

Thromboelastography during adult donor care

Thromboelastography is a test of blood coagulation used to evaluate all components of clot formation and possible abnormal clot dissolution. It supplements traditional laboratory testing by demonstrating the integration of coagulation factors, platelets (number and function), and other factors during coagulation. Analysis of abnormalities demonstrated by thromboelastography can guide organ procurement coordinators in titrating appropriate quantities of fresh frozen plasma, cryoprecipitate, or platelet transfusions during treatment of coagulation in adult donors. (*Progress in Transplantation*. 2010;20:163-168)

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Notice to CE enrollees:

A closed-book, multiple-choice examination after this article tests your ability to accomplish the following objectives:

1. Identify testing for coagulation problems in potential organ donors
2. Determine methods for measuring blood coagulation
3. Describe clinical applications of data derived from the thromboelastogram

Thromboelastography, or thrombelastography, is a test of blood coagulation used to assess normal coagulation, excessive bleeding, or the potential for excessive coagulation (a hypercoagulable state) that may be useful during donor care. This testing method produces a thromboelastogram as a graphic assessment of the clotting capability of the patient/donor's whole blood. Thromboelastography is used to evaluate the strength of clots formed by the donor, components of the coagulation process, possible accelerated clot formation, and whether excessive clot breakdown (fibrinolysis)

may increase ongoing bleeding or potentially initiate hemorrhage.

Historically, the terms "TEG" and "thrombelastograph" were used synonymously and generically to describe the process and product. However both now have become registered trademarks of one of the manufacturers of the thromboelastography device (Haemoscope Corporation, Niles, Illinois). This action restricts use of those terms only to the graphic representations produced by the company's device.¹ Thromboelastography has become more accessible and has been modified to allow faster and potentially bedside ("point of care") testing,² so organ procurement coordinators may wish to incorporate this technique into donor care.

In this article, we review testing methods, interpretation of the thromboelastogram, and clinical applications of the data provided. Information was obtained from searching PubMed citations from 2000 to 2009 and from the author's files. No publication was found that described direct use of thromboelastography in donor care.

Review of Normal Coagulation

Blood coagulation is a normal but complex process intended to prevent undesirable bleeding and to remove

