

Comparison of Thromboelastography to Bleeding Time and Standard Coagulation Tests in Patients After Cardiopulmonary Bypass

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This prospective study of 36 adult patients undergoing cardiopulmonary bypass (CPB) was conducted to determine the utility of thromboelastography (TEG) versus platelet studies (bleeding time, platelet count, mean platelet volume) and standard coagulation tests (prothrombin time, activated partial thromboplastin time, fibrinogen) to more effectively discriminate patients likely to benefit from platelet or fresh frozen plasma (FFP) transfusion. Although the sensitivities of the bleeding time (71.4%) and platelet count (100%) were similar to the TEG (71.4%), the specificity (89.3%) of the TEG was greater than that of the bleeding time (78.5%) and platelet count (53.6%). Seven patients experienced clinically significant hemorrhage; 5 (71.4%) had an abnormal TEG. Three of 8 (38%) other patients with an abnormal TEG had no abnormal bleeding. Only 2 of 27 (7.4%) patients with a

normal TEG had abnormal bleeding requiring platelet or FFP transfusion. Therefore, it is suggested that post-CPB patients with a normal TEG should not receive platelet or FFP transfusions empirically. If excessive bleeding is noted in a patient with a normal TEG, this suggests a surgically correctable etiology. Data from this series suggest that patients displaying an abnormal TEG appear to be at increased risk for hemorrhage; therefore, appropriate blood product support should be initiated at the first sign of accelerated bleeding. *This is a US government work. There are no restrictions on its use.*

KEY WORDS: thromboelastography, hemorrhage, cardiothoracic surgery, coagulopathy, bleeding time

BLEEDING COMPLICATIONS following cardiopulmonary bypass (CPB) continue to be a source of significant morbidity and mortality. Postoperative hemorrhage is most commonly due to inadequate surgical hemostasis. Other causes include inadequate heparin reversal and decreased plasma concentrations of plasma proteins, particularly fibrinogen.¹ Blood contact with synthetic nonendothelial surfaces also causes activation of the intrinsic coagulation pathway even in the presence of heparin.² The concentrations of plasma proteins and coagulation factors generally do not fall below the levels necessary for normal hemostasis,^{3,4} but a decrease in platelet function and quantity is the most important factor contributing to the coagulopathy seen after CPB.⁴⁻⁶

Harker et al³ reported that clinically significant bleeding occurred in the post-CPB period due to platelet dysfunction.³ Mohr et al⁷ stated that patients who displayed abnormal bleeding had a significantly lower mean platelet volume (MPV) (7.7 ± 0.84 v $8.68 \pm 1.1 \mu\text{m}^3$). Although platelet transfusion may correct the bleeding disorder seen in patients with thrombocytopenia and/or platelet dysfunction, prophylactic administration of platelets to all CPB patients after CPB has not demonstrated any clinically significant benefit.^{6,8} Furthermore, a National Institutes of Health consensus conference recommended that prophylactic platelet transfusions not be routinely administered following CPB.⁹

Evaluation of post-CPB bleeding is complicated by the

need for expedient reporting of results of coagulation tests in order to rapidly initiate treatment and, therefore, minimize the risks of morbidity and mortality due to hemorrhage. Thromboelastography (TEG) measures the strength and shear elasticity of a clot as it forms, matures, retracts, and lyses (Fig 1). The TEG was developed by Hartert of Heidelberg, Germany during World War II. The first results were published in 1948.¹⁰ Spiess et al¹¹ compared TEG to the activated coagulation time (ACT), and a coagulation panel consisting of the prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet count, fibrinogen concentration, and concentration of fibrin split products (FSP) in patients following CPB. They found that TEG predicted which patients would have postoperative hemorrhage with an 87% accuracy. Neither the ACT nor the other parameters could predict hemorrhage with greater than a 51% accuracy. In their study, Spiess et al,¹¹ however, did not compare TEG to any test specifically related to platelet function. In a later trial, TEG was found to be equivalent to the Sonoclot analysis for the detection of coagulation defects following CPB.¹² The TEG parameters most closely related to platelet function (α , maximum amplitude [MA], amplitude 60 minutes after MA [A_{60}]) have been shown to significantly correlate with the results of platelet aggregometry, and TEG is technically less demanding.¹³

