27 How do we integrate thromboelastography with perioperative transfusion management?

Duncan MacIvor, Annette Rebel, and Zaki-Udin Hassan

For the foreseeable future, conventional coagulation testing will remain important for anticipation, intervention, and management of hemorrhage and thrombosis in surgical patients. Conventional tests used at our institution include platelet (PLT) count, prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen levels, sometimes other factor levels, and D-dimer. Activated clotting time (ACT; International Technidyne Corp., Edison, NJ) is a point-of-care (POC) test run in our operating room. However, today's complex and prolonged operations increasingly require effective, targeted use of blood products and hemostasis-altering drugs, which in turn demands more complete and timely coagulation information than conventional testing typically provides. Inherently long turnaround times can render laboratory results irrelevant before they can be reported, creating demand for POC testing including ACT and PLT function screening assays such as the PLT function analyzer (PFA-100; Siemens USA, Washington, DC). POC testing has its own limitations, including cost, quality control (QC), equipment maintenance, and correlation with laboratory-based testing. Available, more sophisticated testing can do a better job for complex surgical patients in the operating room.

ABBREVIATIONS: ACT = activated clotting time; aPTT = activated partial thromboplastin time; CPB = cardiopulmonary bypass; LMWH = low-molecular-weight heparin; MA = maximum amplitude; PT = prothrombin time; R time = reaction time; TEG = thromboelastography.

From the Department of Pathology and Laboratory Medicine and the Department of Anesthesiology, University of Kentucky Medical Center, Lexington, Kentucky.

Address reprint requests to: Duncan C. MacIvor, MD, Department of Pathology and Laboratory Medicine, University of Kentucky Medical Center, 800 Rose Street MS117, Lexington, KY 40536; e-mail: dma223@email.uky.edu.

Received for publication December 20, 2011; revision received April 25, 2012, and accepted April 26, 2012.

doi: 10.1111/j.1537-2995.2012.03728.x

TRANSFUSION 2013;53:1386-1392.

Another limitation of most coagulation tests is their artificial, analytical nature, which isolates components of the hemostasis system under contrived laboratory conditions. The in vivo coagulation mechanism resembles an intricate ballet performed by flowing red blood cells (RBCs), PLTs, subendothelial proteins, and various circulating proenzymes and cofactors on a dynamic three-dimensional stage of phospholipid bilayers and meshed fibrin strands, resulting in a clot that stanches hemorrhage, remains localized to the site of injury, and gradually dissolves as healing proceeds. No in vitro coagulation test will ever do full justice to the in vivo system.

While also artificial, whole blood thromboelastography (TEG) nevertheless more closely mimics physiologic hemostasis, providing specific information about coagulation status in real time, and it is currently used extensively at our institution to guide specific interventions with blood product replacement and drug therapy. The basic technology was developed by Hartert in the late 1940s,[1] but was not widely used until much more recently. Two versions of this technique are currently available: TEG (Haemonetics Corp., Braintree, MA) and ROTEM (Tem International GmbH, Munich, Germany). A third method, Sonoclot (Sienco, Inc., Arvada, CO), employs a slightly different clot detection principle. This article will focus on TEG because we currently use it at our institution (Fig. 1).

The test is conceptually simple. In our laboratory, a small quantity of fresh citrated whole blood is mixed with kaolin and excess calcium, much as in the aPTT, except that in TEG, the RBCs and PLTs remain to fulfill their physiologic roles. The multiple variables of TEG include not only the time to initial clot detection (the sole endpoint of the aPTT) but also the subsequent rate of clotting, the strength of the clot over time, and the rate and degree of clot lysis. Since both the primary (PLT-related) and the secondary (factor-related) components of hemostasis participate in the reaction, the features of the curve can identify and guide management of thrombocytopenia, factor deficiencies, hypofibrinogenemia, fibrinolysis, or inappropriate dosing of hemostasis-altering agents. At our institution, we primarily use citrated whole blood samples. Versions of TEG using citrated or very fresh uncitrated blood with or without kaolin are available as

in-laboratory or POC tests. Our experience with alternatives is limited; therefore, we will confine our discussion to the most common method using citrated blood and kaolin.

