

A Reduction in Clot Formation Rate and Strength Assessed by Thrombelastography Is Indicative of Transfusion Requirements in Patients With Penetrating Injuries

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Background: Bleeding is a major cause of death in patients with traumatic injuries. Recently, thrombelastography (TEG) has been suggested as an additional means of evaluating coagulation in trauma patients. We hypothesized that TEG data would aid in defining the coagulopathy of trauma in patients with penetrating traumatic injuries.

Methods: A retrospective study was performed of patients ($n = 44$) with penetrating injuries admitted to a combat support hospital during a 2-month period in 2004. Recorded data included standard laboratory data, TEG parameters, and blood product use in the first 24 hours after admission. Values were compared with clin-

ically accepted ranges and those obtained from the Haemoscope Corporation.

Results: At admission, International Normalization Ratio, prothrombin time, and partial thromboplastin time were increased in 39% (≥ 1.5), 31% (> 16 seconds), and 37% (> 40 seconds) of patients, respectively, suggesting hypocoagulation, but these variables did not correlate with the use of blood products ($p > 0.05$). TEG values obtained within 24 hours of admission ($6 \text{ hours} \pm 5.7 \text{ hours}$; median of 4.5 hours) demonstrated hypocoagulation based on delayed propagation of the clot (increased K time and reduced α -angle) and decreased clot strength (reduced maximal amplitude [MA]). MA correlated

($r = 0.57, p < 0.01$) with blood product use as well as platelet count ($r = 0.61, p < 0.01$). Patients with reduced MA ($n = 23$) used more blood products and had reduced platelet counts and hematocrit.

Conclusion: Thrombelastography was a more accurate indicator of blood product requirements in our patient population than prothrombin time, partial thromboplastin time, and International Normalization Ratio. Thrombelastography enhanced by platelet count and hematocrit can guide blood transfusion requirements.

Key Words: Thrombelastograph, Clot, Transfusion, Trauma, Penetrating Injury.

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Posttraumatic coagulopathy is a common manifestation of patients arriving in emergency departments and is often an early predictor of both eventual blood transfusion requirements and mortality.^{1,2} The hemostatic status of these patients on admission is generally the most reliable indication of outcome.³ However, despite the extreme importance of early identification, standard assays are often inadequate in diagnosing clotting deficiencies.^{4,5} These assays, termed the coagulation profile—prothrombin time (PT), activated partial thromboplastin time (PTT), fibrinogen concentration and platelet count—serve mainly as a measure of time to clot initiation.⁶ Because the most commonly employed assays for clotting efficacy, PT and PTT, are performed on platelet-poor plasma, they are unable to assess the interactions that occur between clotting factors and platelets as clot forms.⁷

Thrombelastograph (TEG) during cardiopulmonary bypass surgery for the detection of coagulopathy has improved accuracy in diagnosing hemostatic abnormalities.⁸ In contrast, though studies with blunt trauma patients have illustrated a correlation between TEG readings and eventual transfusion requirements, this test is largely underutilized in the identification of coagulopathy in trauma patients.⁷

The parameters analyzed on a TEG tracing, the thrombelastogram, produce a more comprehensive illustration of the clotting cascade than is provided by currently used laboratory values.^{4,9} Because it is known which blood components are responsible for the phases of clot formation, irregularity in a specific portion of the TEG serves a diagnostic purpose. These values may direct transfusion of appropriate blood components and drugs, including rFVIIa, for treatment of specific clotting deficiencies. A normal TEG in the presence of abnormal vital signs may indicate surgical bleeding and the need for exploration.^{4,6} This could, theoretically, reduce transfusion requirements of patients arriving in emergency departments, as it has for patients undergoing cardiopulmonary bypass.^{6,10,11} Algorithms directing transfusion have proven to significantly reduce blood product use in for cardiopulmonary bypass.^{6,8}

Based on the TEG parameters, data from studies of blunt trauma patients have indicated that these patients are hypercoagulable at admission.^{1,5} However, studies have also re-

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vealed that those patients with the most severe injuries, as characterized by greater injury severity score, tend to be hypocoagulable.^{1,2} This study was performed to investigate the coagulopathy of penetrating trauma patients, as identified by thrombelastography, and to examine the relationship between this disorder and subsequent transfusion requirements. The relationships between routine coagulation parameters, TEG parameters, and blood product use were analyzed as well.

