THROMBOELASTOGRAPHY (TEG) IN TRAUMA

SUMMARY

Thromboelastography (TEG) is a test of whole blood coagulation that was developed in the 1950's, but was largely passed over in favor of conventional coagulation tests (PT, PTT, platelet count). It has been applied to transplant and cardiac surgery since the 1980's and has been shown to decrease usage of blood products and mortality when used to evaluate the coagulation cascade during these procedures. With new understanding of the "coagulopathy of trauma," there has been considerable interest in the use of TEG in the trauma population. This guideline reviews the interpretation of a thromboelastogram and how it may be used to guide blood product administration.

RECOMMENDATIONS

Level 1
- **None**

Level 2
- **Thromboelastography may be used to screen patients for coagulopathy in the following situations:**
  - **Blunt or penetrating trauma patients who arrive in hemorrhagic shock**
  - **Patients receiving massive transfusion protocol (1:1:1) to evaluate for discontinuation or guided product therapy**
  - **Clinical suspicion for hemorrhage or coagulopathy**

Level 3
- **Thromboelastography may be used to guide blood product administration in bleeding patients as follows:**
  - **TEG-ACT > 140 or R-time > 10 → transfuse fresh frozen plasma**
  - **K-time > 3 or ∝ angle < 53 → transfuse cryoprecipitate**
  - **MA < 50 → transfuse platelets**
  - **LY30 > 3% → administer tranexamic acid**

INTRODUCTION

TEG was developed in 1948 by Hellmut Hartert in Heidelberg, Germany as a test to detect clotting factor deficiencies (1). Its availability in the United States was limited until the 1980's, when the addition of disposable components, tissue activators, and computerized software made the test more practical, reproducible, and timely. A TEG is designed to assist the clinician in identifying whether a patient has normal hemostasis or is bleeding due to a coagulopathy or anticoagulant therapy. If a coagulopathy is identified, the TEG results will point to the specific therapy to treat it, whether using fresh frozen plasma, cryoprecipitate, or an anti-fibrinolytic or thrombolytic drug.

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

Specimen handling is key to the accuracy of the TEG (2). The sample is collected from the patient using a syringe or Vacutainer. Venipuncture must be atraumatic and free of tissue fluid. Stasis from prolonged use of a tourniquet must be avoided. Native whole blood can be used directly from a syringe collection. This requires that the TEG analyzer be in close proximity to where the sample is collected and the sample introduced into the analyzer within 4 minutes. Sodium-citrated whole blood (collected in 3.2%/105M sodium citrate) is used if the TEG is in a remote location and the sample must be transported. TEG analysis should be performed on citrated whole blood within 2 hours of blood collection that is kept at room temperature. Citrated samples are then recalcified prior to analysis.

It is critical to understand the different activators that may be used for thromboelastography to induce the clotting cascade. Conventional TEG is activated with kaolin, which initiates the intrinsic pathway, resulting in the "reaction time" or "R-time" that is similar to a PTT. Rapid thromboelastography utilizes tissue factor (TF) in addition to kaolin, activating both the intrinsic and extrinsic pathways, producing the activated clotting time or TEG-ACT.