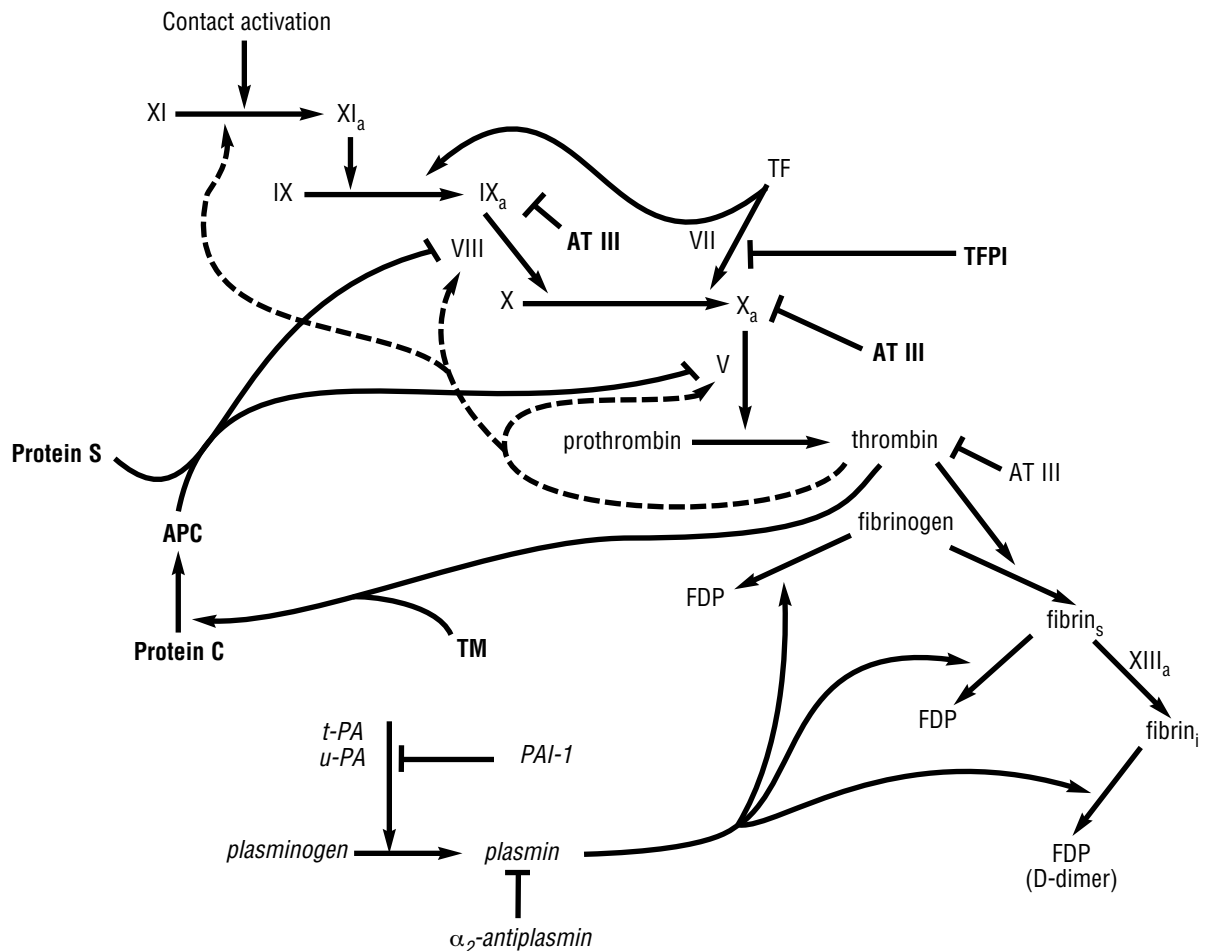


Figure 1 Schematic representation of the normal coagulation system (see text). The regulatory proteins in bold type limit clot size, fibrinolytic proteins are shown in italics, and some normal coagulation proteins are traditionally designated by Roman numerals. The dotted line shows a feedback loop that accelerates clot formation when activated.

Abbreviations: APC, activated protein C pathway; AT III, antithrombin III; FDP, fibrin degradation products; fibrini, insoluble fibrin; fibrins, soluble fibrin; PAI-1, plasminogen activator inhibitor-1; TF, tissue factor from injured (disrupted) tissue; TFPI, tissue factor pathway inhibitor; TM, thrombomodulin; t-PA, tissue plasminogen activator; u-PA, urokinaseplasminogen activator.

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clots when hemostasis is secured (Figure 1). This balance between clot formation and dissolution continuously ensures normal physiological blood flow to all organs and tissues.^{1,3-7}

After trauma, intracranial hemorrhage, subarachnoid hemorrhage, stroke, or other central nervous system catastrophes, clotting is often initiated because of injury or rupture of blood vessels. Abnormal exposure of the inner endothelial lining of the vessel and release of an adjacent tissue protein, tissue factor, initiate a cascade of responses. Circulating proteins (von Willebrand factor and factor VII) in the blood and traumatized area stimulate circulating platelets in the blood to attach to the injured zone. Subsequently, protein coagulation factors are incorporated into the forming clot. One of the clotting factors, fibrinogen, fragments

into fibrin segments that enter and strengthen the evolving clot.

As the clot forms, other proteins (eg, antithrombin, protein C, protein S, thrombomodulin), present within the circulating blood and at the endothelial surface, are also activated and function to slow the coagulation process so as to control the size and location of the clot. These regulatory proteins prevent excessive local thrombosis.

Similarly, fibrinolysis (clot breakdown/dissolution) is initiated by the plasminogen system in response to clot formation, using another series of proteins (eg, plasminogen, plasminogen activator) within the blood and adjacent tissue. The regulatory and fibrinolytic proteins control the extent of clot formation and clot removal so as to ensure blood circulation to distant organs.

