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Practical Use of Thromboelastometry in the Management of Perioperative Coagulopathy and Bleeding

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ABSTRACT

Achieving hemostasis after complex cardiovascular and transplant surgical procedures is one of the greatest challenges anesthesiologists face. Preoperative coagulation disturbances due to underlying disease or antithrombotic therapy are common, and they are worsened by intraoperative blood loss and fluid replacement. The coagulation reactions in vivo are incredibly complex interactions among blood cells, proteins, and vasculature, standing in sharp contrast to rather simple treatment options including transfusion of platelets, plasma, and cryoprecipitate. The long turnaround time of laboratory coagulation testing, and intraoperative heparin use also make timely coagulation assessment difficult during cardiopulmonary bypass, and thus, hemostatic components are often empirically ordered and administered without knowing their actual need or efficacy. However, increasing clinical experience with viscoelastic coagulation testing in cardiac and transplant anesthesia has introduced a paradigm shift, enabling clinicians to obtain clinically relevant coagulation data in a timely fashion and to treat a specific element of coagulation that is dysfunctional. Viscoelastic coagulation testing may facilitate an optimal use of blood components and other hemostatic agents, but its application is often practice specific (ie, type of surgery), and there are technical limitations and learning curves. The aims of this review are thus to summarize recent clinical data on viscoelastic coagulation testing and to provide practical examples of its use in complex cardiac surgical and transplant cases.

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Coagulopathy and bleeding complications have been regarded as a major cause of increased morbidity or mortality after cardiac surgery [1] and major noncardiac surgery [2]. Recent advances in minimally invasive surgical techniques [3] and patient blood management evidently reduced the incidence of allogeneic transfusion across many surgical

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specialties [4-7]. Nonetheless, marked variability in transfusion rates across surgical institutions has been reported in cardiac surgery [8], liver transplantation [6,9,10], and major orthopedic surgery [11]. Rational use of hemostatic components in cardiac surgery is particularly important in reducing blood use because their consumption represents approximately 9% of all units administered in the United States (~2 million units in 2011) [12].

Bleeding management and hemostatic therapy remain crucial aspects of perioperative care due to the aging population, critical illness, and complexity of certain surgical procedures [2,13-17]. Perioperative bleeding and coagulopathy are often multifactorial, and delayed surgical reexploration reveals nonsurgical (medical) coagulopathy approximately one-third of the time [18]. To compound the problem, the nonsurgical bleeders appear to fare worse than the surgical bleeders in terms of acute outcomes and survival [18]. It is therefore important to diagnose coagulopathy in a timely fashion and intervene with a specific component transfusion, thus achieving early cessation of bleeding and lower postoperative complications [5,19,20].

Conventional monitoring of coagulation during and after cardiopulmonary bypass (CPB) involves sequential processing, by which several tests are sent at the same time but their results become available after different time intervals [21,22]. High heparin concentration during CPB hinders the use of standard clotting time (CT) tests including prothrombin time/international normalized ratio (PT/INR) and activated partial thromboplastin time (aPTT). PT and aPTT are ordered only after heparin is neutralized, and thus, these results are unavailable when microvascular bleeding occurs soon after protamine administration [19]. One of the major reasons for perioperative utilization of viscoelastic coagulation tests is to obtain clinically relevant coagulation data in a timely fashion in cases with ongoing bleeding or at a high risk of bleeding. Thrombelastography (TEG; Haemonetics, Niles, IL) and rotation thromboelastometry (ROTEM; TEM Innovations, Munich, Germany) have been incorporated into transfusion guidelines [23] and integrated into transfusion algorithms at many institutions [5,10,24,25]. In our practice, thromboelastometry has become a critically important tool in intraoperative transfusion decision making in complex cardiovascular and transplant surgical procedures. This review, based on our clinical experiences in complex hemostasis management using thromboelastometry, can be informative to those who are new to the field as well as those who are experienced and interested in further study in viscoelastic coagulation testing. The aims of this review are (1) to describe key thromboelastometric parameters in relation to perioperative coagulopathy or bleeding, (2) to discuss practical uses of allogeneic components for complex coagulopathies associated with cardiovascular and transplant surgical procedures, and (c) to summarize what is known about thromboelastometry in the perioperative period to allow for research in blood management.