As the clot begins to form in the presence of the activator, the TEG records the visceroelastic changes that occur in the sample. A pin suspended in the blood within a stationary cup is monitored for motion as fibrin-platelet bonding occurs. This motion is related to the strength of the clot and is analyzed by a computer, which creates a graphical representation.
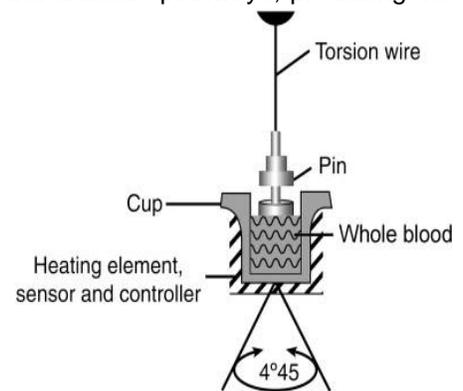
As noted, coagulation factors begin to accumulate producing the R-time or TEG-ACT. These values will be prolonged in the presence of coagulopathy and shortened in hypercoagulability. At this point, fibrin cross-linking begins the initial phases of clot formation. This is measured as both a time index known as the "K-time" (defined as time to 20 mm of clot) and as a rate. This rate can be determined by the slope of the TEG tracing and is expressed as the α-angle. The K-time and α-angle thus reflect the levels of circulating fibrinogen. Platelet aggregation then occurs until maximum clot strength occurs at the "maximum amplitude" (MA). Lysis of the clot may then begin, especially in the presence of severe coagulopathy or of fibrinolytic agents. The percentage of clot that has dissipated at 30 minutes time is expressed as the LY-30. The figure to the left shows the correlation between the coagulation cascade and TEG tracing, and are summarized at the end of this document.(2).
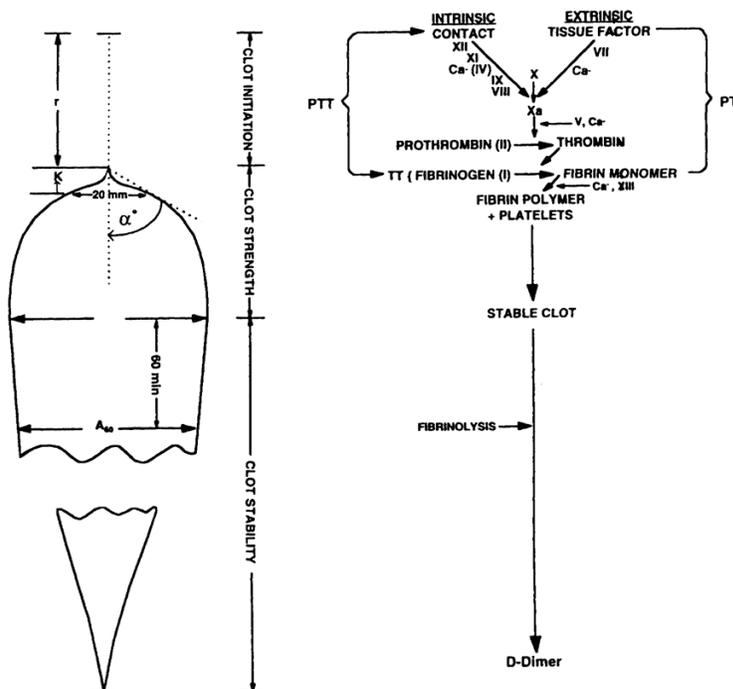
TEG is thus a test of whole blood coagulation, and is typically available within 45 minutes to an hour. Computer software is available that allows the tracing to be displayed electronically at remote locations, such as an operating room or the trauma bay.

Approved 12/04/2013
Revised 12/3/2014

LITERATURE REVIEW
TEG did not come into widespread use in the United States until the 1980's when it became an important tool during orthotopic liver transplantation (3). Although many patients with liver failure will have prolonged PT/INR, they are typically hypercoagulable as evidenced by TEG. Liver transplantation often requires a massive amount of blood transfusion due to blood loss and the complex coagulopathies that occur during the anhepatic and post-reperfusion stages. TEG-guided transfusion algorithms were shown to greatly reduce the requirements for blood product transfusion (3).

By the 1990's, TEG was being applied to cardiac surgery, which consumes 20% of all blood products in the United States. Ten percent of patients have excessive bleeding following cardiopulmonary bypass, 50% of these secondary to coagulopathy. This may occur due to inadequate heparin reversal or the effects of the cardiopulmonary bypass circuit on platelets. The alpha angle was shown to be strongly correlated with total blood loss. The first major study was published by Speiss et al in 1995 in an analysis of 1079 CABG patients (4). A TEG-guided algorithm was shown to decrease overall peri-operative transfusion requirements and the number of re-explorations for bleeding decreased from 5.7% to 1.5%. Ak et al in 2009 randomized 224 CABG patients to a clinician directed transfusion strategy or a TEG-guided algorithm (5). Overall, there was no difference in blood loss, packed red blood cells transfused, or clinical outcome. However, the TEG group received fewer transfusions of platelets, FFP, and tranexamic acid and had a significant cost savings.

