Rotational Thromboelastometry Reduces Fresh Frozen Plasma Requirement in Patients without Liver Disease Undergoing Therapeutic Endoscopic Procedures with Deranged Screening Coagulation Tests—A Pilot Study

P. Krishna Bharadwaj[1]   Ebby George Simon[1]   Rutvi G. Dave[2]   Tulasi Geevar[2]   Sukesh C. Nair[2]   Aby Abraham[3]   A. J. Joseph[1]   Amit Kumar Dutta[1]   Sudipta Dhar Chowdhury[1]   Rajeeb Jaleel[1]   Anoop John[1]   Ajith Thomas[1]

[1] Department of Gastroenterology, Christian Medical College, Vellore, India
[2] Department of Transfusion Medicine and Immunohematology, Christian Medical College, Vellore, India
[3] Department of Haematology, Christian Medical College, Vellore, India

Address for correspondence Ebby George Simon, DM, Department of Gastroenterology, Christian Medical College, Vellore, Ranipet 632517, Tamil Nadu, India (e-mail: ebbysimon@gmail.com).

Abstract

Background/Aims Rotational thromboelastometry (ROTEM) is a viscoelastic test that is used in patients with liver disease for guiding blood component use. This study is aimed at comparing the amount of blood products transfused and bleeding rates in patients without liver disease, who underwent therapeutic endoscopic procedures with deranged screening coagulation tests (prothrombin time [PT]; activated partial thromboplastin time [aPTT]), with and without hypocoagulable ROTEM.

Methods Patients with deranged PT and aPTT without liver disease who underwent therapeutic endoscopic interventions during the period 2020 to 2022 were retrospectively analyzed. Baseline parameters, amount of blood products transfused, and outcomes such as 30-day bleeding and mortality rates were recorded in those with and without hypocoagulable ROTEM.

Results Of the 204 patients with deranged PT/aPTT who underwent therapeutic endoscopy during the study period, 180 of those with liver disease were excluded. Six patients (M:F = 5:1; median age: 37, 20–54 years) had hypocoagulable ROTEM and 18 patients (M:F = 11:7; median age: 56, 20–71 years) had normo-/hypercoagulable ROTEM. There were significant differences in the total amount of fresh frozen plasma (FFP) transfused and FFP transfused per patient between the two groups (9,000 vs. 4,500 mL and 2,000 vs. 1,000 mL; $p = 0.04$, respectively). Two patients with hypocoagulable ROTEM bled within 30 days, while none did in the comparator group

Keywords
► fresh frozen plasma
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► therapeutic endoscopic procedures
► thromboelastometry

($p = 0.03$). One patient in the hypocoagulable group died within 30 days and none in the normo-/hypercoagulable group.

Conclusion The use of ROTEM reduces FFP requirement in patients without liver disease with deranged PT/aPTT undergoing therapeutic endoscopic procedures without any increased risk of early or late rebleeding, and 30-day mortality.

Introduction

Screening coagulation tests which include platelet count, prothrombin time (PT), and activated partial thromboplastin time (aPTT) are routinely performed in some centers prior to surgery and therapeutic endoscopy to identify patients with bleeding disorders, assuming that testing will predict perioperative bleeding which can be prevented by giving necessary treatment.[1–3] There is sometimes also a medicolegal angle for the need of performing these tests.[4] At the same time, there are society guidelines which do not support doing coagulation tests unless there is prior history of bleeding, a clinical condition that predisposes to bleeding or a procedure fraught with high bleeding risk.[5,6] This has led to confusion among physicians as whether to do these tests prior to procedures, leading to varying policies.[4]

Screening coagulation tests are done prior to therapeutic endoscopic procedures in our department based on British guidelines.[5] Abnormal results in these tests often warrant the administration of blood products prior to endoscopy. These can lead to increased cost of care and are fraught with the low but certain risk of transfusion reactions. Viscoelastic tests such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM) are now used to overcome these shortcomings in patients with cirrhosis due to rebalanced hemostasis in liver disease.[7] TEG is a point-of-care test which provides a more global overview of the hemostasis. If TEG is abnormal, then appropriate products are administered.