The purpose of this study was to compare TEG not only to PT, aPTT, and fibrinogen, but more importantly to the bleeding time (BT), platelet count, and MPV as predictors of hemorrhage. In so doing, it was hoped to develop a clinically useful method to identify patients who may benefit from transfusion of platelets and/or fresh frozen plasma (FFP) (ie, those at high risk for hemorrhage), versus those who can safely be followed, thus decreasing the risk of transfusion-associated morbidity.^{14,15}

METHODS

After approval by the institutional review board and appropriate informed consent, 36 patients participated in this prospective

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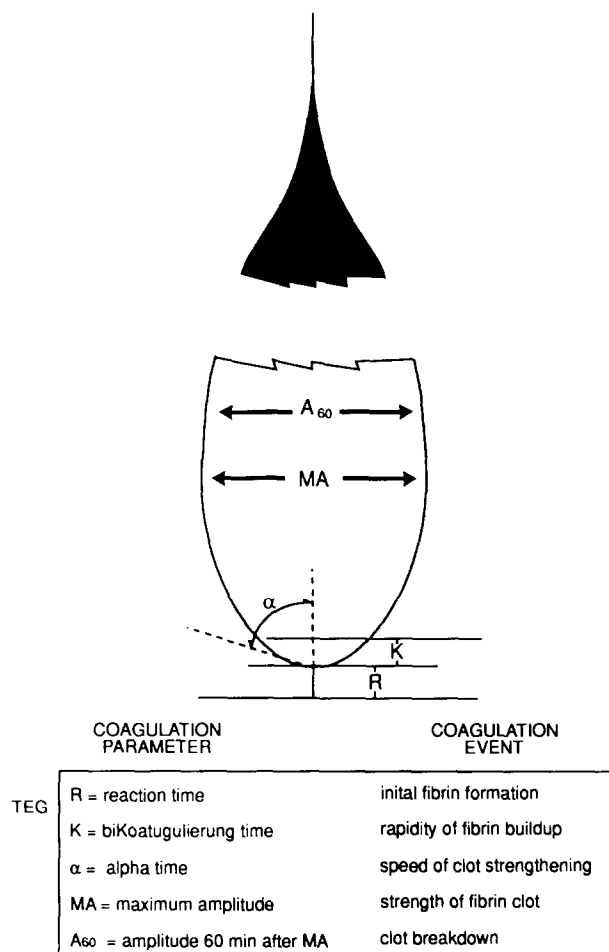


Fig 1. Schematic representation of TEG tracing.

study. All patients underwent cardiac surgical procedures requiring cardiopulmonary bypass. The patients studied were the first 36 who consented to participate and underwent surgery as the first or second case of a weekday in order to allow optimal laboratory support. The CPB circuit included a membrane oxygenator (Bentley, Baxter Healthcare Corp, Irvine, CA) and a centrifugal pump head (Biomedicus, Medtronic Inc, Eden Prairie, MN). Both the venous and arterial lines had 40 μm filters. The circuit was primed with 1,600 mL of crystalloid solution and 200 mL of 25% albumin. Hypothermia to 28°C was used in all cases. Cardiopulmonary bypass flow was 2.4 L/min/m² during normothermia and was tapered to 1.8 L/min/m² during hypothermia. A potassium-blood cardioplegia solution was used.

Prior to cannulation and initiation of CPB, all patients received 300 U/kg of beef lung heparin to produce an ACT of more than 400 seconds. After separation from CPB, protamine reversal of remaining heparin activity was based on the ACT as described by Bull et al.¹⁶

All patients had bleeding times performed preoperatively and upon arrival in the intensive care unit (ICU) postoperatively (within 45 minutes of heparin reversal). Bleeding times were performed using a Simplate II BT-device (Organon Teknika Corp, Durham, NC). A blood pressure cuff was placed on the upper arm of the patient and inflated to 40 mmHg. The volar surface of the forearm was cleansed with 70% alcohol swabs. The device was placed firmly on the forearm, but not pressed down. All incisions

were made in a vertical direction. Every 30 seconds the flow of blood was blotted with circular filter paper without touching the edges of the incision. The blotting was continued until the flow of blood stopped (normal 2 to 9 minutes). All BTs were performed by a trained hematology technician or hematologist.

All patients had an arterial catheter placed immediately prior to surgery. All blood samples were drawn via this catheter after 10 mL of blood was withdrawn and discarded. The blood samples for TEG, PT, aPTT, platelet count, MPV, hemoglobin (Hgb), hematocrit (Hct), fibrin split products (FSP), fibrinogen, and thrombin time (TT) were drawn immediately prior to surgery and upon arrival postoperatively in the ICU. The postoperative samples were obtained before transfusion of any platelets or FFP and after documentation that the ACT had returned to baseline with the administration of an adequate dose of protamine.

