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Rotational thromboelastometry thresholds for patients at risk for massive transfusion

Gregory R. Stettler, MD,[a] *Ernest E. Moore, MD,*[b,*] *Geoffrey R. Nunns, MD,*[a] *Jim Chandler,*[b] *Erik Peltz, DO,*[a] *Christopher C. Silliman, MD, PhD,*[c,d] *Anirban Banerjee, PhD,*[a] *and Angela Sauaia, MD, PhD*[a,e]

[a] *Department of Surgery, University of Colorado, Aurora, Colorado*
[b] *Department of Surgery, Denver Health Medical Center, Denver, Colorado*
[c] *Department of Pediatrics, University of Colorado, Aurora, Colorado*
[d] *Bonfils Blood Center, Denver, Colorado*
[e] *University of Colorado School of Public Health, University of Colorado, Aurora, Colorado*

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ABSTRACT

Background: Goal-directed hemostatic resuscitation based on thrombelastography has a survival benefit compared to conventional coagulation assays. While thrombelastography transfusion thresholds for patients at risk for massive transfusion (MT) have been defined, similar cutoffs do not exist for the other commonly used viscoelastic assay, rotational thromboelastometry (ROTEM). The purpose of this study was to develop ROTEM blood product thresholds in patients at risk for MT.

Methods: ROTEM was assessed in trauma activation patients admitted from 2010 to 2016 ($n = 222$). Receiver operating characteristic curve analyses were performed to test the predictive performance of ROTEM measurements in patients requiring MT. The Youden Index defined optimal thresholds for ROTEM-based resuscitation.

Results: Patients who required MT ($n = 37$, 17%) were more severely injured. EXTEM clotting time (CT) was longer in patients with MT compared to non-MT (87 *versus* 64 s, $P < 0.0001$). EXTEM angle was shallower in MT patients compared to non-MT (54° *versus* 69°, $P < 0.0001$). Clot amplitude after 10 min (CA10) was less in MT compared to non-MT patients (30.5 *versus* 50 mm, $P < 0.0001$). Clot lysis index 60 min (CLI60) was lower in patients who had MT than non-MT (47 *versus* 94%, $P = 0.0006$). EXTEM CT yielded an area under the receiver operating characteristic curve (AUROC) = 0.7116 and a cut point of >78.5 s. EXTEM angle had an AUROC = 0.865 and a cut point of <64.5°. EXTEM CA10 had an AUROC = 0.858, with a cut point of <40.5 mm. CLI60 had an AUROC = 0.6788 with a cut point at <74%.

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* *Corresponding author*. Department of Surgery, Denver Health Medical Center, 655 Bannock StreetDenver, CO 80203. Tel.: +1 303 724 2685; fax: +1 303 720 2682.
E-mail address: ernest.moore@dhha.org (E.E. Moore).

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Conclusions: We have identified ROTEM thresholds for transfusion of blood components in severely injured patients requiring an MT. Based on our analysis, we propose plasma transfusion for EXTEM CT > 78.5 s, fibrinogen for angle <64.5°, platelet transfusion for CA10 < 40.5 mm, and antifibrinolytics for CLI60 < 74%.

Introduction

Uncontrolled hemorrhage is the leading cause of preventable death following trauma, accounting for up to 40% of deaths.[1] An endogenous trauma-induced coagulopathy accounts for most of these hemorrhagic deaths and is a multifocal process attributed to reduced thrombin generation, fibrinogen depletion, platelet dysfunction, and systemic hyperfibrinolysis.[2-5]

Half of deaths from acute blood loss occur within the first 2 h after injury, and hemorrhage accounts for the vast majority of deaths within the first 24 h.[6] Reliable objective means of early recognition and targeted transfusion interventions are the key to successful management of life-threatening trauma-induced coagulopathy.

