CLINICAL ARTICLE

Thromboelastography Predictive of Death in Trauma Patients

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Objectives: To determine if thromboelastography (TEG) is predictive of patient outcomes following traumatic injury.

Methods: A retrospective review of 131 patients with pelvic trauma admitted to a Level II trauma center was conducted over four years from 1 January 2009 to 31 December 2012. Patients were identified retrospectively from a prospectively collected database of acute pelvic trauma ($n = 372$). Eligible patients were identified from billing/coding data as having fractures of the acetabulum, iliac wing or sacral alae. Patients with incomplete TEG data were excluded ($n = 241$), as were patients with pathological fractures. TEG clotting variables and traditional clotting variables were recorded.

Results: Evaluation of TEG data revealed 41 patients with abnormal clotting times (TEG R). TEG R > 6 was an independent risk factor for death (OR, 16; 95%CI 5.4–53; $P = 0.0001$). The death rate was 52% in patients with TEG R values ≥ 6 ($n = 13/25$). There was no significant association between traditional clotting markers and death rate.

Conclusions: TEG reaction time value, representing the time of initial clot formation, was the only hematologic marker predictive of mortality in patients with pelvic trauma. Delay in reaction time was associated with a significantly increased death rate, independent of injury severity. The death rate association was not observed with traditional markers of clotting. Future prospective studies may be warranted to determine the presentation and significance of TEG abnormalities when resuscitating patients with orthopaedic trauma.

Key words: Coagulopathy; Mortality; Thromboelastography

Introduction

The initial workup following a traumatic incident has important clinical correlations that affect the course of treatment and recovery of the patient. Historically, the prothrombin time (PT), partial thromboplastin time (PTT) and international normalized ratio (INR) have been the variables of choice when evaluating the blood content and coagulation state following sustained bleeding. The PT measures the

extrinsic clotting pathway, which is mediated by factors I, II, V, VII and X. The PTT measures the intrinsic clotting pathway, which is mediated by factors I, II, VIII, IX, XI and XII¹. However, these values do not include measures of platelet aggregation or combined extrinsic/intrinsic function. Recently, an old test, thromboelastography (TEG), has been reexamined for its utility in the analysis of several aspects of clot formation and strength^{2–5}. TEG has been available since the 1950's and is

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Fig. 1 Thromboelastography tracing indicating the values provided by the test⁶. α , Alpha angle; K, clot formation speed; MA, maximum angle; R, reaction time.

the only available test that measures the entire clotting cascade, allowing for a profile of the extrinsic and intrinsic arms of the coagulation cascade as well as platelet function. TEG offers a comprehensive bedside analysis of a patient's coagulation state. This information has the potential to guide treatment plans and lead to better patient outcomes and shorter, less expensive hospital stays.

The following four TEG values can be obtained from the blood test (Fig. 1)⁶: reaction time (R), Alpha Angle, K and Maximum Angle (MA). The R value measures the time the first clot takes to form. K measures the speed of clot formation by measuring the time from the end of R until the clot reaches 20 mm. The alpha angle is calculated by taking the tangent of the curve produced to reach the K value and is another measure of clot formation speed. The MA value is a measure of the strength of the clot^{7,8}.

The purpose of this study was to identify whether coagulopathy predicts perioperative morbidity and mortality in patients with pelvic trauma. We hypothesized that TEG values would predict morbidity and mortality. This information could be valuable to clinicians attending patients with pelvic trauma as well as general trauma patients.

Patients and Methods

Upon admission, patients were entered into a prospective database and the data were later retrospectively reviewed following Institutional Review Board approval. The study was a retrospective review of a prospectively collected database of consecutive patients ($n = 372$) with acute pelvic trauma admitted to a Level II trauma center from 1 January 2009 to 31 December 2012. Eligible patients were identified from billing/coding data as having fractures of the acetabulum, iliac wing or sacrum or pelvic polytrauma. Patients with isolated pubic ramus fractures were excluded, as were patients who had not undergone TEG evaluation ($n = 241$). Patients with pathological fractures or systemic polytrauma (visceral organ injury, closed head injury, etc.) were excluded. TEG, PT, PTT and INR are ordered routinely on trauma patients on admission in our

institution. Injury severity score was also calculated from review of the data. Records were reviewed retrospectively by an observer blinded to the coagulation data. Logistic regression analyses were performed to determine the association between TEG statistics, injury severity score and traditional coagulation tests.