Thromboelastography was performed using the Biotoc Elvi thromboelastograph (Logos Scientific, Henderson, NV). The TEG tracings were analyzed for R, K, α, MA, and A₆₀. The normal ranges suggested by the manufacturer are as follows: R = 6 to 12 minutes, K = 3 to 5 minutes, α = 45 to 55°, MA = 55 to 60 mm, and A₆₀ = >0.85 MA (Fig 1). However, patients following CPB commonly demonstrate subclinical abnormalities of the coagulation system,¹⁷ which may alter TEG parameters and make these suggested "normals" less clinically useful than in other populations of patients. Different authors have chosen slightly wider ranges of normal values in various other studies.^{11,12,18} Therefore, the authors established the normal ranges used in this article for post-CPB patients by review of TEG parameters in "bleeders" and "nonbleeders" to optimize sensitivity and specificity. The normal values used in this study are R < 14 minutes, K < 6.5 minutes, α > 38°, MA > 45 mm, and A₆₀ > 0.85 MA.

Postoperatively, the patients were followed for 24 hours with careful notation of blood product transfusion and mediastinal tube (MT) or chest tube (CT) output. Abnormal bleeding was defined as blood loss exceeding 1,500 mL of blood via the MT/CT within the first 24 hours following surgery, or the need to transfuse platelets or FFP postoperatively to control hemorrhage. Platelet and FFP transfusions in the ICU were ordered by the surgery service based on the results of standard coagulation tests or the clinical suspicion of abnormal coagulation. The surgeons were not aware of the TEG results. The need for reexploration was based upon the clinical judgment of the attending cardiothoracic surgeon.

Patients were categorized as "bleeders" and "nonbleeders" based on this definition of abnormal bleeding. The sensitivity, specificity, negative predictive value, and positive predictive value of each coagulation test were calculated according to the following equations:

$$\text{sensitivity} = \frac{\text{true positives}}{\text{true positives} + \text{false negatives}}$$

$$\text{specificity} = \frac{\text{true negatives}}{\text{false positives} + \text{true negatives}}$$

$$\text{positive predictive value} = \frac{\text{true positives}}{\text{true positives} + \text{false positives}}$$

$$\text{negative predictive value} = \frac{\text{true negatives}}{\text{false negatives} + \text{true negatives}}$$

RESULTS

Thirty-six patients were studied: 22 underwent coronary artery bypass grafting (CABG), 9 valve replacements, 3 Kent bundle ablations, and 2 atrial septal defect repairs.

Table 1. Patients With Abnormal Bleeding

Patient Number	Age (years)	Type of Surgery	Preoperative Anticoagulation	Reexploration Required	CT/MT Output in 24 Hours (mL)	Units PRBCs Transfused	Units Platelets Transfused	Units FFP Transfused
1	58	AVR	No	No	1,530	4	12	4
2	63	CABG	No	No	1,805	4	6	2
3	54	CABG	ASA	No	2,275	4	0	0
4	70	AVR	No	Yes	2,330	8	12	6
5	75	CABG	Heparin	Yes	3,407	13	42	6
6	32	Tricuspid annuloplasty, MVR	No	No	1,385	8	6	6
7	32	AVR, MVR, TVR	No	No	544	5	6	3
Mean	55			29%	1,896 ± 899	6.6	12	3.9

One patient with an abnormal TEG and a platelet count of $69 \times 10^9/L$ died 8 hours postoperatively. The chest was not reexplored and an autopsy was not performed. The data from this patient are not included in the analysis. Statistical analysis of preoperative TEG, BT, and laboratory values was not useful in predicting patients likely to bleed. Further values referred to in the paper represent postoperative results unless otherwise specified. Seven of the 35 patients (20%) met criteria for abnormal bleeding (Table 1). Patient characteristics for “nonbleeders” are shown in Table 2. Only one of the patients in this group received platelets postoperatively. This patient was given 6 U of platelets empirically prior to placing a catheter into the femoral artery. His TEG, platelet count, and coagulation studies drawn prior to administration of the platelets (tests pending at time of transfusion) all subsequently returned with values in the normal range.

