The Utility of Viscoelastic Testing in Patients Undergoing IR Procedures

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ABSTRACT

Whole-blood viscoelastic testing can identify patient-specific coagulation disturbances, allowing for targeted repletion of necessary coagulation factors and differentiation between coagulopathy and surgical bleeding that requires intervention. Viscoelastic testing complements standard coagulation tests and has been shown to decrease transfusion requirements and improve survival in bleeding patients. Viscoelastic testing also can be used to predict bleeding and improve the care of patients undergoing interventional radiology (IR) procedures.

ABBREVIATIONS

INR = international normalized ratio, PT = prothrombin time, ROTEM = Rotational Thromboelastometry, TEG = Thromboelastograph

Not all coagulation disturbances are the same, and standard coagulation tests may not give a clear picture of the patient's true ability to form thrombus and achieve hemostasis after a procedure (1), limiting the ability to prevent or limit bleeding during an interventional radiology (IR) procedure. Whole-blood viscoelastic testing can identify patient-specific coagulation disturbances, allowing for targeted repletion of necessary coagulation factors and differentiation of coagulopathy from surgical bleeding that requires intervention.

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PITFALLS WITH ROUTINE COAGULATION TESTING

Routine coagulation tests, including prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time, were developed to assess coagulation in patients with bleeding diatheses, but they do not predict bleeding risk in a nonbleeding patient (2). In the past, a PT of 1.5 times normal (16.5 s, INR 2.5) was suggestive of moderate to severe factor deficiencies (activities $< 30\%$ of normal) and led to the recommendation of plasma transfusion. However, with newer PT reagents, a PT of 1.5 times normal (15.5 s, INR 1.5) reflects only mild deficiency of factor VII, which is clinically insignificant (3). In addition, INRs are not intended and are not reliable for use in patients with an intrinsic coagulopathy (4,5). A review of 25 studies, including 24 observational studies and 1 clinical trial, evaluated the bleeding risk in almost 2000 procedures performed on patients with abnormal coagulation profiles. These procedures included bronchoscopy and biopsy, central line placement, femoral angiography, liver biopsy, renal biopsy, thoracentesis, paracentesis, and lumbar puncture. There was no difference in the frequency of bleeding between the abnormal versus normal coagulation profiles, leading the authors to conclude that mild to moderate elevation of coagulation parameters did not confer an increased risk for periprocedural bleeding (2,6). Other coagulopathies, such as

coagulopathies seen in chronic liver disease, have reduction of all factors produced by the liver, rather than factors selectively targeted by vitamin K antagonists. Patients with chronic liver disease have rebalanced hemostasis with similar (and at times higher) thrombin generation in their plasma compared with normal plasma, causing a global prothrombotic physiologic state (7,8). They may have a higher propensity to form clot, despite an elevated INR.

Optimal platelet counts before a procedure necessary to mitigate bleeding risk are not well defined by adequate studies. One of the main problems with using platelet count to determine bleeding risk is that platelet function is not taken into consideration. Consensus statements use a threshold platelet count of 40–50 $\times$ 10^9/L based on findings from studies in patients with cancer undergoing procedures; however, these patients typically underwent more invasive procedures, such as laparotomies and craniotomies. Bone marrow biopsies have been safely performed in patients with platelet counts $\leq$ 20 $\times$ 10^9/L (9). Additionally, platelet transfusion may not achieve a desired platelet count in patients with chronic liver disease and splenomegaly. In a study tracking the location of transfused radiolabeled platelets in patients with splenomegaly, platelets were shown to disappear from the peripheral circulation into the spleen within 5 minutes of transfusion. Furthermore, this study showed that after intravenous injection of epinephrine, a surrogate for the stress response, platelets would be released from the spleen and reenter the peripheral circulation (10).

VISCOELASTIC TESTING

Viscoelastic analysis is the measurement of whole-blood viscoelastic properties that can provide information on the time to develop a thrombus, the strength of the thrombus, and the degree of clot breakdown (fibrinolysis). There are 2 widely available viscoelastic analyzers on the market: the Thromboelastograph (TEG; Haemoscope Corp, Niles, Illinois) and Rotational Thromboelastometry (ROTEM; TEM Innovations GmbH, Munich, Germany). The basic concept is the same for both analyzers. A sample of whole blood is placed into a cup in which a wire (TEG) or a pin (ROTEM) is immersed into the sample. An oscillation is started (the cup in TEG and the pin in ROTEM), and as the blood clots, a torque is applied to the wire/pin. This increased resistance is displayed graphically onto a computer screen. When the blood is liquid, there is no torque, and the result is a flat graphic line. Clinically, this is related to an upstream sequence of coagulation leading to thrombin generation. Therefore, if the flat line is prolonged, the patient is on an anticoagulant, which will need to be stopped or reversed, or there is a need for replenishing the factors with either plasma or prothrombin complex concentrate. Once the clot begins to form, there is an increase in the resistance measured by the immersed wire/pin, and this is displayed as in increase in the amplitude of the graph. Because the rotation is done in a 180° arc, there is a mirror image on the graph. The amplitude of the graph is correlated with the overall strength of the clot, which relates to the presence and function of platelets and fibrin, and if low should be improved with transfusion of platelets, cryoprecipitate, or fibrinogen concentrate. Although these analyzers work similarly and provide similar-appearing graphs, there are several differences between the machines and graphic results.

TEG

TEG is a point-of-care test of whole-blood coagulation that was first developed by Hellmut-Hartert in 1948 (11). In this test, the sample of blood is placed in an oscillating cup, and a pin is suspended from a torsion wire into the sample. Fibrin strands develop in the blood between the wire and the cup, effectively coupling the wire to the cup. The coupling is directly proportional to clot strength. Increasing tension on the wire is plotted on a graph, and changes in amplitude on the graph correlate with thrombus strength. R-time is the time between the initiation of the test and the start of fibrin formation. K-time is the time required to reach a thrombus strength associated with an amplitude of 20 mm. The alpha angle is a measure of the speed at which fibrin buildup occurs. Maximum amplitude correlates to the maximum clot strength, which is a function of fibrin and platelet bonding and is directly correlated with platelet function (12). Several different TEG-based assays may be performed. The rapid TEG assay uses tissue factor instead of kaolin, which speeds up the test. The heparinase TEG demonstrates heparin effect on thrombosis. A functional fibrinogen TEG demonstrates the role of fibrinogen in clot formation and indicates the need for fibrinogen concentrate transfusion. Finally, the Platelet Mapping TEG demonstrates the functional

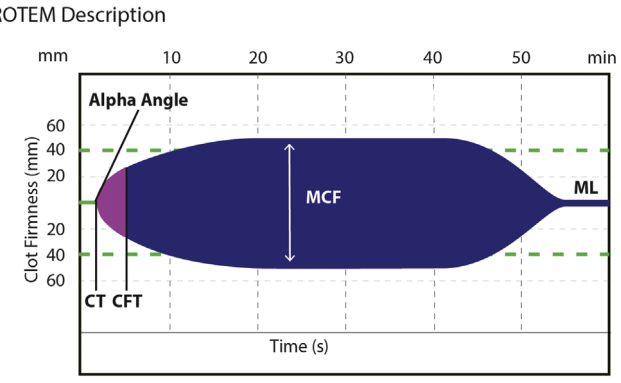

Figure 1. TEMogram with clotting time (CT), alpha angle, clot formation time (CFT), amplitude 10 minutes after clotting time, amplitude 20 minutes after clotting time, maximum clot firmness, and maximum lysis (ML).