EDUCATIONAL COMMENTARY - VISCOELASTOMETRY TESTING: WHEN IS IT USEFUL?

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Learning Outcomes
On completion of this exercise, the participant should be able to:

- describe how viscoelastic tests can be used to make transfusion decisions;
- describe how viscoelastic testing can be used to diagnose fibrinolysis; and
- describe three limitations of viscoelastic testing.

Blood viscoelastometry measures the elastic shear modulus of whole blood as it clots. This is essentially a measure of clot strength and is primarily a function of the platelet count and fibrinogen level in the sample. The two commercial systems available for performing clinical viscoelastometry measurements in vitro, thromboelastography (TEG® [Haemonetics Corporation]) and thromboelastometry (ROTEM® [TEM International GmbH]), produce similar results. In essence, whole blood is added to a sample well followed by activation of clotting (Figure 1). These systems measure the time it takes for a clot to start forming (R value or CT, clot time); the time to reach a specific viscoelastic amplitude, typically 20 mm (K value or CFT, clot formation time); the rate of clot formation (angle); the maximum clot strength (MA, maximum amplitude or MCF, maximum clot firmness); and the loss of clot strength over time, typically due to clot lysis (EPL, estimated percent lysis or ML, maximum lysis). These systems can be run using unanticoagulated whole blood or citrated whole blood. If citrated samples are used, the samples are recalcified as part of the activation step. Coagulation activation can be initiated by calcification alone, but to accelerate and better standardize the activation process, either a contact activator or tissue factor is added. The shortest clotting times and fastest results are typically obtained using a reagent containing tissue factor.

![Figure 1. Example of viscoelastic tracing showing different parameters measured. Equivalent measurements using TEG vs ROTEM listed below the tracing. Abbreviations: CT, clot time; CFT, clot formation time; MA, maximum amplitude; MCF, maximum clot firmness; EPL, estimated percent lysis; and ML, maximum lysis.](image-url)
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Test Interpretation
The time to initial clot formation, R or CT, is related to coagulation factor levels and the presence of anticoagulants. Low coagulation factor levels resulting from blood loss, consumption, vitamin K-dependent factor deficiency, or hereditary factor deficiency prolong clot formation time. Sensitivity to specific factor deficiencies depends on the activator used, similar to prothrombin time (PT) and partial thromboplastin time (PTT). A contact activator is most sensitive to factor VIII and IX deficiency, and less sensitive to deficiencies of factors XI, V, X, and II and fibrinogen. Contact-system deficiencies (factor XII, prekallikrein, and high-molecular-weight kininogen) will also prolong contact-activated clotting times, but are not associated with an increased risk for bleeding. A tissue factor-activator is most sensitive to factor VII deficiency and less sensitive to factors V, X, and II and fibrinogen deficiencies.

Anticoagulants can also prolong clotting times. Heparin prolongs clotting in contact-activated samples more than in tissue factor-activated samples. Direct oral anticoagulants like dabigatran, rivaroxaban, apixaban, and edoxaban can variably prolong the clotting time depending on the activator used and the drug level. Intravenous direct thrombin inhibitors like argatroban and bivalirudin can also prolong viscoelastic clotting time. Standard viscoelastic testing (contact system- or tissue factor-activated) is not sensitive to antiplatelet medications like aspirin or clopidogrel.

The rate of clot formation (angle) is a complex measure that depends on coagulation factor levels, platelet counts, and fibrinogen levels. Some reports have suggested that viscoelastic angle primarily reflects fibrinogen concentration,¹ but this is not correct: platelet count can have an equal or greater effect on angle.²³ The maximum viscoelastic amplitude is directly related to platelet count and fibrinogen, with platelet count having a greater effect in most patients. From a single viscoelastic measurement, it is impossible to tell whether a reduced maximum amplitude is due to the result of a reduced platelet count, a reduced fibrinogen level, or both.⁴ Loss of amplitude suggests increased fibrinolytic activity as indicated by an increased clot lysis parameter (EPL and ML).⁵⁷

Clinical Utility
Emergency Hemostasis Testing
Emergency hemostasis testing is typically performed in the bleeding patient to help assess what blood products are needed to help correct hemostatic deficiencies and stop the bleeding.⁸ This type of testing is different from precision testing to evaluate a hemostatic defect in a patient who is not actively bleeding, where accuracy of diagnosis is most important. In emergency testing, turnaround time is the most important parameter, with test accuracy sufficient to indicate the blood product needed in the shortest time. If the turnaround time is too long, this testing may be of no clinical use, even if the results are accurate. Emergency hemostasis testing can be performed in the clinical laboratory,⁹ in satellite laboratories near the site of care, and through point-of-care testing. In situations where the clinical
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laboratory cannot perform the testing fast enough and a satellite laboratory is not available, viscoelastic testing done at the point of care is often used.10

Emergency Viscoelastic Testing
The major use for viscoelastic testing is rapid transfusion support decisions during and after cardiac and liver transplant surgery, trauma, obstetric hemorrhage, and other major bleeding episodes (Table).10-12 Appropriate use of viscoelastic testing can reduce turnaround times for transfusion support decisions and reduce blood product use, but it does not alter morbidity or mortality.13 For viscoelastic testing to be successful, it is critical to develop an algorithm for blood product use with the clinicians involved. A first step is agreement by all parties that if the viscoelastic testing results are completely normal, no blood products are needed. Without this type of agreement, the reduced blood product use associated with viscoelastic testing is unlikely. A normal viscoelastic test result indicates that coagulation factors, platelets, and fibrinolysis are all normal.

The next step is to develop, with clinicians, a protocol for treatment of bleeding patients with abnormal viscoelastic testing results. Multiple algorithms have been proposed, but currently no standard protocols have shown to be effective in randomized, blinded trials. General guidelines are discussed below.