Three of the 35 patients required reexploration of the chest. One of these patients had a leaking branch from a saphenous vein graft. This was repaired and the patient did not meet criteria for abnormal bleeding. His TEG was normal at the time of reexploration. The other two patients had diffuse oozing without a surgically correctable site of

blood loss, and met criteria for abnormal bleeding. In both instances, these patients had abnormal TEGs that corrected, and bleeding stopped with appropriate transfusion of blood products.

Eight of 35 (23%) patients had at least one abnormal TEG parameter suggesting a hypocoagulable state (Fig 2). Five of the eight (62.5%) developed abnormal bleeding. Two of the three patients who did not hemorrhage yet had an abnormal TEG could have been considered to be at risk for bleeding. One patient had a platelet count of $85 \times 10^9/L$ and a prolonged PT, aPTT, as well as abnormal R, K, α , and MA values. The other patient had a BT of 11.0 minutes, platelet count of $91 \times 10^9/L$, fibrinogen of 89.7 mg/dL (175 to 390 mg/dL), and abnormal K, α , and MA values. The only other patient whose TEG was abnormal, and did not display abnormal bleeding, had an unexplained abnormal TEG preoperatively and postoperatively with normal standard coagulation parameters.

Table 2. Patients Who Did Not Bleed Excessively

Age mean 54 years
Range, 18 to 71 years
Preoperative anticoagulation 12/28 (42.9%)
ASA 8/28 (28.6%)
Therapeutic dosage of heparin within 24 hours of surgery 4/28 (14.3%)
Type of surgery
Valve replacement (5)
Coronary artery bypass graft (18)
Kent bundle ablations (3)
Atrial septal defect (2)
Reexploration
1 of 28 (3.6%)
Chest tube/mediastinal tube output in first 24 hours
Mean 789 ± 319 mL
Blood products required (mean units per patient)
Packed red blood cells 2.8 U
Platelets = 0.86 U (18/24 U given intraoperatively)*
Fresh frozen plasma 0.14 U (all units transfused intraoperatively)

*One patient received 6 U of platelets empirically prior to placement of an introducer into the femoral artery.

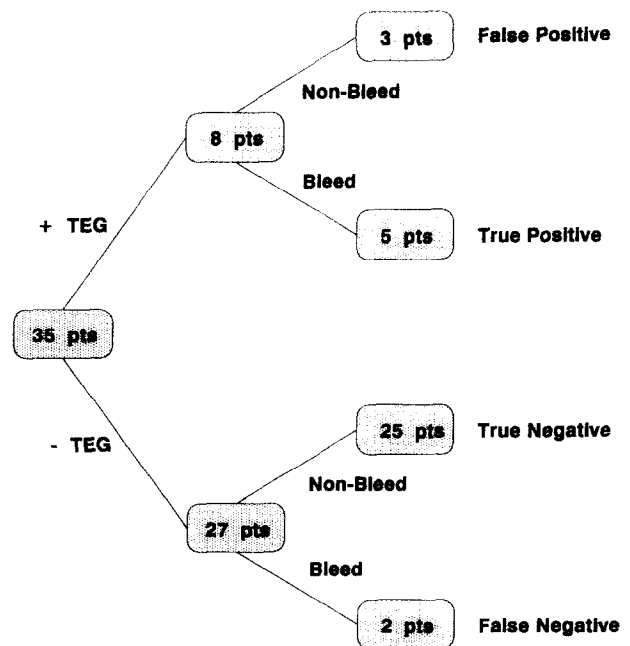


Fig 2. Patient outcome in comparison to TEG results. +TEG, at least one TEG parameter suggesting a hypocoagulable state; -TEG, all TEG parameters in the normal range.

Table 3. Predictive Values of Tests

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
TEG	71.4	89.3	62.5	92.3
Bleeding time (≥ 9 min)	71.4	78.5	45.5	91.7
Platelet count ($< 130 \times 10^9/L$)	100	53.6	31.6	100
MPV ($< 7.4 \mu m$)	14.3	87.5	3.6	18.8
PT (> 13.55 s)	85.7	10.7	19.4	75.0
aPTT (> 30.85 s)	85.7	21.4	21.4	85.7
Fibrinogen (< 175 mg/dL)	85.7	32.1	24.0	90.0
Thrombin time (< 9.95 s)	28.6	78.6	25.0	81.5
Hemoglobin ($< 12g/dL$)	85.7	7.1	18.8	66.7

Twenty-seven of 35 (77%) patients had a normal TEG. All but two (92.5%) of these patients did not meet criteria for postoperative hemorrhage. Thus, TEG in this study displayed a sensitivity of 71.4% and specificity of 89.3% (Table 3).