Imbalance within this complex coagulation mechanism, caused by other factors (eg, cytokines or other inflammatory mediators), may produce excessive or inadequate clotting or excessive clot dissolution. Disseminated intravascular coagulation⁷ is such an example of imbalance in which inappropriate coagulation occurs in tissues distant to the site of injury and is followed by excessive and ongoing fibrinolysis, leading to hemorrhage.

Assessment of Abnormal Clotting Function

The ability of the donor's blood to form a clot may be assessed routinely as part of general donor surveillance or in response to active bleeding. The customary battery of tests includes measurement of prothrombin time, partial thromboplastin time, fibrinogen level, and platelet count. Prothrombin time and partial thromboplastin time measure the time needed to form a clot within a specific laboratory assay and reflect the concentration and function of a variety of protein coagulation factors in the serum. Serum fibrinogen level is a measurement of the concentration of one of those coagulation factors, fibrinogen, and the platelet count quantifies the number of platelets present in 1 mL of blood. Many other coagulation factors can be measured independently but are not routinely assessed.

Prolonged prothrombin times and partial thromboplastin times (in seconds) that are greater than the hospital's normal values usually indicate a deficiency in the amount or concentration of 1 or more of the coagulation factors in the blood. These deficiencies may be caused by consumption of factors during extensive clotting, dilution of factors in the blood after administration of large volumes of fluid that does not contain factors (eg, crystalloid saline), or underproduction of factors within the liver. Hepatic underproduction may be caused by previous liver disease or medication (eg, warfarin [Coumadin]).⁸ A low fibrinogen concentration or platelet count indicates a deficiency of those items, also potentially due to increased consumption, low production, or dilution. Donor acidosis and hypothermia also affect fibrinogen use and limit its effectiveness in thrombin formation within the clotting process.⁹

The competency of the platelets to participate in clot formation (a "qualitative platelet defect") is more difficult to assess,^{10,11} but occurs commonly when aspirin, clopidogrel (Plavix), and/or other platelet "antagonist" drugs have been given. The bleeding time test was previously used to evaluate platelet function (not numbers), but is now rarely offered by hospital laboratories. Flow cytometry, optical aggregation, singlet platelet counting,¹² and other methods or devices to analyze platelet function may be used or are commercially available, but are rarely available in hospitals. A component of thromboelastography does evaluate platelet function and numbers, as discussed later.



Figure 2 Thromboelastography device.

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Fibrinolysis is also difficult to evaluate by laboratory tests. An abnormally severe decrease in the serum concentration of fibrinogen and an increase in the products of fibrinogen destruction, so-called fibrin split products may be suggestive. However, as noted earlier, fibrinogen may also be low for other reasons, and fibrin split products are normally produced during routine clot lysis if any clotting is occurring for any reason. Therefore, fibrin split products are present normally after trauma or any other brain catastrophe that might induce normal coagulation.

Testing Method

Blood is withdrawn from the donor and quickly (minutes) placed in the sample cup (cuvette) of the thromboelastography device (Figure 2). A pin is located within the cuvette and is attached to a wire that transmits the movement of the pin through a transducer, converting the pin's mechanical movement into an electronic signal. The cuvette is rotated at a fixed speed and angle during the thromboelastography measurement. As a clot forms within the cuvette, the blood becomes thicker, and the increased resistance produced by the clotting blood produces movement of the pin and torsion wire. This displacement of the pin and wire causes a change in the electromechanical signal generated as displayed on the graph created (Figure 3).

Clot formation is usually accelerated by the addition of a procoagulant to the cuvette (usually kaolin). The choice of the procoagulant is influenced by special circumstances of testing (eg, more rapid testing required, heparin present in blood).

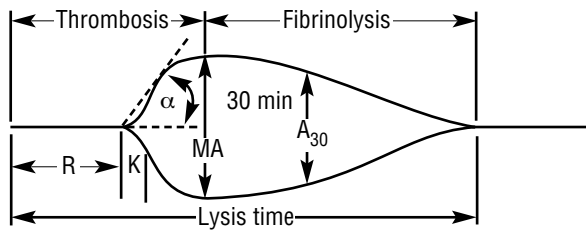


Figure 3 Thromboelastogram® and components (A_{30} means clot amplitude at 30 minutes; see text for explanation of the other abbreviations).

