Journal of Surgical Research **156,** 133–138 (2009)
doi:10.1016/j.jss.2009.03.046

Noncitrated Whole Blood Is Optimal for Evaluation of Postinjury Coagulopathy With Point-of-Care Rapid Thrombelastography[1]

Jeffry L. Kashuk, M.D.,*,[2] Ernest E. Moore, M.D.,* Tuan Le, M.D.,† Jerry Lawrence, B.A.,* Michael Pezold, B.A.,* Jeffrey L. Johnson, M.D.,* Clay C. Cothren, M.D.,* Walter L. Biffl, M.D.,* Carlton Barnett, M.D.,* and Allison Sabel, M.D., Ph.D., M.P.H.‡,§

*Department of Surgery, †Department of Laboratory Medicine, ‡Department of Patient Safety and Quality, and §Department of Biostatistics and Informatics, Denver Health Medical Center, University of Colorado at Denver, Denver, Colorado

Submitted for publication January 8, 2009

Introduction. **Progressive postinjury coagulopathy has become the fundamental rationale for damage control surgery, and the decision to abort operative intervention must occur prior to overt laboratory confirmation of coagulopathy. Current coagulation testing is most commonly performed for monitoring anticoagulation therapy, the results are delayed, and the applicability of these tests in the trauma setting is questionable. Point-of-care (POC) rapid thrombelastography (r-TEG) provides real time analysis of thrombostatic function, which may allow for accurate, goal directed therapy. The test differs from standard thrombelastography (TEG) because the clotting process and subsequent analysis is accelerated by the addition of tissue factor to the whole blood sample, but is limited by the requirement that the analysis be performed within 4 min of blood draw to prevent clot formation. Consequently, citrated specimens have been proposed to obviate this time limitation. We hypothesized that the speed of r-TEG analysis following tissue factor addition to citrated blood might compromise accurate determinations compared with noncitrated whole blood. Additionally, we sought to compare the use of r-TEG with conventional coagulation tests in analysis of postinjury coagulopathy.**

Methods. **We conducted a retrospective study of severely injured patients entered into our trauma database between January and June 2008 who were at risk for postinjury coagulopathy. Patients needed simultaneous conventional coagulation (INR, fibrinogen, platelet count) and r-TEG specimens with either fresh or citrated whole blood for inclusion in the study. κ-Statistics were used to determine the agreement between the tests in predicting hypocoagulability. McNemar's χ^2 tests were used to compare theoretical blood product administration between r-TEG and conventional coagulation tests for noncitrated specimens. Therapeutic transfusion triggers were: INR (>1.5) and r-TEG ACT (>125 s) for FFP administration; fibrinogen (<133 mg/dL) and α-angle ($<63^\circ$) for cryoprecipitate; and platelet count (<100 K) and maximum amplitude (MA) (<52 mm) for aphaeresis platelets. Statistical significance was established as $P < 0.05$ using two-sided tests.**

Results. **Forty-four patients met the inclusion criteria. κ-Values (correlation) were higher in noncitrated versus citrated specimens for all comparisons between conventional and r-TEG tests, indicating better performance of r-TEG with the noncitrated specimens. FFP would have been administered to significantly more patients based on conventional transfusion triggers (61.5% by INR transfusion triggers versus 26.9% by r-TEG-ACT triggers, $P = 0.003$). There was no statistically significant difference in potential cryoprecipitate or aphaeresis platelet administration.**

Conclusion. **POC r-TEG is superior when performed with uncitrated versus citrated whole blood for evaluation of postinjury coagulation status. As a real time measure of total thrombostatic function, our preliminary data suggest that r-TEG may effectively guide transfusion therapy and result in reduced FFP administration compared with conventional coagulation tests.**

Key Words: **thrombelastography; trauma; coagulopathy; goal directed therapy; thrombin release; hypocoagulability; citrate; whole blood.**

[1] Presented at the combined AAS-SUS Academic Surgical Congress, Ft. Myers, Florida, February 5, 2009.

[2] To whom correspondence and reprint requests should be addressed at Department of Surgery, Denver Health Medical Center, University of Colorado School of Medicine, 777 Bannock Street, MC 0206, Denver, CO 80204. E-mail: jeffry.kashuk@dhha.org.

0022-4804/09 $36.00

INTRODUCTION

Progressive postinjury coagulopathy is the fundamental rationale for damage control surgery, and the decision to abort operative intervention must occur prior to overt laboratory confirmation of coagulopathy [1, 2]. Unfortunately, current laboratory coagulation testing was originally designed for diagnosis and treatment of hemophilia [3], and later applied to monitoring of anticoagulant therapy. These tests, however, were not intended to be used for evaluating surgical bleeding or postinjury coagulopathy. When applied to the trauma setting, the results are delayed, and their applicability and accuracy in reflecting the current coagulation state of the patient have been questionable [4].