Tables 4 and 5 show a simple comparison of coagulation parameters post-CPB for "bleeders" and "nonbleeders." Using a two-tailed *t*-test, a statistically significant difference was observed between these groups for BT, platelet count, PT, aPTT, K, α , and MA.

No patients exhibited primary fibrinolysis either preoperatively or postoperatively as defined by TEG criteria ($A_{60} < 0.85$ MA) or by analysis of platelet count, PT, aPTT, fibrinogen, and FSP.

DISCUSSION

Thromboelastography was introduced in the United States for use in monitoring complex and often severe changes occurring in the coagulation system during liver

Table 4. Comparison of Postoperative Values Between "Bleeders" and "Nonbleeders"

Variable	Lab Normals	Bleeders	Nonbleeders	(<i>t</i> -test) P Value
Duration bypass (h)	NA	2.47 \pm 0.91	2.34 \pm 1.1	0.51
Bleeding time	2-9 (min)	13.8 \pm 5.0	8.1 \pm 3.3	0.002*
Hgb	12-18 (g/dL)	10.1 \pm 2.0	9.7 \pm 1.4	0.58
Platelet count	130-400 ($\times 10^9/L$)	70.0 \pm 24.6	136.4 \pm 42.0	0.001*
MPV	7.4-10.4 (μm)	8.21 \pm 0.90	8.42 \pm 0.88	0.60
PT	11.6-13.5 (s)	18.5 \pm 2.2	15.6 \pm 1.6†	0.001*
aPTT	23.5-30.8 (s)	47.5 \pm 12.5	37.1 \pm 9.3†	0.03*
Fib	175-390 (mg/dL)	117.8 \pm 35.7	164.1 \pm 57.1	0.07
TT	9.9-11.9 (s)	12.0 \pm 3.1	13.2 \pm 4.3	0.54

Abbreviations: Hgb, hemoglobin concentration; MPV, mean platelet volume; PT, prothrombin time; aPTT, activated partial thromboplastin time; Fib, fibrinogen; TT, thrombin time.

*Significant differences between groups ($P < 0.05$).

†Denotes values consistent with a hypocoagulable state in nonbleeders.

Table 5. Comparison of Postoperative TEG Values Between "Bleeders" and "Nonbleeders"

Variable	Manufacturer's Normals	Bleeders	Nonbleeders	(<i>t</i> -test) P Value
R	(6 to 12 min)	12.6 \pm 2.2	11.1 \pm 3.0	0.23
K	(3 to 5 min)	10.2 \pm 8.3	4.2 \pm 2.1	0.001*
α	(45 to 55°)	38.9 \pm 7.8	49.5 \pm 8.8	0.008*
MA	(55 to 60 mm)	42.6 \pm 10.5	54.3 \pm 8.4	0.004*

* $P < 0.05$.

transplantation.¹⁸ TEG examines the interaction of the coagulation cascade, fibrinogen, and platelets as an entire unit, rather than individually as do standard coagulation tests.¹⁹ Cardiac surgery induces many of the same coagulation changes seen during liver transplantation. The principal defect post-CPB is most often secondary to platelet dysfunction. Therefore, monitoring patients with standard coagulation tests is often inadequate because the results are not routinely available in a timely fashion and are incapable of detecting qualitative platelet defects.

The present data revealed a sensitivity of 71.4% and specificity of 89.3% for TEG. This study differs from the work of Spiess et al,¹¹ however, in that it included studies of platelet size, quantity, and function in the analysis. Comparison of TEG to BT provides evidence that TEG parallels this test of platelet function just as it does platelet aggregometry.¹³ Though BT proved similar to TEG in the ability to predict "bleeders" versus "nonbleeders," the TEG has several inherent benefits. TEG analysis is performed with only 0.35 mL of whole blood and can be obtained as soon as protamine reversal of heparin is complete, resulting in the return of clinically useful data within only 30 minutes to guide coagulation management. Though the BT is a relatively simple procedure to perform on ambulatory patients, it may be difficult or impossible to perform in cardiac surgery patients when access to an extremity is seldom possible intraoperatively. Patients may not be moved throughout the test (mean 9.1 minutes in these patients), therefore necessitating waiting until the patient has arrived in the ICU postoperatively. In addition, a blood pressure cuff must remain inflated on an extremity during the test, which is often difficult if the patient has multiple arterial and venous catheters in the upper extremities, and has had veins harvested from the lower extremities.