In TEG, the sample clots in a small rotating cup, which oscillates through a fixed small angle every 10 seconds. An initially stationary pin connected to a torsion wire is immersed in the clotting blood. As progressively strengthening fibrin strands bind the pin to the cup, its rotation imparts increasing torque to an electromechanical transducer. Points plotted at the extremes of these excursions describe a bifurcating curve whose components yield a variety of information and which can be printed or transmitted in real time to a remote computer screen (Fig. 2). The distance (in millimeters) between the arms of a TEG curve varies with the strength of the clot, reaching a maximum, and then reconverging as the clot undergoes fibrinolysis.

Fig. 1. Photograph of TEG machine.

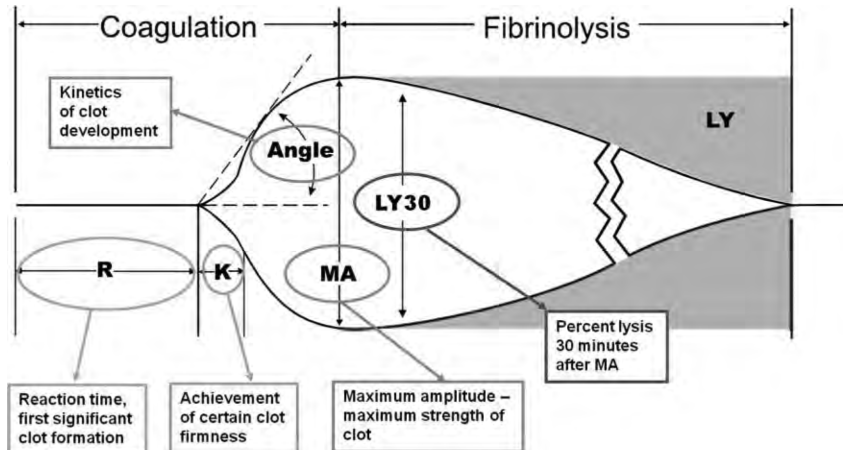

Fig. 2. Components of a TEG curve.

The "reaction time" or R time is the interval between the start of the test and initial clot detection. Like the aPTT, this depends on clotting factor activity or the presence of inhibitors, most often heparin. Prolonged R times suggest clotting factor deficiency or heparin effect and the need for plasma transfusion or heparin adjustment as appropriate. Samples can be run in parallel in heparinase cups to distinguish heparin effect from factor deficiency.

Two related variables illustrate the rate of clot strengthening. The "k time" is the interval between R time and a curve divergence of 20 mm. The faster the clot stiffens, the shorter the k time and vice versa. Similarly, the "alpha angle" between the *x* axis and a line tangent to the developing curve varies with the rate of clot development. These variables depend primarily on fibrinogen concentration and may point to hyper- or hypocoagulable states. For instance, in evolving disseminated intravascular coagulation, a short R time, a short k time, and a large α angle would be expected with thrombotic activity early in the course, but the onset of consumptive coagulopathy and fibrinolysis markedly changes the shape of the curve (Fig. 3).

The maximum amplitude (MA) reflects the maximum strength of the in vitro clot, which is of great interest to surgeons concerned about hemostatic performance in vivo. MA reflects fibrinogen concentration and, especially, PLT function. Throughout clot formation, continuing PLT activity provides the phospholipid scaffolding needed for interaction of clotting factors. Thus, thrombocytopenia or anti-PLT drug effects decrease the MA of the in vitro clot. The most appropriate response to low MA may be PLT transfusion or possibly cryoprecipitate to increase fibrinogen and von Willebrand factor concentration to treat uremic PLT dysfunction. Some practitioners employ derivative variables related to MA such as "time to maximum amplitude" or "projected maximum amplitude" hoping to take corrective action earlier in the test process. We have not found these to be useful at our institution, but we are currently evaluating the coagulation index and the G variable, which are intended to reduce curve complexities to simple numbers.

In certain situations such as thrombolytic drug therapy, or in more advanced disseminated intravascular coagulation, measuring the rate and degree of clot lysis may be helpful. This is most easily done by observing early, excessive curve convergence. Alternatively, the area under the curve between MA and a vertical line drawn at 30 minutes after MA (LY30) can be compared to a similar area between 30

and 60 minutes after MA (LY60). The decrease in area is proportional to the rate of fibrinolysis.

Like any laboratory test, TEG reflects the clinical situation existing at the moment the blood was drawn. During active hemorrhage, rapid transfusion, and corrective drug administration, TEG results can also be overtaken by events. However, consecutive samples can be run simultaneously on multiple TEG channels during evolving situations.