Results

Among the eligible 131 pelvic trauma patients, 70 were male (mean age, 47.9 years) and 61 female (mean age, 55.7 years). The mean injury severity score (ISS) was 25.4. The mechanisms of injury included motor vehicle collision ($n = 66$), fall ($n = 36$), pedestrian struck ($n = 23$), gunshot ($n = 5$), and falling object ($n = 1$). Twenty-six patients required surgical stabilization. The mean clotting time (R) was 4.8 mins (standard deviation [SD], 1.8; normal, 3.8–9.8 mins), mean clot kinematics (K) 2.0 mins (SD, 1.8; normal, 0.7–3.4 mins), mean fibrinogen (Alpha) angle 63° (SD, 13; normal, 48° – 78°) and mean clot strength (MA) 63 mm (SD, 13; normal, 49.7–72.7 mm)⁷. According to the TEG data, 41 patients had abnormal clotting times (TEG R), 16 had abnormal clot kinematics (TEG K), 25 had abnormal fibrinogen angles (TEG alpha) and 56 had abnormal clot strength (TEG MA). Several forms of complications and adverse outcomes were encountered in these patients, including death ($n = 18$), massive transfusion ($n = 19$), pulmonary embolism ($n = 5$), deep venous thrombosis ($n = 1$), myocardial infarction ($n = 1$) and pelvic hematoma ($n = 84$) (Table 1).

There was no statistically significant association between ISS and any TEG values (Spearman's rho, $P > 0.05$). Increasing ISS was found to be associated with an increased risk of pulmonary embolism, massive transfusion and hematoma. TEG R ≥ 6 was found to be an independent risk factor for death (odds ratio [OR] 16; 95% CI 5.4–53; $P = 0.0001$). The death rate was 52% in patients whose TEG R values were ≥ 6 ($n = 13/25$). Using a logistic model of death including all variables (PT, INR, PTT, TEG R, TEG K, TEG Alpha, TEG MA and ISS), TEG R (OR per patient 1.33; 95% CI 1.02–1.73; $P = 0.0358$) was an independent predictor of death (area under the curve 0.841) (Fig. 2). PTT was abnormally high in most patients who died ($n = 12/18$) but was not predictive of death ($n = 12/39$).

Discussion

The data collected indicate that TEG, specifically the R value, predicts mortality independent of traditional coagulopathy tests or injury severity score. TEG R time ≥ 6 is associated with increased clotting time. The normal TEG values used as a standard originated from a study using healthy volunteers⁷, which may indicate why a value determined to be normal ($R = 6$) is clinically associated with increased risk of mortality. Unlike the healthy volunteers, the patients in this study presented with active hemorrhage causing their high normal values to denote a risk of adverse outcomes. Aggressive treatment of patients with pelvic trauma presenting with prolonged TEG R time should be initiated as soon as possible to attempt to prevent mortality and increase the likelihood of

TABLE 1 Complications in relation to TEG values (%)

Complications	Low				Normal				High			
	R	K	α	MA	R	K	α	MA	R	K	α	MA
Hematoma	15.3	0	10.7	16.8	46.6	51.1	48.9	32.8	4.6	14.5	6.1	19.8
DVT	0	0	0	0	0.8	0.8	0.8	0.8	0	0	0	0
PE	1.5	0	0	0.8	2.3	3.1	3.1	0	0	0.8	0.8	3.1
Massive transfusion	3.8	0	6.1	6.9	9.2	8.4	8.4	6.1	3.1	6.9	0.8	3.1
Mortality	3.1	0	5.3	6.1	9.2	8.4	7.6	6.1	2.3	5.3	0.8	2.3
Complications	16.0	0	10.7	17.6	50.4	55.0	52.7	35.1	4.6	13.7	6.1	19.8
No complications	8.4	0	0	0	22.1	30.5	27.5	22.9	0	0	3.1	7.6

