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Does Thromboelastography in Non-Trauma Critical Care Patients Promote The Judicious Use of Blood Products? A Retrospective Exploratory Single Center Observational Study

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ABSTRACT

Background: Thromboelastography (TEG) revolutionized the resuscitation of critically ill trauma and cirrhotic patients by improving blood product utilization and survival outcomes. There is limited data on the application and outcomes of non-trauma critical care (NTCC) patients with TEG use. This study compares the blood product utilization, mortality, and other outcomes of NTCC patients using TEG or CCT-guided transfusion.

Methods: This is a single-center retrospective observational exploratory study of adult NTCC patients admitted to the medical intensive care unit in a rural academic center. Eligible patients received transfusion of blood products (BPs) guided by CCT or TEG studies. The primary outcome compared BPs transfused. Secondary outcomes included methods to achieve hemostasis, 28-day readmission rate after discharge, and 28-day survival.

Results: TEG was used in 80 (70.8%) patients. The TEG group received 4.5 more units of BPs than the CCT group (p=0.003). A clinically significant difference in BPs transfused was seen in packed red blood cells (p=0.064), platelets (p=0.003), and fresh frozen plasma (p=0.020). The methods to achieve hemostasis between the groups were statistically significant (p=0.021). The 28-day readmission-free rate was similar (42.5% vs. 54.5%, TEG vs. CCT, p=0.301), as was the 28-day survival after discharge (p=0.078) in both groups.

Conclusions: TEG-guided transfusion increased the number of BPs transfused compared to CCT in NTCC patients. No difference between the two groups in achieving hemostasis, 28-day readmission rate, or 28-day mortality was observed. This study highlights the need to further analyze TEG-guided resuscitation prior to adopting TEG into routine practice in NTCC settings.

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Abbreviations

Conventional coagulation testing (CCT)
Critical care (CC)
Fresh frozen plasma (FFP)
Intensive care unit (ICU)
Packed red blood cells (pRBCs)
Thromboelastography (TEG)

Key Messages

While thromboelastography (TEG) has revolutionized the resuscitation of critically ill trauma and cirrhotic patients by improving blood product utilization and survival outcomes, there is limited data on its application and outcomes in non-trauma critical care (NTCC) patients.

In this study, TEG use was associated with increase blood product utilization and was no different than conventional coagulation studies in improving mortality outcomes in NTCC patients.

We highlight the need to further analyze TEG-guided resuscitation in NTCC settings prior to its adoption into routine practice.

Introduction

Hemorrhage remains a major cause of potentially preventable morbidity and mortality in adult medical intensive care unit (ICU) patients. Traditionally, conventional coagulation testing (CCT) has been used to guide resuscitation and transfusion of blood product components such as packed red blood cells (pRBCs), platelets, fresh frozen plasma (FFP), and cryoprecipitate. However, CCT may take a considerable amount of time to result. In a clinical scenario where a patient presents with trauma related severe hemorrhagic shock, time is of the essence and patients may

require a large amount of blood products transfusion. While it is common practice to transfuse blood products at a balanced 1:1:1 ratio of pRBC:FFP:platelets for resuscitation, this practice may lead to increased blood product waste [1]. In the search for an expedited, effective point-of-care test to assess coagulopathy in hemorrhagic shock, thromboelastography (TEG) has emerged and shown to be efficacious in acute traumatic hemorrhage. Initially developed in 1948 by Hartert, TEG was largely relegated to use in hematology research for decades due to long assay times and poor accuracy [2]. This changed in the late 1990s when point-of-care models were developed that could report results in minutes and were highly accurate [3, 4]. Since then, TEG has seen increasing usage in multiple clinical scenarios to rapidly assess patients for coagulation deficits and guide transfusion requirements for resuscitation.

TEG is a viscoelastic assay that simulates the clotting of blood under physiologic conditions in real-time and measures the strength of the clot at each phase from formation to breakdown. The appeal of TEG is the promise of individualized transfusion strategies to rapidly correct coagulation deficits specific to individual patients. Initial studies proved that TEG-generated metrics were predictive and correlated with CCT [3, 4]. Subsequent studies showed reduced mortality, reduced blood products transfusion requirements, and improved ICU outcomes for trauma patients who needed massive transfusion protocol randomized to TEG-guided resuscitation [5-7]. The utility of TEG has since been expanded in bleeding cirrhotic patients. It is well recognized that CCT results are not reflective of coagulation status in advanced cirrhosis since chronic liver dysfunction alters the production of coagulation factors that maintain normal hemostasis [8]. Randomized controlled trials have shown TEG-guided transfusion in bleeding cirrhotic patients results in reduced use of blood products without significant differences in mortality or ICU outcomes [9-11]. The benefits of TEG-guided resuscitation in non-traumatic medical ICU patients are, however, not well elucidated. In this study, we compared the utilization of blood products, mortality, and ICU outcomes between TEG- and CCT-guided transfusion in non-trauma critical care (CC) patients in the medical ICU.

