml) is placed into a prewarmed cuvette. A suspended piston is then lowered into the cuvette which moves in rotation of a 4.5 degree arc backwards and forwards. The normal clot goes quite fast through an acceleration and strengthening phase. The fiber strands which interact with activated platelets attach to the surface of the cuvette and the suspended piston. The clot forming in the cuvette transmits its movement onto the suspended piston. A "weak" clot stretches and therefore delays the arc movement of the piston, which is graphically expressed as a narrow thromboelastogram. A strong clot in contrary will move the piston simultaneously and proportionally to the cuvettes movements, creating a thick thromboelastogram.

Figure 2

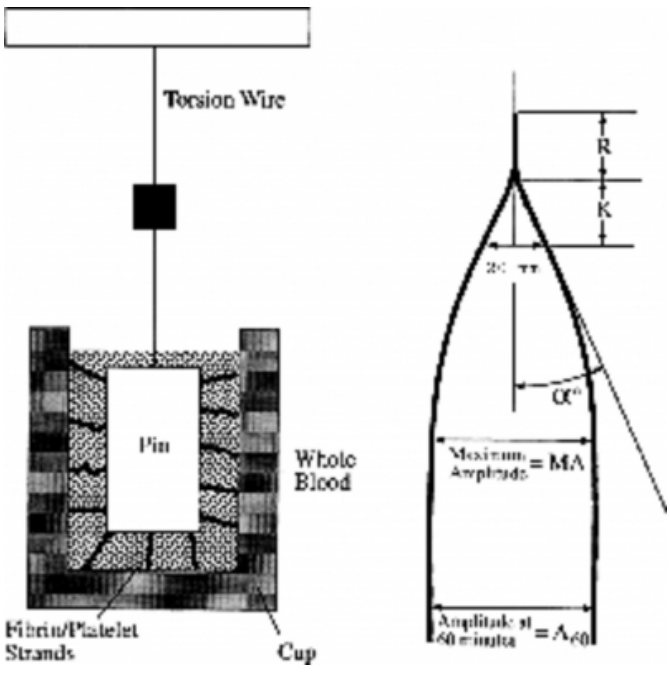
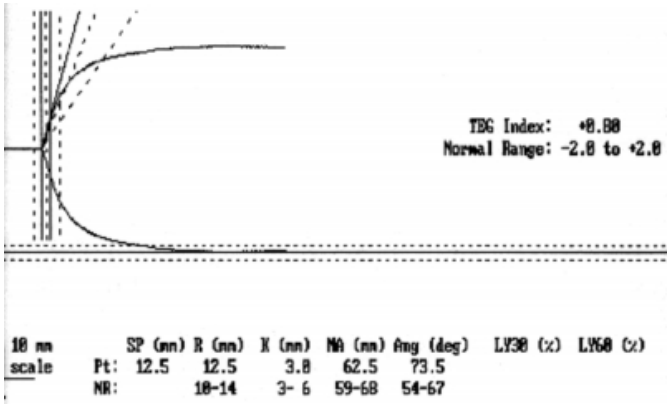


Figure 3

Figure 2: Normal TEG(r)



The strength of a clot is graphically represented over time as a characteristic cigar shape figure. There are five parameters of the TEG(r) tracing: R, k, alpha angle, MA and MA60, which measure different stages of clot development.

R: is a period of time from initiation of the test to the initial fibrin formation.

k: is a measure of time from beginning of clot formation until the amplitude of thromboelastogram reaches 20 mm, and represents the dynamics of clot formation.