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The speed of clot development is evaluated on the horizontal axis of the graphic representation (Figure 3) as follows:

R time: the reaction time from initiation of the test to clot formation as indicated by a 2-mm amplitude deviation from the graphic baseline (normal, 4-8 minutes for whole blood)

K time: time to formation of the initial fibrin cross-links (normal, 1-4 minutes for whole blood)

Alpha angle: formed by a triangle joining the baseline position and K (normal, 47°-74°)

The clot strength and platelet numbers and function are evaluated by the following:

MA: maximum width (amplitude) of the displayed graph measures the composite size and strength of the final clot formed. All components of the clotting process contribute to the final size of the MA (normal for whole blood, 55-73 mm)

“G” factor: derived variable suggesting clot strength (normal, 6-13 dynes/cm²)

Normally, the graphic MA persists through the duration of the thromboelastography testing. However, if accelerated fibrinolysis is present in the blood, the MA may narrow during testing as the clot is liquefied and a “tail” may be seen on the graph (Figure 4D). The thrombolytic process is also represented by the LY30, which measures the amount of clot breakdown that has occurred 30 minutes after the MA is achieved (normal, 0%-8%). (LY60 is the same as LY30, but after 60 minutes.) In addition, the estimated percent lysis is a further assessment of fibrinolysis (normal, 0%-15%) and should not be elevated.

Interpretation and Clinical Application

Inadequate clot formation and strength predispose the donor to increased bleeding and the possible consequences of hemorrhage and hypotension upon organ function. Therefore, the several signs of poor clot formation in laboratory tests, including thromboelastography, should be addressed and treated as directed by the guidelines of individual organ procurement organizations (OPOs).

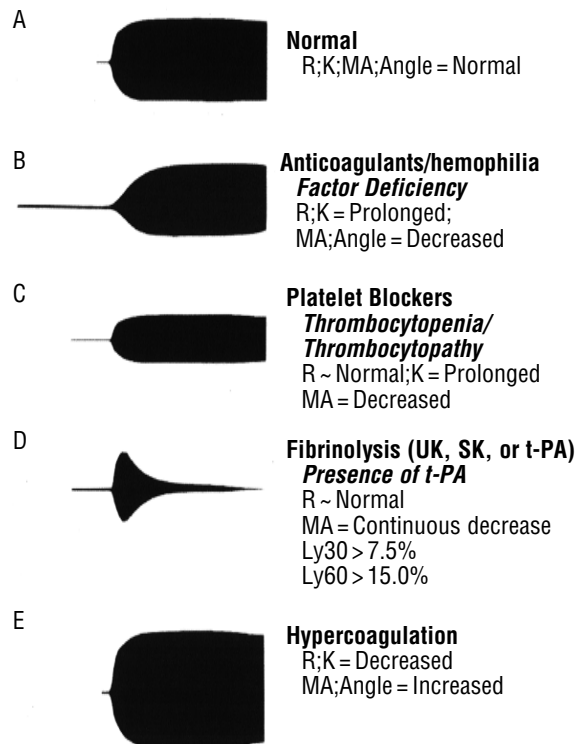


Figure 4 Normal and abnormal thromboelastograms® (see text).

Abbreviations: t-PA, tissue plasminogen activator; SK, streptokinase; UK, urokinase.

Delayed initiation of clot formation is represented by prolonged R and K times above normal values in seconds and a lower alpha angle (Figure 4B). These measures, in general, are roughly correlated with prothrombin and partial thromboplastin times and reflect deficits in the concentration of coagulation factors due to diminished production (eg, liver disease, warfarin treatment), heparin, thrombin inhibitors (eg, argatroban), hemodilution within the serum space, or active consumption. Most of these abnormalities should first be treated by stopping any agents that would interfere with coagulation. Next, administration of fresh frozen plasma (FFP) is used except when a specific coagulation factor is deficient, such as in hemophilia, where administration of a single factor is preferred. Recommendations as to the number of units of FFP needed are difficult to make because the amount of continuing consumption is unknown if bleeding is ongoing. Similarly, if large volumes of intravenous fluid are being given, dilution of existing circulating coagulation factors cannot be predicted. A full replacement estimate of 15 mL of FFP per kilogram of body weight is commonly used, but should be adjusted to meet the guidelines of individual OPOs. Each unit of FFP is about 200 mL, so the number of units of FFP needed for full replacement is calculated as follows:

(Recommended mL of FFP/kg) × (kg body weight) ÷ 200 = number of units of FFP

Subsequent serial measurements of prothrombin time, partial thromboplastin time, or thromboelastography values should be obtained, as directed by guidelines of the OPO, to determine if additional FFP is needed.