Materials and Methods

Study Design and Setting

This was a retrospective observational exploratory study conducted at a rural tertiary academic center and its affiliated hospitals. We extracted data and compared characteristics, interventions, and outcomes of non-trauma CC patients requiring blood products utilizing CCT and TEG to guide transfusion decisions. The "does thromboelastography in non-trauma critical care patients promote the judicious use of blood products? a retrospective exploratory single center observational study" protocol was reviewed and approved by our Institutional Board Review (#2101223301) on February 24th, 2021. Only deidentified data obtained for clinical evaluation purposes was used. The study was conducted in accordance with the institutional ethical standards on human experimentation and with the Helsinki Declaration of 1975. The study was reported in line with the STrengthening the Reporting of Observational Studies in the Epidemiology (STROBE) guidelines [12].

Participants and Study Size

The SlicerDicer application within EPIC electronic health record was utilized to identify adult (>18 years of age) non-trauma CC patients requiring blood product transfusions between January 1, 2020 to January 1, 2021. The Consort Flow Diagram illustrates the patient selection process (Figure 1) [13]. We excluded CC patients who were admitted with traumatic injury (n=12). After an individual review of all cases, patients with insufficient clinical data were excluded (n=19). These included patients with missing key demographic and treatment course and/or outcome data. A total of 113 patients met all the inclusion criteria of the study. Of these, 33 patients underwent CCT while the rest (n=80) underwent TEG testing prior to blood product transfusions. CCT include the performance of prothrombin time, activated partial thromboplastin clotting time, and international normalized ration. Both CCT and whole-blood TEG analysis were performed by the in-hospital clinical laboratory. The need and amount of blood product transfusion were determined by the ICU physicians, based on both laboratory data and clinical judgment.

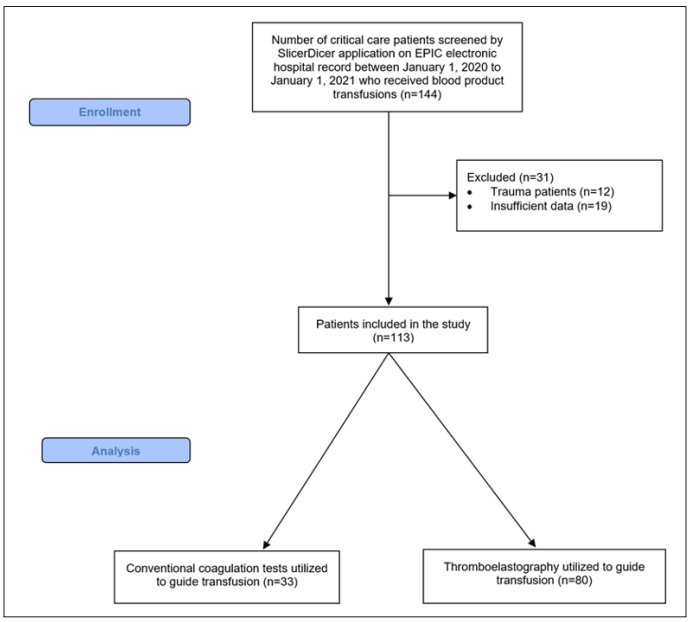

Figure 1: The Consort Flow Diagram illustrating the patient selection process

Outcomes

The primary outcome of this study was the number of units of blood products transfused in the CCT and TEG groups of non-trauma CC patients. We sought to compare and analyze data from both groups as an aggregate total and categories of blood products. The secondary outcomes included methods of achieving hemostasis and 28-day outcomes after hospital discharge (readmission-free rate and median days of survival).

Data Collections

All study records were securely stored in the Research lectronic Data Capture (REDCap) system at our institution.

Statistical Methods

Descriptive analyses were performed for all outcome measures and endpoints. Continuous variables were reported in medians with interquartile range. Categorical data were reported in frequencies and percentages. Statistical analysis was performed with a predetermined significance level of 0.05. Categorical variables were analyzed using Pearson chi-square or Fisher exact test and nonparametric numerical variables were analyzed using the Wilcoxon rank-sum test.