METHODS

The Institutional Review Board at Brooke Army Medical Center approved review of patient records in the Joint Theater Trauma Registry maintained at the United States Army Institute of Surgical Research. A retrospective study was performed on patients admitted to a combat support hospital (CSH) during November and December of 2004. Inclusion criteria included traumatic penetrating injury, a TEG taken within 24 hours of admission, and the availability injury description and laboratory results in patient charts. Iraqi detainees and those who died intraoperatively or upon arrival at the CSH were excluded from the study. Data compiled included age, source of injury (either gun shot wound or explosion), time of admission and of first TEG, vital signs, coagulation profile, Injury Severity Scores (ISS), TEG data, and transfusion requirements during the first 24 hours after admission. Vital signs taken at admission were systolic blood pressure (SBP), pulse rate, respiratory rate, Glasgow Coma Score, and body temperature. Recorded vital signs and compiled laboratory results were the earliest available after admission. Blood samples taken at admission provided platelet count (Plt), hematocrit (Hct), hemoglobin concentration (Hb), activated prothrombin time (aPTT), PT, International Normalization Ratio (INR), base excess (BE), and pH. Blood values were measured using standard clinical chemistry techniques. Total transfusion requirements in the first 24 hours after admission included all blood components (units of packed red blood cells + fresh frozen plasma + fresh whole blood). Fresh whole blood was calculated as 1 unit plasma and 1 unit packed red blood cells. ISS were calculated from patient medical records according to the published guidelines of Baker et al.¹²

Thrombelastography

A Computerized Thrombelastograph Coagulation Analyzer (TEG model 5000, Haemoscope Corporation, Niles, IL) was used for the analyses and the data were recorded and modeled. TEG was obtained at the discretion of the attending physician. The patients' whole blood was assayed within 4 minutes of phlebotomy to prevent the initiation of clotting before TEG. About 360 μ L of whole blood were added to 1% celite-treated cups, which were then placed in the TEG apparatus. The samples were run at patient temperatures to accurately reflect their in vivo coagulation status. Analyzed parameters included R time, K time, α -angle, and maximal amplitude (MA). The normal ranges for each of these values, corresponding to celite-activated whole-blood samples, were

obtained from the Haemoscope Corporation and the data were thus classified as normal or abnormal.

Statistical Analysis

Data were analyzed with use of SAS version 8.1 (SAS Institute Inc., Cary, NC). Demographic data were expressed as mean $\pm$ SD. Univariate analysis was performed by two-sample Student's *t* test or Wilcoxon Rank Sum test for continuous variable and χ^2 test for categorical variables. Patients with MA <54 mm, the reported low value of "normal" range, were compared with those with MA $\geq$ 54 mm. In addition, Pearson correlation coefficients were calculated to determine relationships between continuous variables, between dichotomous and continuous variables (called Point-biserial correlation), and between dichotomous variables (Phi). Significant differences were determined at a *p* < 0.05.

RESULTS

Eight hundred fifty patients were admitted to the CSH during the 2-month period. Seventy-six patients had a TEG performed. Thirty-two patients were excluded from the study because of lack of complete patient files, TEG data taken after 24 hours after admission, nonpenetrating traumatic injuries, or detainee status. Therefore, 44 patients met the criteria for analysis.

Vital signs and laboratory values of the patient population are presented in Table 1. Of the patients in the study,

Table 1 Patient Vitals and Laboratory Values at Admission

Vital signs	
SBP (mm Hg)	123 $\pm$ 23.6
Pulse (bpm)	104 $\pm$ 24.7
Respiration rate (per min)	16 $\pm$ 6.8
GCS	10 $\pm$ 5.6
Temperature ($^{\circ}$ C)	36.9 $\pm$ 1.1
ISS	21 $\pm$ 9.4
Laboratory values	
Hb (g/dL)	10 $\pm$ 2.6
Hct (%)	29 $\pm$ 7.7
Plt (10^3 cells/mm ³)	211 $\pm$ 161.2
BE (mEq/L)	-5.8 $\pm$ 5.2
pH	7.33 $\pm$ 0.09
aPTT (s)	39.4 $\pm$ 16.5
PT (s)	14.1 $\pm$ 3.1
INR	1.44 $\pm$ 0.34
TEG values	
R (min)	3.6 $\pm$ 1.08
K (min)	3.5 $\pm$ 3.0
α -angle ($^{\circ}$)	55.5 $\pm$ 13.6
MA (mm)	52.6 $\pm$ 12.5
Blood products	
PBRC (units)	5 $\pm$ 4.4
FFP (units)	3 $\pm$ 3.2
FWB (units)	1 $\pm$ 2.1
Cyro (units)	1 $\pm$ 2.9
Blood transfused (units)	12 $\pm$ 10.6

The use of blood products was during the first 24 h after admission.