Coagulopathy of Trauma
With its usefulness in detecting complex coagulopathies and facility for directing blood product transfusion, TEG has more recently been used in the trauma population. In the setting of massive hemorrhage, the body rapidly activates coagulation pathways to prevent ongoing blood loss. However, a delicate balance must occur to prevent a prothrombotic state which has complications such as deep venous thrombosis and pulmonary embolism. This results in the so-called "coagulopathy of trauma," which is poorly understood, but an intense area of research. Niles (2008) described 391 military casualties in Iraq of whom 38% arrived to the receiving facility coagulopathic (6). Brohi (2003) found that of 1,008 patients arriving to a Level 1 trauma center, 25% arrived coagulopathic (7). Cotton (2008) found that among 211 patients requiring massive transfusion protocol, 75% had demonstrated coagulopathy upon admission (8). The exact mechanism of this coagulopathy is unclear, but appears to be at least partially regulated by protein C. Cohen et al examined 203 trauma patients with serial PT, PTT, Va, VIIIa, protein C, t-PA, and D-dimer levels at arrival, 6 hours, 12 hours, and 24 hours. Patients with tissue hypoperfusion and severe traumatic injury showed strong activation of protein C which was associated with coagulopathy. Furthermore, elevated activated protein C levels were significantly associated with organ failure, infection, and death (9). The recently published PRospective Observational Multicenter Major Trauma Transfusion (PROMMTT) study evaluated 1,198 trauma patients of whom 41.6% were coagulopathic (10). While also implicating protein C, depletion of factors I, II, V, VII, VIII, IX, and X was additionally identified in these patients.

Trauma surgeons have traditionally employed conventional coagulation tests to evaluate trauma patients for coagulopathy. These include prothrombin time and partial thromboplastin time, tests that were developed to guide coumadin and heparin therapy as well as test for clotting factor deficiencies. Platelet count is useful in determining the number of circulating platelets, but tells nothing about platelet function.

TEG has thus emerged as a test than can provide an accurate and real-time picture of whole blood coagulation in the bleeding trauma patient. In one of the first major studies in trauma, TEGs were drawn on 69 trauma patients over a 6 month period at a single institution (11). Only TEG and injury severity score (ISS) were found to be predictive of blood transfusion in this population.

TEG vs. Conventional Coagulation Tests
In a porcine model, Martini (2008) examined PT, PTT, activated clotting time (ACT), and TEG after induced hypothermia and hemorrhagic shock (12). Hypothermia was found to inhibit clotting times and clotting rate, whereas hemorrhage impaired clot strength. Combining hypothermia with hemorrhage impaired all of these clotting parameters. PT and PTT were not sensitive whereas ACT was not specific

in detecting coagulation defects. Only TEG differentiated the mechanism related to clotting abnormalities, leading the authors to conclude that TEG better allows focused treatment of coagulopathy associated with hypothermia and hemorrhagic shock.

Holcomb (2012) evaluated a series of 1974 trauma patients with a median ISS of 17, 25% of whom presented in shock and 28% of whom were transfused (13). After controlling for age, mechanism, revised trauma score, base excess, and hemoglobin, the authors found that r-time predicted RBC transfusion and α angle predicted massive transfusion better than PT or PTT. The α angle was superior to fibrinogen in predicting plasma transfusion, and the MA was superior to platelet count in predicting platelet transfusion. These correlations improved for transfused, shocked, or head injured patients.