Beyond being more convenient, and often faster, in certain situations the TEG is superior to coagulation tests such as the BT, MPV, and the platelet count by providing additional clinical information. For example, the TEG can provide evidence of disseminated intravascular coagulation or primary fibrinolysis, which would not be suspected by the performance of platelet-specific coagulation tests.²⁰

Most cases of serious bleeding following CPB occur due to a specific surgically correctable bleeding site. The authors believe that the TEG may be helpful in differentiating a surgical versus a medical cause for bleeding. In this study, three patients required reexploration of the chest to evaluate initial excessive postoperative bleeding. Indeed, the

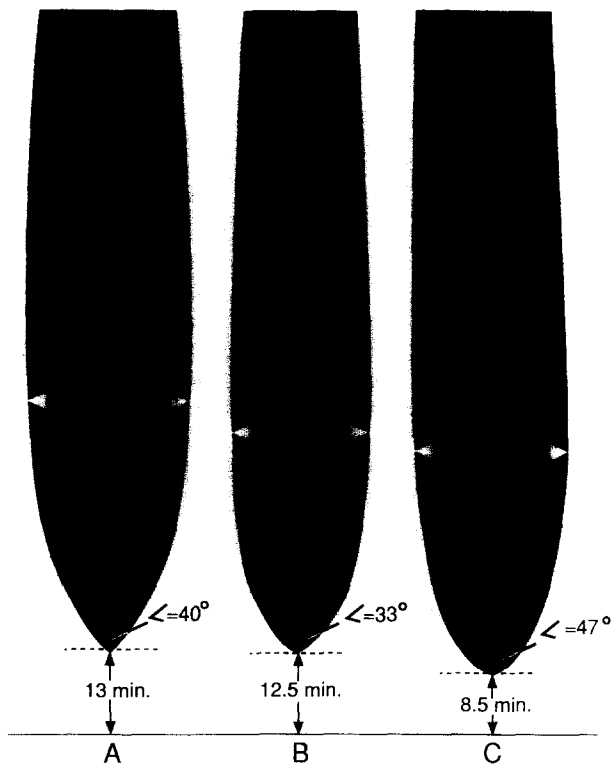


Fig 3. A patient with a coagulopathy after surgery (patient #4). (A) Preoperative TEG tracing, all values are within normal limits. (B) TEG performed upon arrival to ICU postoperatively. Note decreased α , MA, and A_{90} . (C) TEG after transfusion of 2 U FFP, 2 U PRBCs, and 6 U of platelets given during reexploration. Note normalization of the TEG, including shortening of already normal R value, consistent with transfusion of FFP.

only patient with a normal TEG was found to have surgical bleeding due to a leaking saphenous vein graft. After repair of this graft the patient did well, and importantly, transfusion of platelets or FFP was avoided. He lost a total of 1,310

mL via chest and mediastinal tubes, and, therefore, did not meet the criteria of this study for abnormal bleeding. The other two patients, having abnormal TEGs consistent with a coagulopathy, had diffuse oozing at the time of reexploration, and subsequently required a combined total of 54 U of platelets, 18 U of FFP, and 29 U of packed red blood cells over 24 hours to stabilize and control their bleeding (Fig 3). This is not to say that reexploration of the chest should be avoided in the face of an abnormal TEG. Specific blood product therapy could be infused while preparations are being made to return to the OR, and prompt improvement in coagulation may potentially obviate the need for reexploration if the bleeding stops.

This study suggests that TEG may be a useful tool in monitoring the coagulopathy that develops after cardiac surgery. The TEG complements the results of standard coagulation testing, and often provides reliable results faster. In addition, because the TEG reflects the interaction of the entire coagulation system, it is useful in determining specific therapy that can be given thereby avoiding the empiric administration of multiple blood products, while reserving this expensive resource for appropriate indications, and decreasing the incidence of disease transmission. It is suggested that patients with a normal postoperative TEG not receive platelets or FFP empirically, while infusion of appropriate blood products in patients displaying an abnormal TEG could be initiated early in patients with accelerated bleeding. A larger trial is required to verify the results obtained from this initial study, since the normal TEG values for patients after CPB were derived from data obtained in this trial.

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