Table. Therapy indicated by abnormal coagulation results.

<table>
<thead>
<tr>
<th>Viscoelastic Parameter</th>
<th>Hemostatic Parameter</th>
<th>Therapy if Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>R, K, CT, CFT</td>
<td>Coagulation factors</td>
<td>Plasma, factor concentrate</td>
</tr>
<tr>
<td>MA, MCF, angle</td>
<td>Platelets, fibrinogen</td>
<td>Platelets, cryoprecipitate, fibrinogen concentrate</td>
</tr>
<tr>
<td>Lysis, EPL, ML</td>
<td>Fibrinolytic activity</td>
<td>Antifibrinolytic</td>
</tr>
</tbody>
</table>

Abbreviations: CT, clot time; CFT, clot formation time; EPL, estimated percent lysis; K, clot formation time; MA, maximum amplitude; MCF, maximum clot firmness; ML, maximum lysis; and R, clotting time.

Viscoelastic testing can be used to evaluate need for coagulation factor replacement, but the R value, K value, CT, and CFT measurements used to assess clotting time and estimate factor levels are not sensitive or specific.3,14 If clotting time is substantially prolonged, factor replacement using fresh frozen plasma or factor concentrates is likely needed. Cutoffs used for determining treatment depend on the activator used; no consensus is currently available.

If the patient is bleeding and the angle and/or amplitude are reduced, the most common cause is reduced platelet count. Many centers immediately transfuse platelets while checking platelet count and fibrinogen levels to determine the cause of the reduction. Amplitude cutoffs for treatment in the 46 to 50 mm range have been used in several studies, but each institution will need to develop its own protocol depending on specific clinical use.4,12,15 Viscoelastic testing can also be used to estimate the whole blood fibrinogen level, providing a rapid point-of-care differentiation of platelet loss vs decreased fibrinogen.16 If the whole
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blood viscoelastic fibrinogen level is low, the patient needs fibrinogen replacement; if borderline, a plasma fibrinogen level may need to be obtained to assess the true level. In the past, a fibrinogen threshold of 1 g/L was often used for treatment decisions, but more recent studies have suggested that in bleeding patients, fibrinogen in the 1.5 to 2 g/L range may be needed. This is equivalent to a whole blood fibrinogen specific amplitude of approximately 10 mm. Whole blood fibrinogen measurements are affected by sample hematocrit levels. Because fibrinogen is in the plasma fraction of blood, higher hematocrit levels lead to lower sample plasma fractions and potentially falsely low fibrinogen levels (Figure 2).

![Figure 2](image)

**Figure 2.** Effect of hematocrit concentration on the ratio of adjusted whole blood fibrinogen (AWBFIB) to plasma fibrinogen (FIB). As hematocrit increases, the plasma fraction of the sample containing the fibrinogen falls, leading to falsely low fibrinogen estimates. From Bollinger et al.

Fibrinolytic Bleeding

Viscoelastic testing is the only rapid test available to detect clinically significant fibrinolytic bleeding. If the whole blood percent lysis (EPL or ML) is elevated, it may indicate excessive fibrinolysis, and antifibrinolytic therapy is needed. Excessive fibrinolysis can occur during liver transplant, cardiac surgery, after trauma, and in other situations. Increased fibrinolysis is associated with increased mortality in trauma patients. The primary clinical issue with this type of testing is the turnaround time. It may take up to an hour for the increased fibrinolysis to appear on the viscoelastic tracing. Decreases in amplitude of 8% to 15% have been used as an indication of clinically significant fibrinolysis. In the worst case, the tracing shows early, near 100% lysis. These patients often bleed from all wound sites, including those caused by trauma, surgery, and intravenous and intra-arterial lines. All other parameters on the results of viscoelastic testing (clotting times, amplitude) and conventional testing (PT, PTT, fibrinogen, platelet count) may be normal. D-dimer is not a good test for increased fibrinolysis since it measures intravascular fibrin, not fibrinolytic activity. D-dimer levels are often elevated in patients who have reduced fibrinolysis but a high clot burden.
Limitations

Interference

Viscoelastic parameters such as amplitude and angle are affected by multiple factors, including platelet count and fibrinogen and coagulation factor levels, limiting their predictive ability for specific defects. Establishing reference ranges that accurately predict bleeding risk is problematic. In one study, approximately 9% of healthy subjects were predicted to have coagulopathy when manufacturers’ reference ranges were used. As discussed under fibrinogen estimates, because viscoelastometry uses whole blood, viscoelastic parameters may be affected by changes in hematocrit concentration, leading to decreased amplitude as hematocrit increases and increased amplitude when hematocrit falls. Lysis-like artifacts can appear on viscoelastic tracings if the pin is not seated correctly in the TEG system and have also been reported with the use of some heparinase cups. The specificity of lysis on viscoelastometry can be confirmed by adding an antifibrinolytic, but this adds time and complexity to the evaluation. Viscoelastic testing in heparinized patients may require heparin removal with heparinase before testing.

Platelet Function Testing

In standard viscoelastic testing of whole blood, a contact-system activator or tissue factor is added to blood, leading to thrombin generation and clot formation. Thrombin generated in the assay is the primary platelet activator. Thrombin activation of platelets through the PAR1 receptor is so powerful that standard antiplatelet medications such as aspirin and clopidogrel cannot be detected using standard viscoelastic testing. Attempts have been made to modify viscoelastic assays to detect platelet dysfunction due to antiplatelet medications, but issues have been raised in regard to assay design, sensitivity, specificity, and accuracy. This type of testing is time-consuming and complex, and is seldom used for emergency hemostasis testing.

References

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