TEG-Guided Transfusion
As a test of whole blood coagulation, TEG can be used to guide blood product administration. Using remote tracing software in the emergency department, this can allow rapid decision making to be made early in a patient's resuscitation. In a study of 272 trauma patients, Cotton's group was able to view r time and k time within 5 minutes, and α angle and MA within 15 minutes (14). Conventional coagulation tests were not available for 48 minutes. R time and k time were found to strongly correlate with PT/INR and PTT, whereas MA and alpha angle were found to strongly correlate with platelet count. Controlling for demographics and ED vitals, r time best predicted massive transfusion in the first 6 hours. These findings were echoed in a recent study of pediatric trauma (15).

An interesting study was published out of Ben Taub General Hospital, which up until 2009 used a TEG-guided massive transfusion algorithm before switching to the now common 1:1:1 (pRBC:FFP:platelet) massive transfusion protocol (MTP) (16). TEG-guided resuscitation was equivalent to standardized MTP in patients receiving 6 or more units of pRBC's. However, MTP worsened mortality in penetrating trauma patients receiving 10 or more units pRBC's.


RECOMMENDED PRACTICE AT ORMC
TEG is obtained in trauma patients in the following situations:
- Blunt or penetrating trauma patients who arrive in hemorrhagic shock
- Patients receiving massive transfusion protocol (1:1:1) to evaluate for discontinuation or guided product therapy
- Clinical suspicion for hemorrhage or coagulopathy

The TEG may be repeated serially until normalized. Suggested transfusion triggers are outlined in the Table 2. A decision tree for trauma patients in hemorrhagic shock is delineated in Figure 2.


Figure 1: TEG tracing
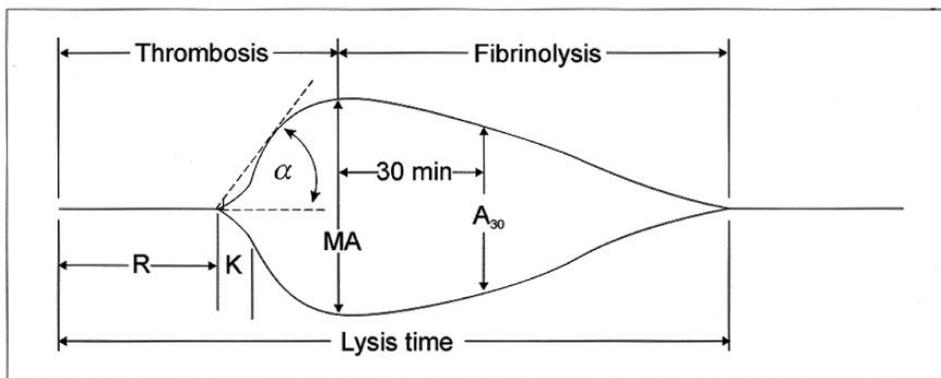
Table 1: TEG values and interpretation

TEG Value	Normal*	Description	Measures
TEG-ACT (rapid)	80 - 140 sec	"Activated clotting time" to initial fibrin formation	clotting factors (extrinsic/intrinsic pathways)
R time (conventional)	5.0 - 10.0 min	"Reaction time" to initial fibrin formation	clotting factors (intrinsic pathway)
K time	1.0 - 3.0 min	"Kinetic time" for fibrin cross linkage to reach 20 mm clot strength	fibrinogen, platelet number
α angle	53.0 - 72.0 degrees	Angle from baseline to slop of tracing that represents clot formation	fibrinogen, platelet number
MA	50.0 - 70.0 mm	Maximum amplitude of tracing	platelet number and function
G value	5.3 - 12.4 dynes/cm^2	Calculated value of clot strength	entire coagulation cascade
LY 30	0 - 3%	Clot lysis at 30 minutes following MA	fibrinolysis

Table 2: Suggested TEG-guided transfusion

TEG Value	Transfuse
TEG-ACT > 140	FFP
R time > 10	FFP
K time > 3	cryoprecipitate
α angle < 53	cryoprecipitate +/- platelets
MA < 50	platelets
LY30 > 3%	tranexamic acid