The parameters in TEG are R-time, K-time, angle, maximal amplitude (MA), and LY30. R-time is the time taken to initiate clot formation, and it reflects clotting factor levels. K-time represents the time taken to reach certain level of clot strength. Angle denotes kinetics of clot strength and clot build up. K-time and angle reflect fibrinogen contribution up to 80% and platelets up to 20%. MA indicates maximum clot strength contributed by platelets up to 80% and fibrinogen up to 20%. LY30 is a measure of fibrinolysis, and it refers to the percentage in amplitude reduction after 30 minutes of MA.[8]

ROTEM is also a point-of-care viscoelastic test similar to TEG. In TEG, the pin is stationary and the cup oscillates, whereas in ROTEM, the pin oscillates and the cup is stationary. The parameters in ROTEM are clotting time (CT), clot formation time (CFT), α angle, maximum clot firmness (MCF), and maximum clot lysis and their counterparts in TEG are R-time, K-time, angle, MA, and LY30, respectively.[9]

A previous study attempting to understand the relationship between TEG and ROTEM showed linear association with strong correlation for CFT with K-time and MA with MCF. Rest of the parameters showed either moderate or poor correlation.[10]

The use of TEG in nonliver patients to guide transfusion requirements is a recent concept which can be useful in patients with deranged screening coagulation parameters based on its success in other clinical situations.[11] With this background, our study is aimed to compare the amount of blood products transfused and bleeding rates in patients with and without hypocoagulable ROTEM who underwent therapeutic endoscopic procedures with deranged screening coagulation tests (PT and aPTT) without liver disease.

Materials and Methods

A retrospective study of all patients with deranged PT or aPTT, without liver disease, who underwent therapeutic endoscopic interventions under the department of medical gastroenterology at our hospital, a tertiary care center in South India, between January 1, 2020, and May 31, 2022, was conducted. ROTEM was done only in those patients who had deranged PT or aPTT. Deranged PT was defined as PT more than 12.5 seconds or international normalized ratio (INR) $\geq$ 1.4.[12,13] Deranged aPTT was defined as aPTT more than 40.4 seconds.

Viscoelastic testing was performed with citrated whole blood on ROTEM (Tem International, Munich, Germany) using modified EXTEM mode. EXTEM reagent with low tissue factor (TF) concentration was used to reflect physiological conditions.[14] The test was performed by trained personnel and activated using TF. The TF was prepared by dilution of PT reagent, Innovin (Dade Behring, United States) at 1:2,000 dilution, modified from the method described by Sørensen et al.[15] The variables assessed were CT, CFT, α angle (α), MCF, and maximal lysis. The reference ranges for these parameters were established using samples from more than 300 blood donors.

A hypercoagulable state was defined as two or more of the following: short CT and/or CFT time, increased α-angle, and increased MA. Hypocoagulable state was defined as two or more of the following: prolonged CT and/or CFT, decreased α-angle, and decreased MA. Normal state was defined as all indices being within the normal ranges. In case, if ROTEM that did not fall into one of the three categories above (i.e., only a single abnormality or mixed hyper- and hypoindices in the same ROTEM), the predominant abnormality was used to categorize the ROTEM into the most appropriate category.[16]

The amount of blood products transfused was decided by clinician by the advice of hematologist and/or transfusion medicine specialist. Patient details were collected through

the hospital computerized data system. Data consisting of demographics, etiology of primary gastrointestinal disease, screening coagulation parameters, therapeutic intervention performed, amount of blood products transfused, and important outcomes such as 30-day bleeding and 30-day mortality were recorded and compared between those with and without hypocoagulable ROTEM. Vitamin K was not given for patients with cholestasis prior to therapeutic intervention as utility of ROTEM was being studied in deranged coagulation.

Statistical analysis was performed using the chi-square test or Fisher's exact test, as applicable for categorical data. Mann–Whitney's U test was used for continuous data. The data were analyzed with SPSS v. 21.0 data (Statistical Package for the Social Sciences, SPSS Inc., Chicago, Illinois, United States). A p-value of < 0.05 was taken to be statistically significant.

This study was approved by our Institutional Review Board (Ref: IRB: 14844 [Retro] dated October 26, 2022), and being a retrospective study, there was waiver of consent.