Massive transfusion protocols (MTPs) offer a proven benefit in resuscitation of patients in hemorrhagic shock. Much effort has been directed to identifying the ideal ratio of blood products in resuscitation strategies.[6,7] Traditional interventions have been guided by conventional coagulation assays (CCAs), such as international normalized ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen level, and platelet count. Our group has shown that a goal-directed, thrombelastography (TEG)-guided MTP improves survival as compared with MTP guided by CCAs. Furthermore, these results were achieved with the transfusion of less plasma and platelets during the early phases of resuscitation.[8]

We have defined optimal transfusion thresholds using TEG for patients at risk for massive transfusion (MT) as an activated clotting time (ACT) < 128 s, angle <65°, a maximum amplitude (MA) < 55 mm, and lysis 30 min after achieving MA (LY30) >5%.[7] However, these thresholds are not directly translatable for use in rotational thromboelastometry (ROTEM), another commonly used viscoelastic assay because of differences in instrumentation and reagents.[9] Therefore, we hypothesize that we can identify ROTEM measurements that indicate the need for MT in injured patients using ROTEM and thresholds for specific blood component therapy in these high-risk patients.

Methods

Study design

This is an analysis of prospectively collected data from our Trauma Activation Protocol registry, which includes consecutive adult (age ≥ 18 y old) patients who met criteria for the highest level of trauma team activation at the Denver Health Medical Center, an American College of Surgeons-verified and state-certified level 1 trauma center affiliated with the University of Colorado Denver and were at risk for MT. Exclusion criteria were unsalvageable injuries (defined by patients in asystole at emergency department arrival), isolated gunshot wounds to the head, pregnancy, documented chronic liver disease, or a known coagulation disorder.

The studies contributing to this database were approved by the Colorado Multiple Institution Review Board and performed under a waiver of consent. Trained research professional assistants performed all viscoelastic assays within 1-h post-injury. Clinicians were blinded to these research data. TEGs were ordered at the discretion of the care team and processed in the hospital clinical laboratory to guide resuscitation in injured patients.

The transfusion of products other than red blood cells during this period was guided by rapid thrombelastography (rTEG) criteria, as previously described.[8,10] The primary endpoint of this study was MT, defined as >10 units of red blood cells or death in first 6 h from injury based on findings previously published by our group.[11]

TEG is used at our institution and more commonly in the United States, while ROTEM is used widely in European centers.[9] Although the technologies and reagents are somewhat similar, the measurements reported are not the same and cannot be generalized from one instrument to the other.[12]

Rotational thromboelastometry

ROTEM was performed on whole blood collected in vacuum tubes with citrate added to prevent clotting before the analysis. The specific ROTEM assays used were EXTEM (activated with tissue factor), FIBTEM (activated similar to EXTEM but with cytochalasin D to inhibit the contribution of platelets to the clot),[13] and APTEM, which is a modified EXTEM, in which aprotinin inhibits plasmin *in vitro* if systemic fibrinolysis is present.[14] ROTEM tests yield the following variables that were used to assess the dynamic process of clot formation and breakdown in this study: time to clot initiation (clotting time [CT, s]), dynamics of clot formation (angle [degrees] and clot formation time [CFT, s]), clot strength (maximum clot formation [MCF, mm] and clot amplitude after 10 min [CA10, mm]), and fibrinolysis (clot lysis index at 30 min [CLI30, %] and 60 min after CT [CLI60, %]).[14] Prolonged clot initiation is an indication for plasma and reflected by EXTEM CT. Abnormal dynamics of clot formation is an indication for fibrinogen products and reflected by EXTEM CFT, EXTEM angle, FIBTEM angle, FIBTEM MCF, and FIBTEM CA10. Low clot strength is an indication for platelets and reflected by EXTEM CA10 and EXTEM MCF. Increased fibrinolysis is an indication for antifibrinolytics and reflected by EXTEM CLI30 and CLI60. Clinicians based blood product transfusions on clinical rapid TEG and were blinded to ROTEM values.

Rapid thrombelastography

Thrombelastography (TEG-5000 analyzer; Haemonetics Corp, Stoughton, MA) was performed on whole blood collected in