Table 2 The Patient Population was Split Into Two Groups Based on MA Values: Those Below the Normal Range (<54 mm) and Those Above

	MA <54	MA ≥54
Vital signs		
SBP (mm Hg)	119 ± 26.0	130 ± 19.7
Pulse (bpm)	110 ± 28.9	97 ± 17.9
Respiration rate (per min)	16 ± 7.4	15 ± 6.4
Temperature (°C)	36.8 ± 1.22	37.1 ± 0.84
GCS	9 ± 5.7	10 ± 5.6
ISS	21 ± 9.5	21 ± 7.2
Laboratory values		
Hb (g/dL)	9 ± 2.3	10 ± 2.9
Hct (%)	26 ± 6.3*	31 ± 8.3
Plt (10 ³ cells/mm ³)	130 ± 73.8*	300 ± 185.7
BE (mEq/L)	-6.7 ± 4.86	-4.8 ± 5.44
pH	7.33 ± 0.09	7.33 ± 0.10
aPTT (s)	42 ± 16.0	36 ± 17.0
PT (s)	14 ± 3.6	14 ± 2.7
INR	1.45 ± 0.40	1.41 ± 0.28
TEG values		
R (min)	3.8 ± 1.00	3.4 ± 1.14
K (min)	5.2 ± 3.37*	1.67 ± 0.44
α-angle (°)	47 ± 11.5*	65 ± 8.2
MA (mm)	43 ± 8.3*	63 ± 8.3
Blood transfused (units)	16 ± 11.4*	6 ± 6.5

The means and standard deviations for the parameters were calculated following this division.

* Significantly different ($p < 0.05$) from MA ≥54.

34% were admitted after gunshot wounds and 55% for injuries caused by explosions. Six records did not indicate a source of injury. In the patient population, 11.3% had SBP below 90 mm Hg; 5.1% pH below 7.2; 22% hemoglobin level below 8 g/dL; and 3.3% temperature below 35°C. Abnormal PTT values, defined as greater than 40 seconds, was recorded in 14 patients (37%); PT greater than 16 in 12 patients (32%); and INR greater than 1.5 in 15 patients (39%) (Table 1). Although these values are indicative of hypocoagulation, they showed no significant correlations ($p > 0.05$) with subsequent blood product requirements, undermining the diagnostic capabilities of these parameters to identify nonsurgical bleeding in patients with penetrating injuries.

TEG normal ranges, obtained from Haemoscope Corp., are an R of 4 to 8 minutes, K within 0.5 minutes to 3.7 minutes, α-angle of 47 degrees to 74 degrees, and MA of 54 mm to 73 mm. The percentages of the patient population outside these normal ranges were 59%, 27%, 27%, and 56.8%, respectively, with abnormal R, α-angle, and MA values below the normal range and K values longer than normal, with few exceptions (Table 2). A shortened R time denotes a hypercoagulable status whereas reductions in α-angle and MA represent a hypocoagulable state. Regression analysis indicated that the MA values correlated with eventual transfusion requirements and platelet counts of patients (Fig. 1A and B). Patients with low MA values (<54 MA; $n = 23$) had significantly increased use of blood products and significantly

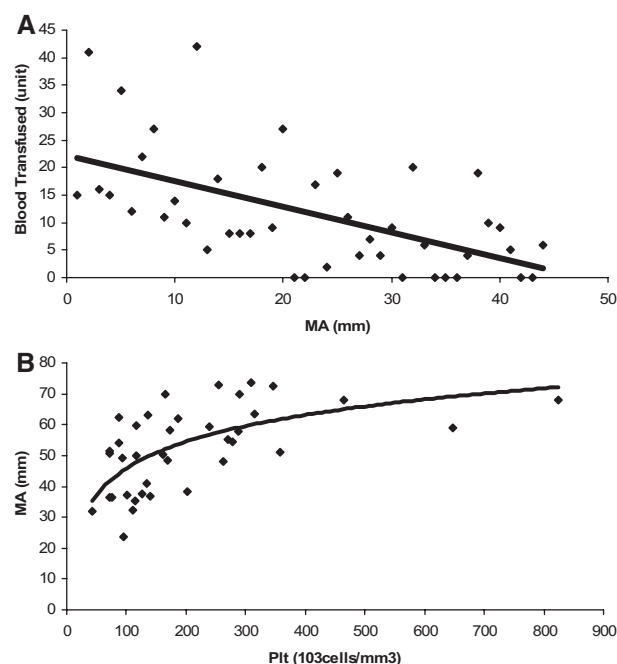


Fig. 1. (A) Correlation of TEG-MA with the blood product requirements of each patient ($r = 0.57$, $p < 0.001$). (B) Correlation of TEG-MA with patient platelet counts ($r = 0.61$, $p < 0.001$).