A low alpha angle may also reflect a selective fibrinogen deficiency and should be correlated with its direct laboratory measurement. Low fibrinogen may also occur because of increased and/or continuing consumption, dilution, or underproduction as discussed earlier, thereby making the prediction of replacement amounts also difficult. FFP contains a modest concentration of fibrinogen, but cryoprecipitate is the blood product of choice for hypofibrinogenemia. The OPO's guidelines should specify at what serum concentration of fibrinogen (usually 100-150 mg/dL) treatment should begin and the number of units of cryoprecipitate ("cryo") to order. Usually 6 to 10 units are given, followed by serial measurements of fibrinogen and administration of additional units of cryoprecipitate until the fibrinogen level specified in the guidelines is reached.

A more narrow MA most often reflects low platelet numbers (thrombocytopenia) or diminished qualitative platelet function (thromboasthenia) during clot formation. As discussed earlier, medications that alter platelet function include aspirin, clopidogrel, ticlopidine (Ticlid), and dipyridamole, among others. Because coagulation factors are also an integral component during clot development, the MA may also be diminished when clotting factor concentrations are low (Figure 4C). Platelet replacement should be considered if the platelet count is low as defined by the guidelines of the individual OPO or if those guidelines recommend platelet transfusion if the donor has received any of the listed medications. In general, the platelet count can be increased by about 10 000 platelets for each platelet unit given. However, again, if active bleeding is continuing, some of the new platelets may immediately be consumed. When aspirin, Plavix, Ticlid, or the other medications listed have been given, all "native" platelets must be considered nonfunctional. Assuming no further drug is freely circulating, OPO guidelines should direct a full replacement dose, usually 6 platelet units ("packs"). Serial platelet counts for thrombocytopenia and serial evaluations using thromboelastography for thrombocytopenia are helpful in determining if more platelet transfusions are needed.

Hypercoagulation

A short R and/or K time and/or an increased (more acute) alpha angle may indicate accelerated clot formation as a hypercoagulable condition (Figure 4E) and have been observed after trauma, burn injuries, or as a predictor of thrombotic complications.^{8,13,14} More rapid clotting or a tendency toward generalized or disseminated

clot formation may also place donor organs at risk. If hypercoagulation is suspected, other diagnostic studies may be sought, such as tests showing low protein C or antithrombin III levels. However, because treatment of a hypercoagulable condition would require active anticoagulation, considerable discussion should occur before initiating any therapy, especially as the donor will be undergoing surgery soon.

Summary

Thromboelastography complements traditional laboratory measurements of blood coagulation. It provides unique information about the combined and integrated processes of all components of clot formation, strength, and lysis. Platelet function and the possibility of a hypercoagulable condition, difficult to assay with other tests, can also be evaluated. Thromboelastography may provide the organ procurement coordinator with another tool to titrate the administration of blood products so as to control bleeding during donor care.

Financial Disclosures

None reported.

