Thromboelastography®
Past, Present, and Future

THIS issue of Anesthesiology contains an article by Camenzind et al.1 regarding the influence of citrate storage on thromboelastography® (TEG® Haemascop Corp.). Although the TEG® is most commonly performed on a native (uncitrated) sample, the use of citrated blood permits longer delays after sample acquisition, thus facilitating ancillary or research laboratory analysis. Camenzind et al.1 nicely outline some of the issues related to the impact of sample storage on the TEG®. Anesthesiology, as a specialty, has taken a leading role in evaluating the TEG® as a near-site monitor of hemostasis in several clinical settings. Many issues, however, remain unresolved about how to use the TEG® to guide clinical decision-making. The purpose of this Editorial View is to briefly review studies that have lead to current applications of the TEG® and to outline future challenges that need to be addressed for its broader use.

General

The use of the TEG® to monitor whole-blood coagulation was first described by Hartert in 1948.2 The TEG® measures shear elastic modulus (dynes per centimeters squared) during clot formation in whole or recalcified citrated blood.2,3 The global nonspecific nature of the TEG® measurement may be both its greatest weakness and strength. Although specific coagulation assays rarely correlate with blood loss, they do provide specific diagnoses that respond to specific treatments. The TEG® maximum amplitude (MA) is a complex integrated measurement that has been associated with blood loss. The chief limitations of the TEG® include its: (1) inability to diagnose a specific hemostatic lesion; (2) weak correlation with specific assays (prothrombin and activated partial thromboplastin times); and (3) inability to consistently detect benefits of fractionated blood product therapy.4 Since 1948, the technique has enjoyed periods of popularity but has never achieved widespread use in the United States. In the early 1980s, the TEG® was used routinely for coagulation monitoring during liver transplantation.5 The TEG® has now found additional applications in a diverse group of clinical settings, including cardiovascular surgery, obstetric anesthesia, and trauma anesthesia (massive transfusion).

Liver Transplantation

Each of the three phases of orthotopic hepatic transplantation has associated metabolic, hemorrhagic, and other derangements that complicate the preexisting coagulopathy present in these patients. Transfusion requirements are highly variable, but sudden massive blood loss occurs in conjunction with hyperfibrinolysis, coagulation factor and inhibitor deficiencies, and/or thrombocytopenia. Without prompt and effective treatment, these complicated clinical coagulopathies can result in dramatic hemorrhagic consequences. Kang et al.5 demonstrated that the use of the TEG® for monitoring hemostasis during liver transplantation decreases blood transfusion requirements. However, a study of low-dose tranexamic acid showed that inhibition of fibrinolysis as measured by the TEG® during orthotopic hepatic transplantation had no influence on transfusion of blood products.6

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Both Dr. Whitten and Dr. Greilich are currently participating in research protocols for which Haemascop Corporation has provided cups and pens for the TEG® machines at a discount rate.

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Cardiovascular Surgery

Many clinicians believed that the TEG® would be useful in determining which component of hemostasis (thrombocytopenia/thrombocytopathy, coagulation factor deficiencies, hyperfibrinolysis) is the primary cause of the coagulopathy associated with cardiopulmonary bypass surgery. Although several studies have demonstrated that the TEG® MA is associated with excessive hemorrhage, its direct correlation with blood loss has never been established.7-9 Studies in both pediatric and adult populations demonstrate that the TEG® MA is no better than platelet count for prediction of blood loss after cardiopulmonary bypass.10,11

The TEG® MA has been found in several studies to demonstrate good accuracy and even a better negative predictive value for excessive blood loss after cardiac surgery.7-9 The high negative predictive value can facilitate early identification and appropriate treatment of surgical bleeding by distinguishing it from a significant coagulopathy. Incorporation of the TEG® into clinical decision-making has resulted in decreased blood loss and transfusions in one large retrospective and two prospective studies.8,9,12 Finally, Tuman et al.15 demonstrated that heparinase-treated whole blood may be used to measure the TEG® during cardiopulmonary bypass to facilitate prompt treatment of significant coagulopathy immediately after heparin reversal.

Obstetric Anesthesia

The physiology of pregnancy results in a hypercoagulable state that prepares the parturient for the hemorrhage of childbirth. Several factors involved in the coagulation cascade and platelet reactivity increase during pregnancy, while naturally occurring anticoagulants decrease. The TEG® is capable of detecting the hypercoagulable state of normal parturients and the coagulopathy associated with pregnancy-induced hypertension or preeclampsia.14 Preeclampsia is associated with thrombocytopenia, coagulation factor deficiencies, and hypothermia. In a recent study by Kaufman et al.16 only the injury severity score and the TEG® were predictive of early transfusion. Historically, patients with an intense systemic response to massive penetrating and/or blunt trauma will almost immediately develop a hypocoagulable state. If surgical control of bleeding cannot be obtained rapidly, the ensuing coagulopathy can be severe in nature and will require aggressive resuscitation. The use of the TEG® to reduce the morbidity and mortality associated with bleeding and transfusion therapy in a major trauma center needs to be explored.

Future Challenges for TEG®

Although standard laboratory tests are poor predictors of bleeding, transfusion medicine specialists have been reluctant to accept whole-blood assays.17 Their justification has been: (1) the nonspecific nature of the TEG® measurement; (2) lack of quality-assurance methodologies required by regulatory agencies such as the American Association of Blood Banks, Federal Drug Administration, and College of American Pathologists; and (3) insufficient scientific evidence or appropriately powered outcome studies. Any near-site bioassays intended to guide clinical decision-making must adhere to rigid guidelines with respect to clear clinical and laboratory indications, quality assurance, and hospital-specific laboratory transfusion “triggers.” Institutions that have undertaken this rigorous task have seen significant improvements in their clinical practice.9

Many transfusion medicine specialists feel that near-site hemostasis monitoring could significantly improve clinical decision-making in patients undergoing surgery. Until recently, the vast majority of studies using the TEG® have been descriptive in design and, therefore, have had a limited impact on clinical decision-making. The next major advance will require a multicenter, interdisciplinary approach to design the studies needed to establish evidence-based transfusion algorithms. If multidisciplinary teams do not address these remaining issues, use of the TEG® in the perioperative period will remain limited.

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Trauma Anesthesia

Massive trauma results in a profound coagulopathy associated with thrombocytopenia, coagulation factor deficiency, and hypothermia. In addition to detecting thrombocytopenia/thrombocytopathy and coagulation factor deficiency, the TEG® has also been shown to be responsive to the influence of hypothermia.15 In a recent study by Kaufman et al.16 only the injury severity score and the TEG® were predictive of early transfusion. Historically, patients with an intense systemic response to massive penetrating and/or blunt trauma will almost immediately develop a hypocoagulable state. If surgical control of bleeding cannot be obtained rapidly, the ensuing coagulopathy can be severe in nature and will require aggressive resuscitation. The use of the TEG® to reduce the morbidity and mortality associated with bleeding and transfusion therapy in a major trauma center needs to be explored.
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