lower platelet counts (Table 2), whereas standard indicators of coagulability, including PT, PTT, and INR, exhibited no significant differences (Table 1). Hematocrit and platelet count were significantly decreased in patients with a low MA. Hematocrit was also significantly correlated to total blood product use ($p = 0.0024$). This relationship was expected, as hematocrit levels are a factor in the decision to transfuse patients, independent of coagulation status.

DISCUSSION

Our results indicate that there was a significant correlation between MA values and blood product use. As there was also a significant correlation between MA and platelet counts, this information could serve as a valuable indicator of hemostatic needs in trauma patients. These findings support results of previous work stating that the maximal clot strength and shear modulus were dependent on platelet functional status and were not affected by the fibrin polymerization process.¹³ Notably, MA provides information on both the number and functional status of platelets, unlike platelet count alone which does not reflect the condition of the platelets.

Because of the correlation between MA, eventual blood product use, and platelet counts, we propose that platelet deficiencies were a contributing factor to the coagulopathy in the trauma patients that received the most blood. Slight differences in platelet function were heavily reflected in MA, suggesting that both platelet function and platelet number were deficient in the patients studied.¹⁴

Physiologic measures (SBP, heart rate, BE, pH, and temperature) and hemostatic measurements (INR, PT, and

PTT) were not found to relate to subsequent transfusion requirements in the present study. Although PT and PTT are measures of clotting time that serve to identify abnormalities in clotting factors, these measures are unable to identify which portion of the clotting cascade is to blame for a coagulopathy.⁵ Through the use of TEG, a more specific diagnosis of this dysfunction may be made.

Reliable and early hemostatic information will help to guide physicians in evaluating the blood component needs of their patients. Thrombelastography was introduced to the medical field in 1947, but was rarely used until recently, as the development of disposable components, tissue activators, and computer software added to the speed and ease of use of the technology. If the capacity of the TEG is to be fully used, i.e., identifying abnormal clotting function even in the absence of excessive bleeding as well as during hemorrhage, it must be initiated early on. Models with a rapid turnaround time and reliable results are necessary if this method of diagnosis is to become widely adopted. New designs are currently being introduced to the market that will accomplish these goals. There have been reported issues of run-to-run variability with the current TEG equipment.¹⁵ The ROTEG, developed by Pentapharm Co. (Nairobi, Kenya), uses a ball-bearing system that reduces the impact of vibration or mechanical stress on the results.¹⁶

TEG measures the entire process of the clotting cascade, from initial clot formation through complete clot lysis.¹⁷ Currently, the initial results of a TEG are available in 10 minutes to 15 minutes, excluding fibrinolysis data, whereas PT and PTT, because of the logistical restraints of hospital laboratories, require 45 minutes to 60 minutes.⁸ Thus, information from an MA concerning platelet number/function is acquired within 10 minutes to 15 minutes, whereas a platelet count from the laboratory may not be available for another 20 minutes to 30 minutes. It has been shown that the use of tissue factor as an activator does not affect TEG results and will further reduce running time by 6 minutes to 8 minutes.

Algorithms designed and experimentally implemented during cardiopulmonary bypass have used TEG parameters to direct transfusion in the operating room.¹⁰ An abnormal R time, the time to clot initiation, relates to the concentration of clotting factor, and a reduced MA, maximal clot strength, indicates a deficiency in number and/or function of platelets. Platelet function and number affect the kinetics of clot formation and therefore are also reflected in the α -angle. Treatment based on these "decision trees" has resulted in significant reductions of 45% and 76% in blood product use.^{6,8,10}

Our conclusions based on the results of this study contradicted previous notions concerning the state of coagulopathy in trauma. This may be a result of several different aspects of our study. Whereas trauma patients analyzed by Schreiber et al.⁵ and Kaufmann et al.¹ were determined to be hypercoagulable at admission, the patients in our study exhibited indices of hypocoagulability. These differences in classification of clotting deficiencies may be attributed to the mode of injury, our study analyzing those patients with pen-

etrating injuries, whereas Schreiber and Kaufmann evaluated those with injuries caused by blunt trauma.^{1,5} However, Faringer et al. showed that the magnitude of blood loss rather than the mode of injury was the primary indicator of coagulopathy incidence during transfusion.¹⁸