References

1. Ganter MT, Hofer CK. Coagulation monitoring: current techniques and clinical use of viscoelastic point-of-care coagulation devices. *Anesth Analg*. 2008;106:1366-1375.
2. Jeger V, Zimmermann H, Exadaktylos AK. Can RapidTEG accelerate the search for coagulopathies in the patient with multiple injuries? *J Trauma*. 2009;66:1253-1257.
3. Roberts HR, Monroe DM, Escobar MA. Current concepts of hemostasis. *Anesthesiology*. 2004;100:722-730.
4. Powney DJ, Reich HS. Regulation of coagulation abnormalities and temperature in organ donors. *Prog Transplant*. 2000;10:146-153.
5. Hess JR, Brohi K, Dutton RP, et al. The coagulopathy of trauma: a review of mechanisms. *J Trauma*. 2008;65:748-754.
6. Dahlbäck B. Blood coagulation. *Lancet*. 2000;355:1627-1632.
7. Carey MJ, Rodgers GM. Disseminated intravascular coagulation: clinical and laboratory aspects. *Am J Hematol*. 1998;59:65-73.
8. Schöchel H, Frietsch T, Pavelka M, Jámor C. Hyperfibrinolysis after major trauma: differential diagnosis of lysis patterns and prognostic value of thrombelastometry. *J Trauma*. 2009;67:125-131.
9. Martini WZ. Coagulopathy by hypothermia and acidosis: Mechanisms of thrombin generation and fibrinogen availability. *J Trauma*. 2009;67:202-209.
10. Pai M, Hayward CP. Diagnostic assessment of platelet disorders: what are the challenges to standardization? *Semin Thromb Hemost*. 2009;35:131-138.
11. Gibbs NM. Point-of-care assessment of antiplatelet agents in the perioperative period: a review. *Anaesth Intensive Care*. 2009;37:354-369.
12. Craft RM, Chavez JJ, Bresee SJ, Wortham DC, Cohen E, Carroll RC. A novel modification of the thrombelastograph assay, isolating platelet function, correlates with optical platelet aggregation. *J Lab Clin Med*. 2004;143:301-309.
13. McCrath DJ, Cerboni E, Frumento RJ, Hirsh AL, Bennett-Guerrero E. Thromboelastography maximum amplitude predicts postoperative thrombotic complications including myocardial infarction. *Anesth Analg*. 2005;100:1576-1583.
14. Park MS, Martini WZ, Dubick MA, et al. Thromboelastography as a better indicator of hypercoagulable state after injury than prothrombin time or activated partial thromboplastin time. *J Trauma*. 2009;67:266-276.

CE Test Test ID 4000-142: Thromboelastography during adult donor care

Learning objectives: 1. Identify testing for coagulation problems in potential organ donors 2. Determine methods for measuring blood coagulation 3. Describe clinical applications of data derived from the thromboelastogram

1. Following trauma or intracranial bleeding, the clotting cascade is initiated as a result of exposure of the inner endothelial lining of blood vessels. The extrinsic cascade is initiated by which of the following tissue proteins?

- a. Von Willebrand factor
- b. Factor VIII
- c. Factor X
- d. Tissue factor

2. A test that measures the amount of time needed to form a clot is which of the following?

- a. Serum fibrinogen
- b. Liver function tests
- c. Prothrombin time
- d. Platelet count

3. Fibrinogen utilization is affected by which of the following clinical situations?

- a. Hypotension
- b. Acidosis
- c. Hyponatremia
- d. Hypokalemia

4. The blood product of choice for hypofibrinogenemia is which of the following?

- a. Fibrin split products
- b. Platelets
- c. Fresh frozen plasma
- d. Cryoprecipitate

5. Which of the following drugs alter platelet function?

- a. Clopidogrel
- b. Acetaminophen
- c. Heparin
- d. Tenormin

6. Each platelet unit given can be expected to increase the platelet count by which of the following?

- a. 100 000
- b. 5000
- c. 2500
- d. 10 000

7. Analysis of thromboelastography provides organ procurement organization coordinators with guidance in which of the following clinical decisions?

- a. Amount of platelets required
- b. Amount of cryoprecipitate needed
- c. Quantities of fresh frozen plasma needed
- d. All the above

8. Information derived from thromboelastography includes which of the following?

- a. Elements of Protein C function
- b. Elements of Protein S function
- c. Components of clot formation strength
- d. Components of platelet aggregation

9. Inadequate clot formation predisposes the donor to increased bleeding and which of the following complications?

- a. Thrombocytosis
- b. Hypotension
- c. Thromboembolism
- d. Hypertension

10. Regulatory proteins are present in the circulatory system and function to prevent excessive local thrombosis. Examples of these regulatory proteins that become activated and slow the coagulation process include which of the following?

- a. Protein C
- b. Protein S
- c. Antithrombin
- d. All the above

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