CLINICAL UTILIZATION OF TEG

In addition to conventional coagulation variables (PT, aPTT, and/or PLT count), TEG can be extremely helpful in perioperative blood product use by providing specific information about coagulation status and the nature of coagulation dysfunction. Use of the TEG curves can be as simple as learning to recognize the characteristic patterns associated with various coagulation problems (Fig. 3). Here we discuss a few settings illustrating the benefits of TEG use in the perioperative period.

Trauma

Trauma-associated coagulopathy is common and is in turn associated with increased mortality risk. The coagulopathy can be *dilutional* due to a relative decrease of coagulation factors by large-volume resuscitation with crystalloid or colloid fluids and/or *consumptive* due to local and systemic release of tissue factor from ischemic tissue during shock. In addition, recent literature has suggested that hyperfibrinolysis (perhaps mediated by widespread activation of protein C) is a key feature of trauma-associated coagulopathy, which may require antifibrinolytic therapy in addition to blood product replacement.[2-4] It is important to note that hyperfibrinolysis is not detected by conventional laboratory testing but can be reliably identified with the TEG curve. Timely diagnosis and specific therapy of the coagulation disturbance can be important to improved survival of the initial injury. TEG has been shown to be a feasible technique for obtaining timely coagulation information in emergency departments, operating rooms, and combat settings to guide blood component therapy and direct resuscitation efforts.[5-7] If the TEG is based in the laboratory, the turnaround time from receipt of the TEG sample to initial results can be less than 15 minutes if the TEG is continuously operational and therefore faster than other coagulation variables (PT, aPTT, and fibrinogen). In a recent review article, aggressive, proactive, TEG-guided coagulation therapy with blood components and factor concentrates appears to promise improved morbidity and mortality in massively injured patients.[8]

Deep vein thromboprophylaxis

Since TEG surveys the properties of viscoelastic blood clot formation, this technique can also evaluate potential

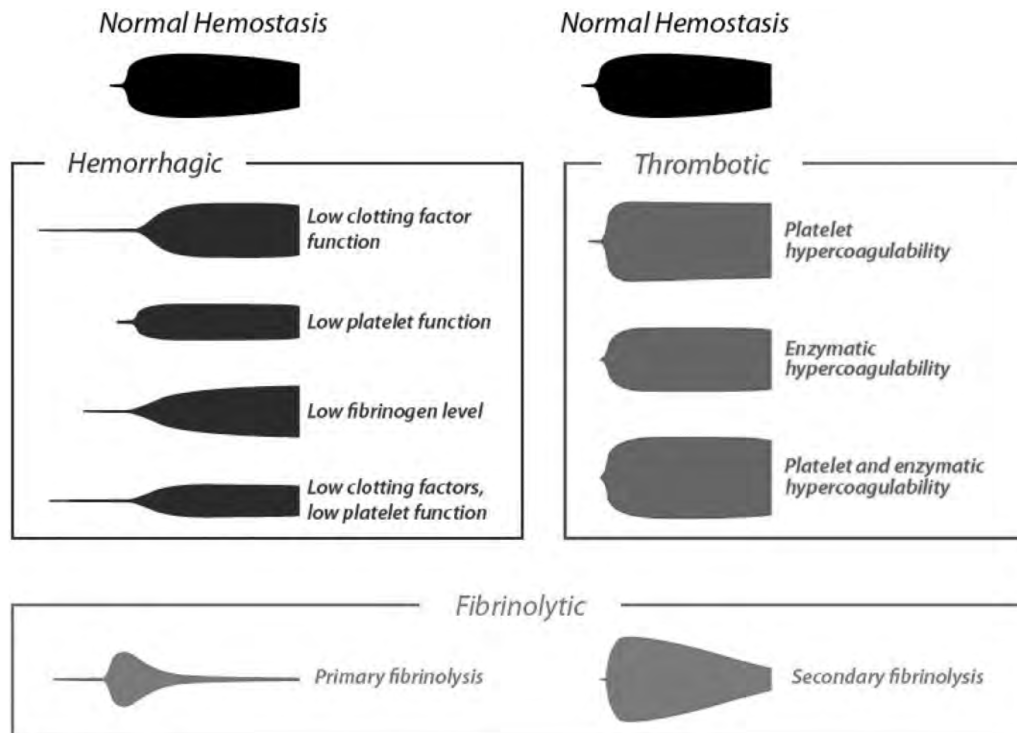

Fig. 3. Characteristic TEG curve patterns in various disorders.