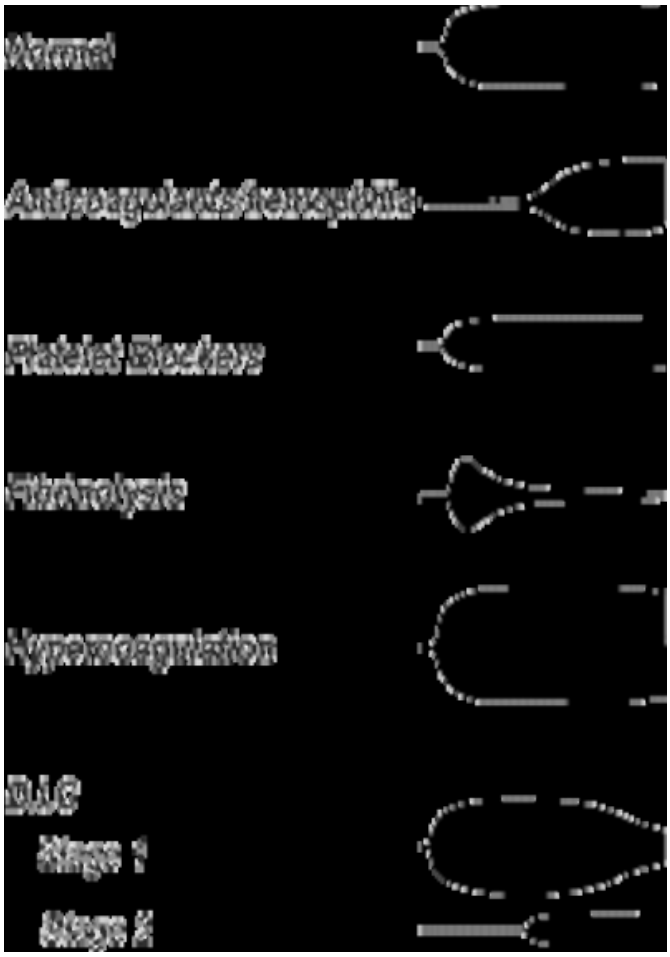
alpha angle: is an angle between the line in the middle of the TEG(r) tracing and the line tangential to the developing "body" of the TEG(r) tracing. The alpha angle represents the acceleration (kinetics) of fibrin build up and cross-linking.

MA - Maximum amplitude reflects strength of a clot which is dependent on number and function of platelets and its interaction with fibrin.

MA60: measures the rate of amplitude reduction 60 min. after MA and represents the stability of the clot.

Figure 4

Overview of TEG(r) interpretation:



Thromboelastographic evaluation of clot formation during heparinization (i.e., cardiopulmonary bypass) is now available. Recently, heparinase (an enzyme breaking heparin) has been introduced to the TEG(r) technology, allowing identification of abnormal coagulation in "heparinized" patients, prior to heparin reversal with protamine. This test may prove particularly useful during long pump runs, deep hypothermia, use of ventricular assist devices or complicated major vascular cases i.e.: repair of thoracoabdominal aneurysm. The test will also detect if more protamine is needed to fully reverse heparin.

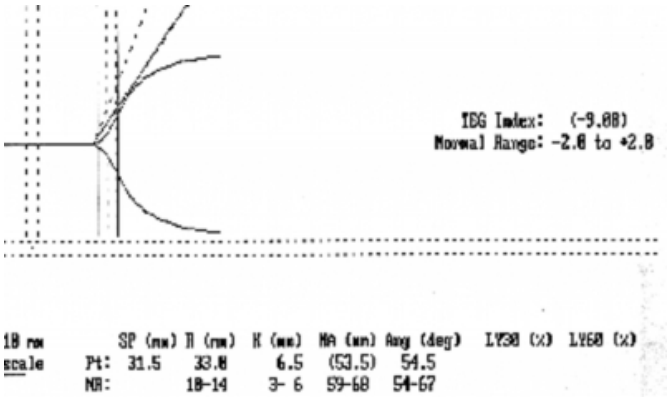
Other reagents that may be added to the whole blood sample are antifibrinolytic agents such as Epsilon-Aminocaproic Acid, Tranexamic acid and Aprotinin. This will test their effectiveness in treatment of fibrinolysis.

Another modification of the TEG(r) will enable to determine the specific contribution of platelets and fibrinogen to the MA value of the TEG(r) tracing. Adding c7E3 Fab (REOPRO), a recently FDA approved monoclonal antibody

which binds to the platelet GPIIb/IIIa receptors, to the TEG(r) sample will eliminate platelet function from the thromboelastogram ($_3$). The MA will become a function of fibrinogen activity (MAR). Therefore subtraction of (MAR) from a whole blood MA (without REOPRO) (MAW), will result in determining specific contribution of platelets function to MA (MAP).