Note: Ranges for low, normal and high TEG values as determined by Scarpelini *et al.*⁷ based on TEG of healthy volunteers. α , alpha angle; DVT, deep venous thrombosis; K, clot formation speed; MA, maximum angle; PE, pulmonary embolism; R, reaction time.

positive patient outcomes. It is also worth noting that although an abnormally low R time ($R < 3.8$)⁸ was not found to be correlated with mortality (Table 2), patients with abnormally low R times had a greater mortality than those whose values were in the moderate range. Fig. 2 reflects this observation by showing the increased mortality at both extremes of this measurement. A short clotting time (low R) for example, may represent a disseminated intravascular coagulation state characterized by hypercoagulability and simultaneous fibrinolysis and hemorrhage; end organ injury can occur in this state. TEG has been shown to be able to diagnose and predict the likelihood of a patient developing a hyper-coagulable state^{9–12}, which corresponds with the noted increase in mortality in this study¹³.

When comparing the TEG data with the traditional markers of coagulation, TEG is able to provide essential information on patients' hemostatic state much quicker, namely, at the bedside. The increased speed of the test is attributable to the ability to perform the analysis in the trauma resuscitation bay rather than having to send the sample to the laboratory to be analyzed. Increased PTT was also found to be loosely associated with mortality but lacked the ability to predict death that was found for TEG R.

Fig. 2 Graph showing relationship between TEG R and mortality rate.

To our knowledge, this study is one of the first to report TEG values in patients with orthopaedic trauma and to identify a clinical association in these patients. Previous studies have demonstrated that coagulopathy is a leading cause of death in patients with orthopaedic trauma as well as in general patients; thus, the management of hemostatic imbalances following a traumatic incident is vital for the survival of these patients¹⁴. Abnormal TEG values following orthopaedic trauma have been associated with poor outcomes such as the development of deep venous thrombosis in patients with proximal femoral fractures that require surgical stabilization¹⁵. TEG has also been shown to predict the occurrence of pulmonary emboli in trauma patients¹⁶ and has been used to diagnose cases of acute ischemic strokes¹⁷ and hypo- and hyper-coagulability induced by sepsis¹⁸. TEG-directed aggressive administration of blood products based on standing protocols based on TEG data has been shown to produce positive patient outcomes when used in patients who require transfusions following trauma^{19–21}. TEG has also recently been utilized to guide transfusions for injured soldiers on the battlefield by the USA Military²² and the UK Defense Medical Service²³. Previous studies have compared TEG with traditional coagulation tests and found that the cost, speed and treatment-guiding ability of these tests merits replacing the traditional tests with TEG in the emergency department^{24–26}. This supports the contention that aggressive TEG-guided treatment of trauma patients provides an efficient means of managing traumatic injuries at the bedside. A recent study in which TEG tests were performed upon entry of pediatric patients with trauma to a

TABLE 2 Relationship between mortality rate and TEG R values

R value	Death (cases)	Mortality (%)
<3.8 (n = 36)	4	11.1
<6 (n = 106)	5	4.7
≥6 (n = 25)	13	52.0

trauma service found a similar correlation between mortality and both TEG values and traditional coagulation markers²⁷. That study was conducted on a very specific and smaller group of patients; however, the results obtained from it support our contention that there is an association between TEG and mortality rates and that early TEG guidance is critical in the initial work-up of trauma patients. Because of the speed with which information from the test can be obtained, TEG has also been utilized in the evaluation of orthopaedic surgical patients²⁸ and to monitor coagulation changes intraoperatively²⁹. TEG has been used to compare the coagulation ability of salvaged blood with that of circulating blood while transfusing intraoperatively; it was found that the coagulation abilities of the recovered blood were significantly inferior to that of the circulating blood³⁰.