Other reasons for the differences between our study and previous work may be related to interpretation of the TEG. In the study by Schreiber et al.⁵ hypercoagulability was defined as an increase in the R-time, representing an earlier onset of clot formation. By this definition, 62% of their patients were hypercoagulable in the absence of α -angle and MA changes. We found a similar incidence of shortened R-time (59%), however, there were significant reductions in α -angle and MA. In the study by Kaufmann and coworkers,¹ their criteria were changes in two or more TEG parameters. Ten percent of their patients who were diagnosed as hypocoagulable had severe injuries and required transfusions. Differences in interpretation of the TEG between studies seem to be a factor in the determination of the coagulation status. In the present study, we related MA to blood product requirements, suggesting this TEG parameter may be a principal indicator of hypocoagulation.

Whereas only male patients were included in our study, other studies have included analysis of both male patients and female patients. Schreiber et al.⁵ illustrated that female patients exhibit greater hypercoagulability after blunt trauma than male patients. Thus, this feature may have provided further grounds for differences between our studies. Times between admission and TEG readings differed between the study by Schreiber et al. (17.3 hours $\pm$ 5.7 hours) and our own (6 hours $\pm$ 5.7 hours; median, 4.5 hours), as well. Because of the extensive variability in hemostatic status over time, this time variation may have been a large factor in the subsequent conflict of results.

In the study by Kaufmann et al.,¹ those patients with the most severe injuries (mean ISS, 29) were hypocoagulable, whereas those with less severe injuries (mean ISS, 13) were hypercoagulable by TEG parameters. The mean ISS of the patients in our study was 21. Therefore, the greater severity of injury in our study may have played a role in the differences in coagulopathy profiles compared with previous studies.

A problem faced by the military physicians caring for coagulopathic patients in combat situations has been the lack of platelet units available for transfusion. The initiation of clotting is maintained at normal to above normal rates because of the early transfusion of plasma, while clot strength remains low. Platelets, having a short 5-day shelf life, are in low supply in the CSHs because of difficulties in transport and storage.¹⁹ Therefore, in CSHs and for the patients in this study, fresh whole blood units were transfused to supply platelets. According to the results obtained in this study, many of the patients were lacking functional platelets, indicating that alterations in transfusion practice, as guided by TEG results, may aid in the correction of these coagulopathies early in the course of care. A TEG-based algorithm

directing treatment could enhance the accuracy with which physicians prescribe blood components.

When analyzing the TEG results of the CSH patients, the MA values were low in 57% of the patients and the R-times were below the normal range in 59%. This indicates a rapid onset of clotting producing a low-strength clot. The treatment, had these been cardiopulmonary bypass patients under a TEG algorithm-directed transfusion protocol, would often have included transfusion of platelet units.⁸ The MA significantly correlated with platelet counts and subsequent blood product use, further supporting the recommendation for platelet replacement. The lack of correlation between PT, PTT, and INR with either TEG parameters or blood product use illustrates the diagnostic inadequacy of these tests for our patient population.

There were a number of limitations in the present study. First, it was a retrospective study from a single facility in a difficult working environment. Second, was the timing of TEG measurements that averaged 6 hours after admission, in contrast to standard coagulation measures that were obtained immediately at admission. However, this delay is still less than that reported in earlier studies of trauma patients.⁵ Third, the delay in the measurement of TEG means that some of the patients may have received blood products before the measurement which could have affected the results. The timing of the TEG relative to the administration of blood products was not available from the data. A fourth limitation was the use of total blood products. We have presented the total number of units infused of various blood products (packed red blood cells, fresh frozen plasma, and fresh whole blood) irrespective of the effect of individual components on clotting. Future efforts should be directed at relating specific changes in components of the TEG profile with the type of blood component required to correct the abnormality.

Decisions concerning blood transfusions are often made empirically in the emergency and operating room because of the lack of a fast and reliable method to test a patient's coagulation status.²⁰ A rapid TEG would provide information upon which physicians could develop a transfusion protocol that would best suit each patient's hemostatic needs. In addition, presently available data, such as platelet counts and hematocrit, with appropriate interpretation may support TEG findings to provide adequate guidelines. The risk of viral infection, immunosuppression, and microcirculatory damage combined with the high costs of blood transfusions warrant the development of such a system.^{4,20,21}

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