Figure 5

Figure 3: TEG(r) Example 1

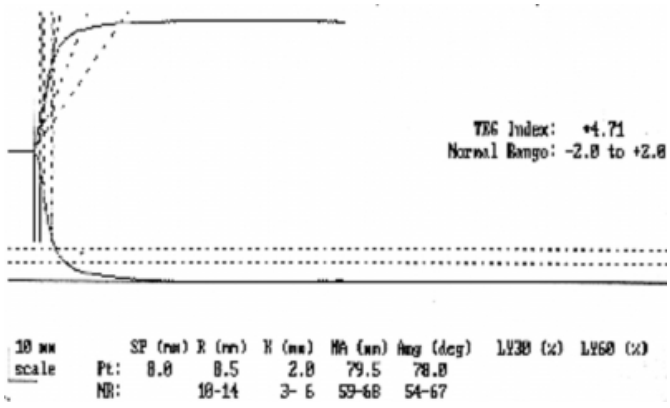


EXAMPLES

For training purposes we would like that you study the TEG(r)'s below. Please make a diagnosis and suggest a treatment for each TEGTM. Click on the links below the TEG(r) examples to check your answers.

Figure 6

Figure 4: TEG(r) Example 2



Answer to TEG(r) Example 1

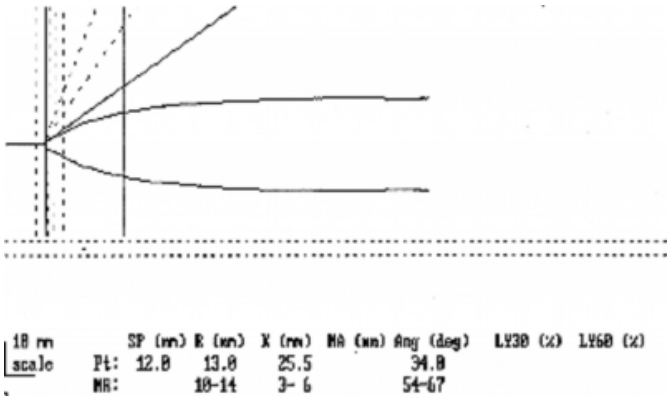
Diagnosis: R parameter elongated: Delayed clot formation; suspect

Treatment: Measure an activated clotting time (ACT) and repeat TEG(r) with Heparinase.

1.

Figure 7

Figure 5: TEG(r) Example 3



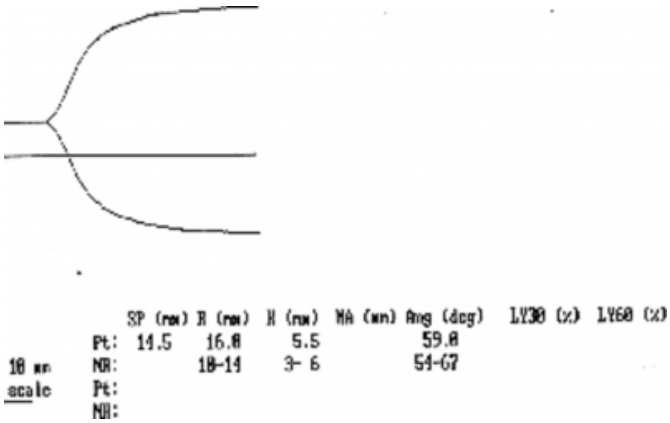
Diagnosis: Short R and K, large a and MA, no fibrinolysis: Hypercoagulable state.

Can be found:

Treatment: Depending on the clinical situation:
may be treated with anticoagulant drug therapy such as

Figure 8

Figure 6: TEG(r) Example 4



Answer to TEG(r) Example 3

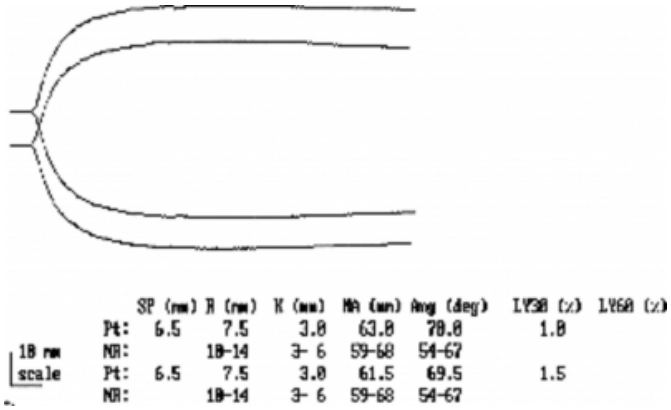
Diagnosis: a and MA are small: Weak Clott Formation indicative of hypofibrinogemia and/or thrombocytopenia/poor platelet function.