Limitations of this study include the retrospective nature of the analysis. Retrospective studies may be more susceptible to selection bias. Additionally, many otherwise eligible patients attending our center did not undergo TEG tests because of the inconsistent utilization of TEG by the trauma service. It is also possible that an unknown confounder, such as a systemic inflammatory response syndrome, underlies the observed correlation. Therefore, it is possible that the coagulopathy is not the cause of death but a side effect of another, fatal condition. Precise information on the cause of death, such as exsanguination or myocardial infarction, is also unavailable because the patients who died did not undergo autopsies. There are many causes of death or complications in trauma patients other than coagulopathy. Other confounders of mortality include patient age, injury severity score and time between sustaining trauma and treatment. Additionally, it is unknown whether the findings would be the same in patients with different fracture types (other than pelvic trauma) or other types of trauma such as visceral organ injury. Most patients who died or experienced

complications had normal TEG values. However, patients with TEG abnormalities had a disproportionately high incidence of perioperative morbidity. The precise cause of death was not recorded in all cases. Additionally, due to the retrospective nature of the database, some possibly relevant patient and clinical variables, such as the precise fracture type and mechanism of injury, were unknown. TEG findings upon hospital admission are dependent, to some extent, upon time from injury and extent of in-field resuscitation. Another limitation is that some medical complications may be associated with other complications that could ultimately lead to death. Serial TEG on hospitalized patients with pelvic trauma may be a better indicator of post-injury coagulopathy because the coagulopathy cascade may occur up to several days after admission for trauma.

Based on our findings, we conclude that future prospective studies may be warranted to determine if TEG better improves the outcomes of resuscitation of pelvic trauma patients than traditional clotting variables. If TEG data were collected as a standard practice among all arriving orthopaedic trauma patients, there would be a more comprehensive data-bank from which correlations between abnormal TEG values and patient outcomes could be better examined. Also the Coagulation Index could be examined to incorporate that information into prediction of individual patient risks.

Coagulation profiles are important in critically injured patients. The results of this study suggest that TEG testing can predict the probability of mortality in patients with pelvic trauma presenting with TEG R values of 6 or greater. Based on these findings, we recommend that TEG be used to screen all patients with pelvic trauma to evaluate for coagulopathy. Early identification and correction of coagulopathy can potentially improve patient outcomes and decrease mortality rates.

References

- Kamal A, Tefferi A, Pruthi R. How to interpret and pursue an abnormal prothrombin time, activated partial thromboplastin time, and bleeding time in adults. *Mayo Clin Proc*, 2007, 82: 864–873.
- Wozniak D, Adamik B. Thromboelastography. *Anestezjol Intens Ter*, 2011, 43: 244–247.
- Campion EM, Mackersie RC. Recent developments in the assessment of the multiply injured trauma patient. *Curr Opin Crit Care*, 2014, 20: 620–625.
- Brummel-Ziedins KE, Wolberg AS. Global assays of hemostasis. *Curr Opin Hematol*, 2014, 21: 395–403.
- Palmer L, Martin L. Traumatic coagulopathy—part 1: pathophysiology and diagnosis. *J Vet Emerg Crit Care (San Antonio)*, 2014, 24: 63–74.
- Kroll M. Thromboelastography: theory and practice in measuring hemostasis. *Clin Lab News*, 2010, 36: 8–10.
- Scarpelini S, Rhind SG, Nascimento B, *et al*. Normal range values for thromboelastography in healthy adult volunteers. *Braz J Med Biol Res*, 2009, 42: 1210–1217.
- Karon BS. Why is everyone so excited about thromboelastography (TEG)? *Clin Chim Acta*, 2014, 436: 143–148.
- Cotton BA, Harvin JA, Kostousov V, *et al*. Hyperfibrinolysis at admission is an uncommon but highly lethal event associated with shock and prehospital fluid administration. *J Trauma Acute Care Surg*, 2012, 73: 365–370.
- Kostousov V, Wang YW, Cotton BA, Wade CE, Holcomb JB, Matijevic N. Influence of resuscitation fluids, fresh frozen plasma and antifibrinolytics on fibrinolysis in a thromboelastography-based, in-vitro, whole-blood model. *Blood Coagul Fibrinolysis*, 2013, 24: 489–497.
- Jacob M, Kumar P. The challenge in management of hemorrhagic shock in trauma. *Med J Armed Forces India*, 2014, 70: 163–169.
- Gonzalez E, Moore EE, Moore HB, Chapman MP, Silliman CC, Banerjee A. Trauma-induced coagulopathy: an institution's 35 year perspective on practice and research. *Scand J Surg*, 2014, 103: 89–103.
- Pawelczyk NS, Huby Mdel P, Salisbury JR, *et al*. Association of hemodilution and blood pressure in uncontrolled bleeding. *J Surg Res*, 2013, 184: 959–965.
- Maegle M, Schöchl H, Cohen MJ. An update on the coagulopathy of trauma. *Shock*, 2014, 41 (Suppl. 1): 21–25.
- Wilson D, Cooke EA, McNally MA, Wilson HK, Yeates A, Mollan RA. Changes in coagulability as measured by thromboelastography following surgery for proximal femoral fracture. *Injury*, 2001, 32: 765–770.
- Cotton BA, Minei KM, Radwan ZA, *et al*. Admission rapid thromboelastography predicts development of pulmonary embolism in trauma patients. *J Trauma Acute Care Surg*, 2012, 72: 1470–1475.
- Rowe AS, Greene CL, Snider CC, *et al*. Thromboelastographic changes in patients experiencing an acute ischemic stroke and receiving alteplase. *J Stroke Cerebrovasc Dis*, 2014, 23: 1307–1311.
- Muller MC, Meijers JC, Vroom MB, Juffermans NP. Utility of thromboelastography and/or thromboelastometry in adults with sepsis: a systematic review. *Crit Care*, 2014, 18: R30.
- Johansson PI, Sorensen AM, Larsen CF, *et al*. Low hemorrhage-related mortality in trauma patients in a Level I trauma center employing transfusion packages and early thromboelastography-directed hemostatic resuscitation with plasma and platelets. *Transfusion*, 2013, 53: 3088–3099.
- Meyer AS, Meyer MA, Sørensen AM, *et al*. Thromboelastography and rotational thromboelastometry early amplitudes in 182 trauma patients with clinical suspicion of severe injury. *J Trauma Acute Care Surg*, 2014, 76: 682–690.