Figure 2: TEG Decision Tree
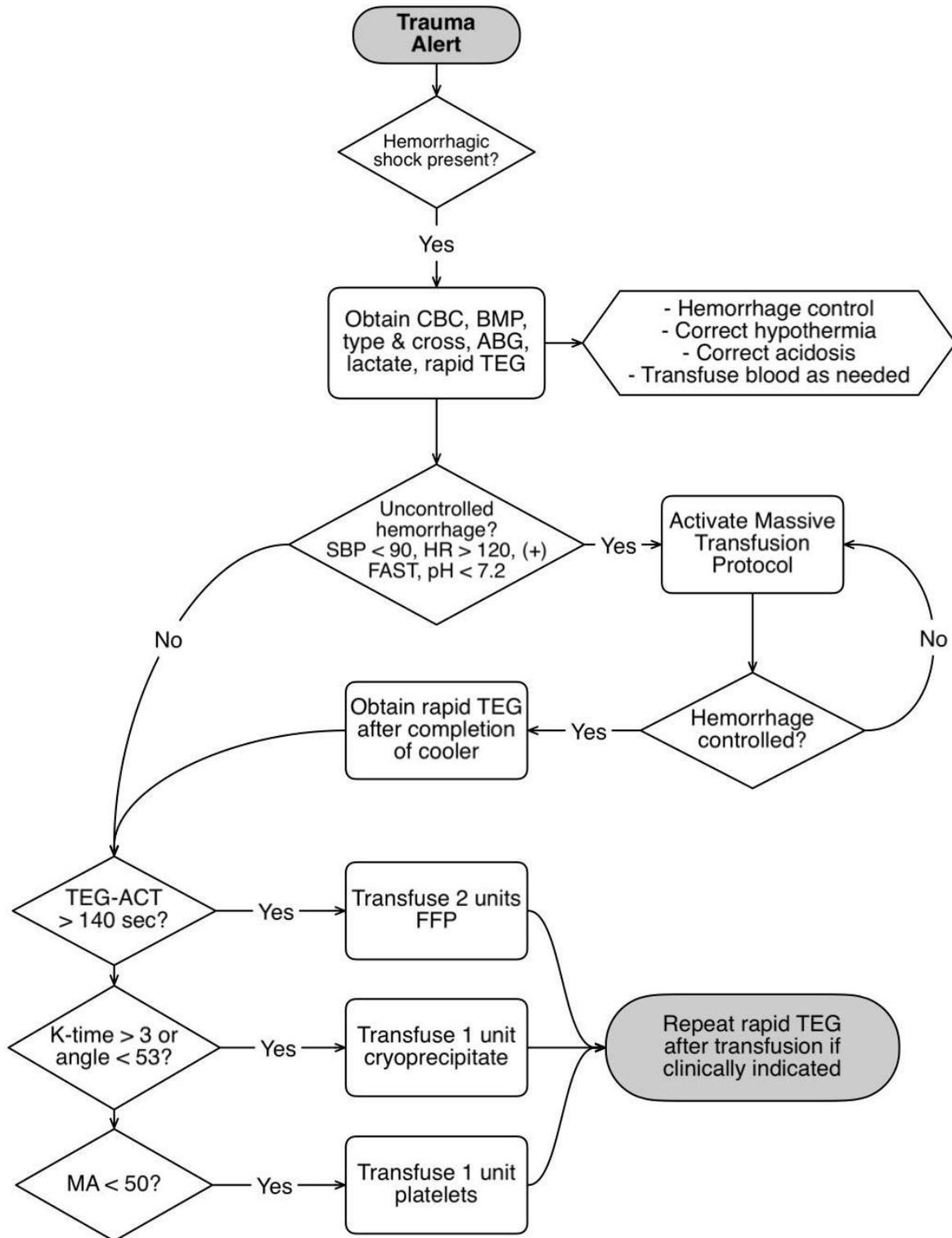
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Surgical Critical Care
Evidence-Based Medicine Guidelines Committee

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Editor: Michael L. Cheatham, MD
Last revision date: December 3, 2014

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