Treatment: Requires administration of FFP, platelets and possible cryoprecipitate. Adding c7E3 Fab (REOPRO) to the TEG(r) sample will eliminate platelet function from the TEG(r) tracing. The MA will become a function of fibrinogen activity. Low fibrinogen activity can be corrected by administration of cryoprecipitate or FFP.

A repeat TEG(r) should be performed post treatment.

Figure 9

Figure 7: TEG(r) Example 5

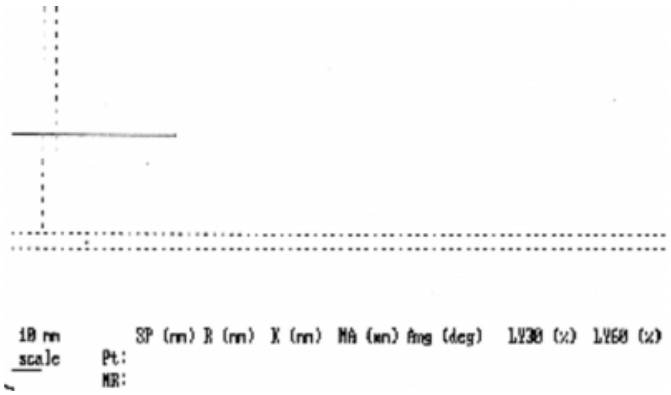


Diagnosis: Heparin Effect. The top curve represents a TEG(r) with Heparinase (heparin activity eliminated) and the bottom trace is the same sample without Heparinase.

Treatment: Reverse the heparin and repeat the TEG(r).

Figure 10

Figure 8: TEG(r) Example 6

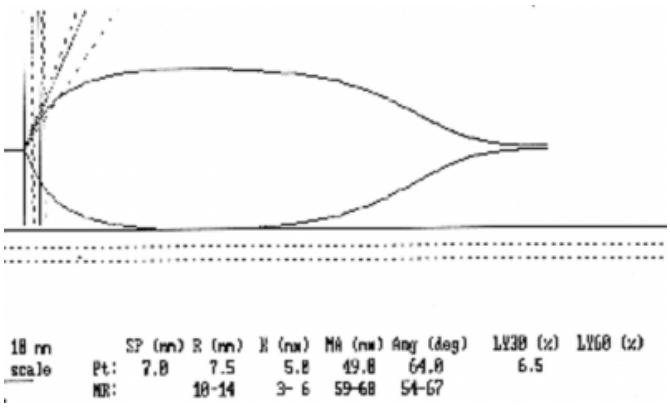


Diagnosis: Normal Coagulation Profile. This is a TEG(r) from the same patient shown in example 4. The heparin was reversed with protamine. The top curve represents a TEG(r) with Heparinase (heparin activity eliminated) and the bottom trace is the same sample without Heparinase. Since both traces are identical all heparin was reversed by protamine.

Treatment: If there is still bleeding the surgeon will have to perform a better job.

Figure 11

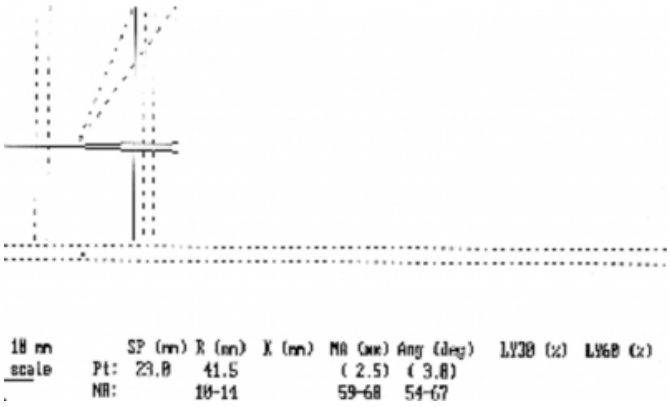
Figure 9: TEG(r) Example 7



Treatment:

Figure 12

Figure 10: TEG(r) Example 8



Diagnosis: (Short R) MA borderline, Lysis30 6.5%: Poor platelet function and fibrinolysis

Treatment: Administer platelets and antifibrinolytics (such as e-Aminocaproic Acid, Tranexamic Acid or Aprotinin). The antifibrinolytics can be added to the TEG(r) to pre-evaluate their effectiveness. Repeat the TEG post treatment.