- 21.** Feinman M, Cotton BA, Haut ER. Optimal fluid resuscitation in trauma: type, timing, and total. *Curr Opin Crit Care*, 2014, 20: 366–372.
- 22.** Spinella PC, Holcomb JB. Resuscitation and transfusion principles for traumatic hemorrhagic shock. *Blood Rev*, 2009, 23: 231–240.
- 23.** Keene DD, Nordmann GR, Woolley T. Rotational thromboelastometry-guided trauma resuscitation. *Curr Opin Crit Care*, 2013, 19: 605–612.
- 24.** Holcomb JB, Minei K, Scerbo ML, *et al.* Admission rapid thromboelastography can replace conventional coagulation tests in the emergency department: experience with 1974 consecutive trauma patients. *Ann Surg*, 2012, 256: 476–486.
- 25.** Martini WZ, Cortez DS, Dubick MA, Park MS, Holcomb JB. Thromboelastography is better than PT, aPTT, and activated clotting time in detecting clinically relevant clotting abnormalities after hypothermia, hemorrhagic shock and resuscitation in pigs. *J Trauma*, 2008, 65: 535–543.
- 26.** 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: 266–275.
- 27.** Vogel AM, Radwan ZA, Cox CS Jr, Cotton BA. Admission rapid thromboelastography delivers real-time “actionable” data in pediatric trauma. *J Pediatr Surg*, 2013, 48: 1371–1376.
- 28.** Topçu I, Civi M, Ozturk T, *et al.* Evaluation of hemostatic changes using n thromboelastography after crystalloid or colloid fluid administration during major orthopedic surgery. *Braz J Med Biol Res*, 2012, 45: 869–874.
- 29.** Horlocker TT, Nuttall GA, Dekutoski MB, Bryant SC. The accuracy of coagulation tests during spinal fusion and instrumentation. *Anesth Analg*, 2001, 93: 33–38.
- 30.** Oswald E, Streif W, Hermann M, Hengster P, Mittermayr M, Innerhofer P. Intraoperatively salvaged red blood cells contain nearly no functionally active platelets, but exhibit formation of microparticles: results of a pilot study in orthopedic patients. *Transfusion*, 2010, 50: 400–406.