The purpose of this study was to perform a limited, pilot investigation to evaluate the potential usefulness of rapid thrombelastography (r-TEG), an emerging technology that allows "goal directed therapy" of specific coagulation aberrations in patients at risk for postinjury coagulopathy. r-TEG differs from conventional TEG because tissue factor is added to the noncitrated whole blood specimen, resulting in an accelerated reaction, but is limited by the requirement that the analysis be performed within 4 min of blood draw to prevent clot formation. Consequently, citrated specimens have been proposed to obviate this time limitation. We hypothesized that the speed of r-TEG analysis following tissue factor addition to citrated blood might compromise accurate determinations compared with noncitrated whole blood specimens, and therefore sought to compare analyses between citrated and whole blood specimens. We further theorized that accurate POC monitoring and timely treatment of postinjury coagulopathy could result in a reduction of blood product use. Accordingly, we also sought to compare transfusion triggers and theoretical blood product administration if monitoring and treatment were based upon r-TEG or conventional coagulation tests.

METHODS

A retrospective study was conducted of severely injured trauma patients at risk for postinjury coagulopathy who were admitted to our academic level 1 trauma center between January and June 2008. Patients were identified from our electronic trauma registry. Demographic characteristics and laboratory values were abstracted from our electronic medical record. Conventional coagulation tests (INR, fibrinogen, platelet count) and r-TEG specimens (with either fresh or citrated whole blood) were collected at similar time period during resuscitation.

A computerized thrombelastograph coagulation analyzer (TEG model 5000; Haemoscope, Niles, IL) was used in this study. Quality control checks were completed within 8 h of blood collection per the manufacturer. Within 4 min of obtaining the blood sample, 10 μL of r-TEG assay (consisting of 8% kaolin, human recombinant tissue factor, phospholipids, buffers, and stabilizers) [5] was added and mixed to 0.35 mL of whole native blood or citrated whole blood. The resulting specimens were than added to each cup and temperature setting checked for accuracy. The r-TEG was than initiated and then stopped after reaching complete tracings. All r-TEG parameters: TEG ACT, α angle, K value, maximum amplitude (MA), G value (clot strength, expressed as dynes/cm), and estimated percent lysis (EPL) were recorded on standard tracings. Theoretic blood product administration was estimated by two methods. For conventional coagulation specimens, current transfusion thresholds from our institution's massive transfusion protocol were utilized. For r-TEG specimens, transfusion triggers were based upon the manufacturer's guidelines for normal ranges. Therapeutic transfusion triggers were: INR >1.5 and r-TEG ACT >125 s for FFP administration, fibrinogen <133 mg/dL and α-angle $<63^{\circ}$ for cryoprecipitate, and platelet count <100 K and MA <52 mm for aphaeresis platelets.

Univariate analyses were done with frequencies, percentages, means, standard deviations, medians, and interquartile ranges as appropriate. McNemar's χ^2 tests were used to show if there was a significant difference in the theoretical blood product administration between conventional coagulation and r-TEG transfusion triggers. Cohen's κ-statistics were used to show the agreement in predicting hypocoagulability between the conventional coagulation and r-TEG tests. Since r-TEG ACT represents the enzymatic contribution to clot formation and, when prolonged, is most responsive to fresh frozen plasma, its ability to predict hypocoagulability was compared with INR. Similarly, because α angle represents the initiation of fibrin crosslinking due to thrombin's effects on soluble fibrinogen, its correlation with fibrinogen level was chosen. Since MA represents the contribution of platelet function to clot strength, we chose platelet count as a correlate. Statistical analyses were performed using SAS, version 9.0, 1999 (SAS Institute, Inc. Cary, NC). Statistical significance was established as $P < 0.05$ using two-sided tests.

RESULTS

Forty-four severely injured trauma patients had simultaneous conventional coagulation and r-TEG tests during our study period. Seventeen patients had citrated specimens and 27 had noncitrated whole blood specimens. The general demographics of our patient population are shown in Table 1. As expected, this cohort is predominately young males with severe injury patterns as reflected by their overall median of 29 y (interquartile range 22–35] and elevated shock indices.

Cohen's κ-values for the citrated tests ranged from 0.17 to 0.39, whereas the noncitrated specimens ranged from 0.26 to 0.48 (Table 2). MA and platelet count in the noncitrated samples had the highest κ-value at 0.48, which was the only comparison to show moderate agreement between the conventional and r-TEG tests [6]. All but one of the other comparisons demonstrated fair agreement. The lowest κ-score was for r-TEG ACT and INR in the citrated samples, and this indicates only slight agreement between the conventional and r-TEG tests. This likely reflects the difficulty of attempting to correlate a static single test (conventional) to a functional, dynamic evaluation of blood clotting via r-TEG.

After ascertaining that noncitrated whole blood appeared to be preferable for r-TEG analysis of coagulation compared with standard coagulation tests, we limited our theoretical blood product administration analysis to this group. Overall, conventional