{image:12}

Diagnosis: R eleongated, K not readable, MA very small, a very small: Technical error in processing TEG(r) or severe coagulopathy (correlate with clinical scenario)

Treatment: Repeat TEG(r)

DISCUSSION

The TEG(r) enables global assessment of hemostatic function. While other conventional tests stop with the formation of the first fibrin strands, the TEG(r) begins to evaluate clot formation at this point and collects data as

clotting continues through to eventual clot lysis or retraction 2. Therefore, one single test produces information about several steps in the coagulation process. Unlike laboratory tests of hemostatic function which are measured in plasma, the TEG(r) measures clotting in whole blood and thus the interaction between fibrinogen, platelets and the protein coagulation cascade. Poor correlations are seen between most conventional coagulation tests and TEG(r) measurements ([4]) ([5]). The only significant correlation could be shown between the maximum amplitude MA of the TEG(r) and platelet aggregometry ([6]).

The modification of the TEG(r) through the addition of other substances such as heparinase or the monoclonal antibody fragment c7E3 (REOPRO) allow evaluation of heparin reversal with protamine or further differentation of coagulopathies. The heparinase-modified TEG(r)-assay proved to be more sensitive in detecting very low levels of heparin in patients undergoing cardiopulmonary bypass surgery compared to the activated clotting time (ACT) ([7]). Data gathered in the same study identified the presence of heparin before systemic heparinization or protamin reversal, and evaluated platelet-fibrinogen interaction in patients receiving systemic heparin. The use of heparinase-guided thrombelastography was as well described in the assessment of a parturient who had been anticoagulated with heparin for suspected thromboembolic disease ([8]). TEG(r)-controlled heparin reversal in this case resulted in safe performance of regional anesthesia. In pediatric patients undergoing open heart surgery, the TEG(r) was able to predict with 100% accuracy increased postoperative bleeding. The specificity of TEG(r) prediction of future bleeding was 73% ([9]).

On the other hand, standard coagulation tests in adult patients undergoing cardiopulmonary bypass could only explain 12% of the observed variation in blood loss ([10]). The TEG(r) seems therefore to be superior in the assessment of postoperative coagulopathies. This hypothesis correlates with the observation made by the authors of this article. Another study compared the usefulness of the TEG(r) in post-cardiopulmonary bypass coagulopathies ([11]). Thrombelastography was a significantely better predictor (87% accuracy) of postoperative hemorrhage and need for reoperation than the activated clotting time ACT (30% accuracy) or coagulation profile (51% accuracy). Changes in transfusion therapy after institution of a blood management program based on TEG(r) in cardiac surgery patients resultet in a significantly lower incidence of overall transfusion (78.5% vs. 86.3%) during hospitalization and in total transfusion in the operating room (57.9% vs. 66.4%) ([12]). Mediastinal reexploration for hemorrhage was 5.7% before institution of TEG(r)-based coagulation monitoring and 1.5% in TEG(r)-monitored patients. The authors concluded that the use of TEG(r)-monitoring decreased the costs and potential risk for patients undergoing coronary artery bypass grafting surgery.

SUMMARY

The usefulness of thrombelastography has been sufficiently documented in general surgery ([13]) ([14]) ([15]), cardiac surgery (10-12) ([16]), urology ([17]), in obstetric patients ([18]) ([19]) ([20]), in pediatric patients ([21]) ([22]), and in liver transplantation ([23]) ([24]). TEG(r) certainly takes an important place among the different coagulation tests. It is the only test measuring all dynamic steps of clot formation until eventual clot lysis or retraction. The cost-effectiveness of TEG(r) could be demonstrated in several studies. A comprehensive knowledge of the method is necessary in order to make appropriate decisions. Better management of coagulopathies will result in a decrease of donor exposure and the risks accompanying transfusion of heterogeneous blood products. The authors hope to provide a better understanding and an increase in popularity of the TEG(r) among health care providers.

SUGGESTED READING

Seminars in Thrombosis and Hemostasis 1995, Volume 21, Supplement 4 was dedicated to thrombelastography and reviews most of the aspects of this technique.

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