Bias

This cross-sectional study describes the blood product usage in non-trauma CC patients in the rural Appalachian region at a

specified time point. We attempted to minimize selection bias by having 3 independent reviewers determine the suitability of patients included in the study. Four reviewers performed independent chart reviews to extract and analyze data. Any disagreements were reconciled with a consensus decision. The retrospective nature of the study may lead to information bias. The need and amount of blood product transfusions were determined by the ICU physicians, based on both laboratory data (CCT and TEG) and clinical judgment. Individual physicians' preference may influence the amount of blood products transfused.

Results

Participants

Baseline patient characteristics all patients included in the study are shown in Table 1. All 113 non-trauma CC patients were included in the final analyses. TEG was utilized in most patients (n=80, 70.8%) of non-trauma CC patients. Overall, demographics between the TEG and CCT groups were not statistically or clinically different. The median age of the TEG and CCT group were 61.5 and 63.0 years (p = 0.576) respectively. A majority of patients were males in both groups (TEG; n=48, 60%, CCT; n=21, 63.6%). Both groups also had a majority of White patients (TEG; n=72, 93.8%, CCT; n=33,100%) with 8 non-White patients analyzed in the TEG group. Comorbidities of patients in the TEG and CCT group did not significantly defer. Each category of anticoagulation or antiplatelet medication that was taken prior to admission was analyzed separately and the percentage of patients taking these medications was uniformly similar between TEG and CCT groups. The most common reason for transfusion in the TEG group (n=58, 72.5%) was acute blood loss, while in the CCT group hemoglobin count of less than 7 g/dL (n=16, 48.5%) was the most common cause of transfusion followed by acute blood loss (n=15, 45.5%). There was a statistically significant difference in the TEG group compared to CCT group in the transfusion indication for acute blood loss (p=0.009).

Table 1: Baseline characteristics of patients

Characteristics	TEG (n=80)	CCT (n =33)	p-value
Age: median (IQR)	61.50 (48.50, 72.75)	63.00 (54.00, 74.00)	0.576
Gender: n (%)			
• Male	48 (60.0)	21 (63.6)	0.833
• Female	32 (40.0)	12 (36.4)	
Race: n (%)			
• White	72 (93.8)	33 (100)	
• African American/Black	5 (6.0)	0	
• Asian	1 (1.2)	0	
• Other (Asian and Native American)	2 (2.4)	0	0.559
Comorbidities: n (%)			
• Coronary artery disease	22 (27.5)	22 (27.5)	0.373
• Atrial fibrillation	15 (18.8)	6 (18.2)	1.000
• Venous thromboembolism	7 (8.8)	3 (9.1)	1.000
• Cerebrovascular accident	7 (11.3)	0	0.104
• Hypertension	49 (61.3)	16 (48.5)	0.295
• Diabetes Mellitus	30 (37.5)	15 (45.5)	0.527
• Inflammatory bowel disease	1 (1.3)	0	1.000
• Cancer	16 (20.0)	13 (39.4)	0.037
• Coagulopathy	11 (13.8)	3 (9.1)	0.753
• Cirrhosis	10 (12.5)	5 (15.2)	0.763
Anticoagulant and/or antiplatelet usage prior to admission: n (%)			
• Aspirin	21 (26.3)	8 (24.2)	1.000
• Anti-P2Y12 inhibitors	11 (13.8)	1 (3.0)	0.175
• Warfarin	4 (5.0)	1 (3.0)	1.000
• Direct-acting oral anticoagulants	14 (17.5)	5 (12.5)	0.793
• Heparin derivatives:	9 (11.3)	5 (15.2)	0.754
Non-steroidal anti-inflammatory drug usage: n (%)	5 (6.3)	0	0.319
Transfusion indication: n (%)			
• Acute blood loss	58 (72.5)	15 (45.5)	0.009a
• Hemoglobin < 7 g/dL	45 (56.3)	16 (48.5)	0.535
• Unexplained symptomatic anemia	3 (3.8)	4 (12.1)	0.191
• Preoperative transfusion	5 (6.3)	1 (3.0)	0.669
• Intraoperative transfusion	4 (5.0)	3 (9.1)	0.415
• Post-operative transfusion	15 (18.8)	8 (24.2)	0.608
• Hemoglobin > 7 g/dL with pre-existing cardiovascular disease	3 (3.8)	0	0.555
• Coagulopathyb	6 (7.5)	3 (9.1)	0.719
• Thrombocytopenia	8 (10.0)	1 (3.0)	0.280
• Otherc	1 (1.3)	1 (3.0)	0.501

CCT, conventional coagulation testing; TEG, thromboelastography.