Types of Viscoelastic Coagulation Tests

The concept of viscoelastic coagulation testing (1948) came after Quick's description of PT (1935) but predates the development of aPTT (1953) [26,27]. Nonetheless, widespread adoption of viscoelastic testing has been slow because of difficulty in standardizing techniques and reagents in addition to a steep learning curve in interpreting numerous variables [28-30]. Modern technology and improved reagents have made such tests more user friendly and clinically applicable [31,32]. The initial clinical application of TEG (Haemonetics, Niles, IL) (Table 1) occurred in liver transplantation in the mid-1980s when massive hemorrhage was common [33]. However, a paradigm shift occurred when a rapid assessment of fibrin-specific clot formation became available as FIBTEM [31,34,35] on thromboelastometry (Table 1). FIBTEM complements tissue factor (TF)-activated EXTEM, which is used to assess overall clot firmness (ie, platelet-fibrin interaction) and fibrinolysis. Prior to this advance, a slow rate of clot development (α angle) was used to diagnose hypofibrinogenemia [33]. However, thrombocytopenia is also associated with a reduced α angle [36], and platelet transfusion remained the mainstay therapy in most TEG-based bleeding management protocols [37,38]. The functional fibrinogen assay became available on TEG as a FIBTEM alternative but has not been as widely used because of concerns regarding its accuracy [29,39].

There are several differences between TEG and ROTEM, which may have some clinical implications, although there is no evidence to substantiate clinical outcome differences between clinically used TEG and ROTEM. Firstly, TF-activated EXTEM and FIBTEM allow for a faster onset of clotting (normally <80 seconds) compared with the conventional kaolin-based TEG (normal, 240-480 seconds). Rapid TEG is a modified activated clotting time (ACT), which is triggered by a mixture of TF and kaolin. Secondly, EXTEM CT is more sensitive to the deficiency of vitamin K–dependent (VKD) factors observed during warfarin therapy or in cirrhosis when compared with contact-activated INTEM, kaolin TEG, or rapid TEG [40,41]. Thirdly, clinical detection of hyperfibrinolysis is also variable depending on the type of TEG or ROTEM assays. Contact-activated tests are less sensitive to fibrinolysis [42]. Abuelkasem et al. [30] recently compared the sensitivity of kaolin TEG, EXTEM, and FIBTEM in diagnosing hyperfibrinolysis (lysis at 30 minutes >8% on TEG or maximum lysis [ML] >15% on ROTEM) during liver transplantation. The sensitivity of FIBTEM (94%) was superior to that of kaolin TEG (23%) or EXTEM (46%). Lastly, EXTEM, FIBTEM, and APTEM reagents contain polybrene, which neutralizes heparin (up to 4-6 U/mL), allowing testing during CPB [43]. HEPTEM is also available when a higher circulating heparin level (4-8 U/mL) is anticipated [43]. Our heparin management protocol includes the HMS Plus (Medtronic, Minneapolis, MN), which allows monitoring of heparin concentrations, and thus, INTEM and HEPTEM are omitted [44,45].

Table 1
Types of tests on thromboelastometry and TEG

Test	TF	Contact	Heparin effect	Detectable condition(s)	Hemostatic Interventions
EXTEM	+		−[a]	Extrinsic pathway, PLT count, fibrinolysis	Plasma, PCC, or PLTs
FIBTEM	+		−[a]	Fibrinogen level[b]	Cryo or fibrinogen conc.
APTEM	+		−[a]	Systemic fibrinolysis	Antifibrinolytics[c]
INTEM		+	+	Intrinsic pathway, PLT count, fibrinolysis	Plasma, protamine, or PLTs
HEPTEM		+	−[a]	Heparin effect	Same as INTEM
ROTEM platelet[d]			−	$P2Y_{12}$ inh., aspirin	PLTs
Kaolin TEG		+	+/−	Intrinsic pathway, PLT count, fibrinolysis	Plasma, protamine, PLT, Cryo, or antifibrinolytics
Rapid TEG	+	+	+/−	ACT, PLT count, fibrinolysis	Plasma, PLT, Cryo, or antifibrinolytics
FF TEG		+	+/−	Fibrinogen level[b]	Cryo or fibrinogen conc.
Platelet mapping[e]			−	$P2Y_{12}$ inh., aspirin	PLTs

Cryo, cryoprecipitate; $P2Y_{12}$ inh., platelet ADP receptor inhibitor; PLT, platelet; Contact, contact activator (ellagic acid or kaolin); +/−, heparin (up to 6 U/mL) is neutralized in the heparinase cup.

[a] Heparin can be neutralized by the reagent at concentrations of up to 4-6 U/mL on EXTEM/FIBTEM/APTEM and 8 U/mL on HEPTEM [43].

[b] Confirmatory test for hypofibrinogenemia; low clot firmness (amplitude) on other ROTEM/TEG tests may indicate either thrombocytopenia or hypofibrinogenemia.

[c] Confirmatory test for fibrinolysis; fibrinolysis may be shown on all the other ROTEM tests.

[d] Impedance aggregometry in heparinized or citrated whole blood (available in Europe).

[e] Viscoelastic testing using reptilase, activated FXIII, and platelet agonist in heparinized whole blood.