[a]Statistically significant value; [b]Includes disseminated intravascular coagulation, thrombotic thrombocytopenic Purpura, and idiopathic thrombocytopenic purpura; [c]Patients who required extracorporeal membrane oxygenation, and/or COVID-19 patients were included.

Table 2: Blood product utilization, measures of hemostasis and outcomes

Blood Product Usage	TEG (n=80)	CCT (n=33)	p-value
Units of blood products transfused: median (IQR)			
• pRBCsa	3.50 (2.00, 7.00)	2.00 (1.00, 4.00)	0.064
• FFPa	1.00 (0, 3.00)	0 (0, 1.00)	0.020a
• Platelets	1.0 (0, 1.75)	0 (0, 0)	0.003a
• Cryoprecipitate	0 (0, 0.75)	0 (0,0)	0.067
• Total blood products	7.50 (3.00, 12.00)	3.00 (1.00, 6.50)	0.003a
Methods to achieve hemostasis: n (%)			
• Bloods products alone	43 (53.8)	19 (57.6)	0.075
• Blood products and procedure	32 (40.0)	8 (24.2)	
• Hemostasis not achieved	5 (6.3)	6 (18.2)	
Time to hemostasis: n (%)			

• < 1 hour	8 (10.0)	11 (33.3)	0.021[a]
• 1-3 hours	12 (15.0)	6 (18.2)	
• 3-6 hours	9 (11.3)	2 (6.1)	
• > 6 hours	51 (63.8)	14 (42.4)	
Mechanical ventilation: n (%)	41 (51.3)	15 (45.5)	0.680
Vasopressor support: n (%)	53 (66.3)	23 (28.8)	0.827
Rebleeding event after hemostasis: n (%)	12 (15.0)	1 (3.0)	0.104
28-day outcomes after discharge from hospital			
• Free of readmission: n (%)	34 (42.5)	18 (54.5)	0.301
• Days to readmission: median (IQR)	28.0 (17.0, 28.0)	28.0 (0, 28.0)	0.482
• Survival: n (%)	75 (93.8)	27 (81.8)	0.078

CCT, conventional coagulation testing; FFP, fresh frozen plasma; pRBC, pooled red blood cells; TEG, thromboelastography.
aStatistically significant value.

Outcome Data

On average, the patients that had TEG-guided transfusion received 4.5 more units of total blood products than CCT-guided transfusion (p=0.003). This statistically significant difference was accounted for by FFP and platelets use between each group, where the median number of units transfused of FFP was 1 in the TEG group and 0 in the CCT group (p=0.020) and median number of units transfused for platelets was 1 in the TEG group and 0 in the CCT group (p=0.003). Blood product utilization and measures of hemostasis are presented in Table 2. 53.8% (n=43) of TEG patients and 57.6% (n=19) of CCT patients achieved hemostasis with blood products alone, while 40% (n=30) of TEG and 24.2% (n=8) of CCT patients required blood products and procedural intervention for hemostasis. Death occurred in 6.3% (n=5) of the TEG group due to the absence of hemostasis compared to 18.2% (n=6) from the CCT group. Overall, the methods of achieving hemostasis between groups were not statistically significant (p=0.075). The time to hemostasis was less than 1 hour for 10% (n=8) of TEG patients compared to 33.3% (n=11) of CCT patients, and greater than 6 hours for 63.8% (n=51) of TEG patients compared to 42.4% (n=14) of CCT patients. When all time frames are considered, there is both clinical and statistical difference in time to hemostasis (p=0.021) favoring the CCT group for non-trauma CC patients. The 28-day free of readmission rate for the TEG group was 42.5% (n=34) compared to 54.5% (n=18) in the CCT group (p=0.301). The median days of survival following discharge were at the maximum outcome days of 28 days for both groups (p=0.078). The 28-day survival was 93.8% (n=75) for the TEG group compared to 81.8% (n=27) for the CCT group (p=0.078).

Discussion

Key Results

Our study is focused on TEG-guided transfusion in non-trauma CC patients and does show a clinically and statistically significant difference in units of blood products transfused between the TEG and CCT groups. Patients that underwent TEG-guided transfusion received 4.5 more units than CCT-guided transfusion (p=0.003). This contrasts with studies of different applications that showed reduced blood product usage with TEG [5-7, 14]. Similar to the reported studies, this study also showed no benefit in 28-day survival and readmission rate between the two groups [9-11]. Importantly, there is both clinical and statistical difference in time to achieve hemostasis (p=0.021) favoring the CCT group for non-trauma CC patients.

Since the advent of accurate, point-of-care TEG systems, there have been an increasing number of indications to utilize TEG in guiding the transfusion of blood products. It has been used routinely in cardiac and transplant surgery, both scenarios that often require transfusion of multiple units of blood products and present with significant coagulation deficits [15, 16]. It has also been proven to be cost-effective and superior to CCT in trauma settings, and new studies are showing TEG-guided transfusion does reduce blood product utilization in cirrhosis patients presenting with bleeding, although no benefit to mortality or ICU outcomes has been shown [5-7, 9-11].

TEG offers an expedient and accurate evaluation of coagulation deficits; it has not yet been shown to be superior to CCT in the medical ICU setting. A variety of factors may be contributing to its limited utility. First, the amount of blood products transfused in reaction to TEG analysis is not uniform or based on formal guidelines, instead is dependent on provider interpretation and experience. This may result in minor coagulation deficits noted on TEG being ignored or overcorrected depending on the clinical scenario. Given its limited usage outside of trauma settings thus far, more training and experience are needed to optimize its benefits. It is not yet known whether establishing a formal guideline for transfusion based on TEG parameters would lead to more judicious use of blood products.

Another rationale for the evidence of this finding may be the fact that in a non-traumatic setting, there may be factors outside of the coagulation factors that determine transfusion need. Instead, patients may have underlying processes that may cause slow loss or breakdown of blood and/or impaired erythropoiesis. In these cases, treatment of underlying abnormality can often correct coagulation deficits without transfusion. For instance, if a patient presents with gastric ulcer bleed, blood product resuscitation blood products alone may not achieve hemostasis. To achieve hemostasis, the patient may require an endoscopic or surgical intervention in addition to blood products transfusion.

While there was no significant difference between methods to achieve hemostasis, there was statistical significance observed in time to hemostasis between the TEG group and the CCT group (p=0.031). Compared to the TEG group, the CCT group appeared to have a lower time to achieve hemostasis compared to that of TEG group, with a majority of the TEG group (61.6%) achieving hemostasis in greater than 6 hours since the initial blood transfusion product, compared to the 42.1% observed in the CCT group. This may suggest that the utility of TEG depends on the correct clinical context, and perhaps in non-traumatic settings it may not be appropriate. Additionally, in comparison to trauma or cases requiring massive transfusion protocol, medical ICU patients are not as reliant on aggressive transfusion and early hemostasis to prevent worsening hemodynamic instability.

While the study result shows statistical significance seen in the total amount of the blood products utilized, the only clinically significant results are seen within the pRBC, FFP, and platelets group. These results may be impacted by the suboptimal sample size evaluated by this study. In this study, we assumed that TEG would decrease the utilization of blood products compared to the CCT group within the study group based on the available data on TEG in the literature. As there is a wide range of 14% - 56% reduction of blood transfusion products reported from the literature, our study

made the best estimate of blood product reduction of 15% as part of this study in the non-trauma CC patient population [17]. From this, we have achieved adequate power as stated in the method section, however, this may have not been enough to see a clinical significance in subgroups of transfusion products.

Limitations

This study has limitations and readers should be mindful when applying these results into their clinical practice. This is an exploratory retrospective single-center study. The sample size and patient demographics limit the generalizability of these outcomes. Nearly all the patients in the study were White. This is due to the racial distribution unique to the rural West Virginia Appalachian region where our tertiary academic center is located. Second, the retrospective nature of the study may potentially lead to information and selection bias. Attempts to minimize these biases have been outlined in the methods section. The need and amount of blood product transfusion were determined by the ICU physicians, based on both laboratory data (CCT and TEG) and clinical judgment. Individual physicians' preference may play a role in the amount of blood products transfused.

Conclusions

TEG is an attractive method to determine the transfusion needs of patients in a critical care setting. While this study does not provide evidence advocating for the use of TEG in the judicious use of blood product transfusion in non-trauma CC patients, further studies are warranted to elucidate the expansion of TEG use in non-trauma CC patients to improve the utilization of blood products. This study further bolsters the need for randomized controlled trials to compare TEG and CCT-guided transfusion in non-trauma CC patients prior to adoption into routine practice.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Author Contributions

SY and BB had full access to all study data and takes responsibility for the integrity of the data and the accuracy of the data analysis. SY, BB, WF, and RS were involved in the study conception and design. SY, OL, TM, and GP were involved in data acquisition. SY, BB, OL, TM, GP, and RS interpreted the data. RS and WF provided statistical analysis reported in the study. SY, OL and BB were involved in drafting and writing the manuscript. All authors contributed to the critical revision of important intellectual content and approved the final version for publishing.

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