Results

A total of 204 patients who underwent therapeutic endoscopic procedures had deranged screening coagulation parameters during the study period. After excluding 180 patients with liver disease, 24 patients were included for the study (►Fig. 1).

Six patients (M:F = 5:1; median age: 37, 20–54 years) had hypocoagulable ROTEM and 18 patients M:F = 11:7; median age: 56, 20–71 years) with either normo-/hypercoagulable ROTEM. Both groups were comparable in baseline characteristics except platelet count ($p = 0.04$) and aPTT level ($p = 0.04$) (►Table 1)

►Table 2 depicts comparison of blood products transfused and outcomes between both the groups. There was significant difference in total amount of fresh frozen plasma (FFP) infused and FFP infused per patient between the groups (9,000 vs. 4,500 mL and 2,000 vs. 1,000 mL; $p = 0.04$), respectively.

Two patients with hypocoagulable ROTEM bled within 30 days and none in the other group ($p = 0.05$). Only one patient in the hypocoagulable ROTEM group died.

Discussion

TEG-guided transfusion strategy has been shown to significantly decrease the blood component requirement in patients with advanced cirrhosis, coagulopathy, and non-variceal upper gastrointestinal bleeding.[17] It is already known that PT and INR do not predict bleeding risk in liver disease because it relies on thromboplastins and measures only the activity of procoagulants and not of the anticoagulants, both of which may be depressed in patients with advanced liver disease.
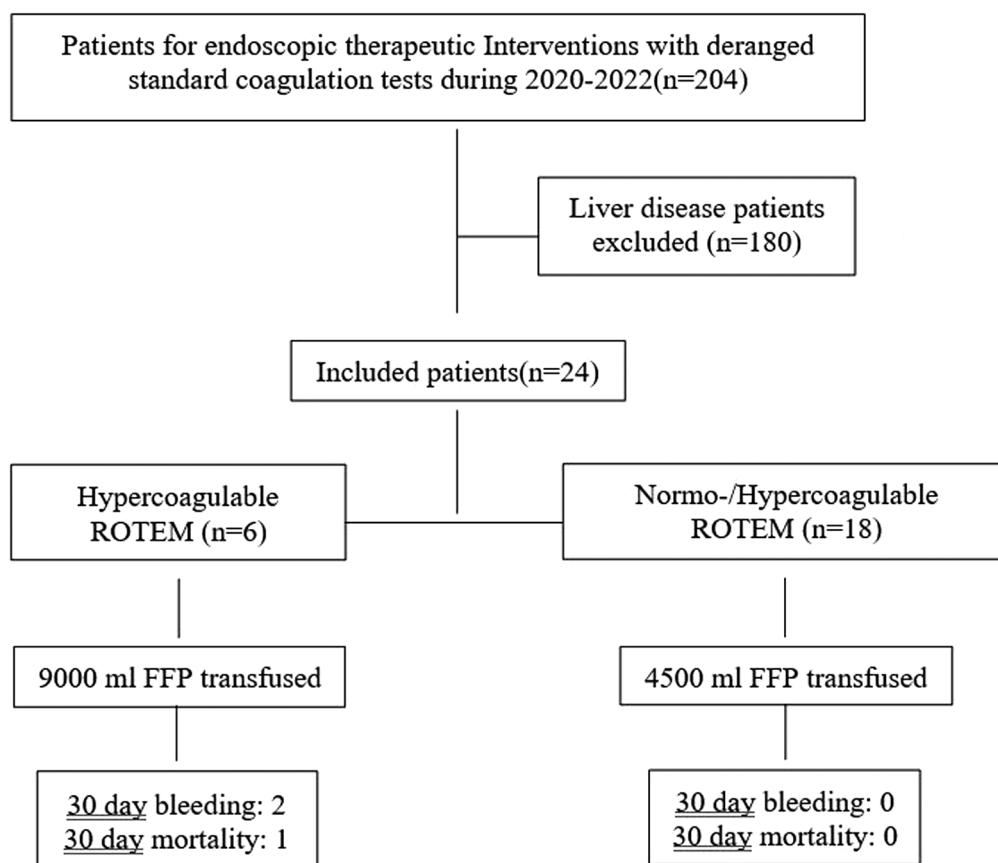

Fig. 1 Patient flow diagram. FFP, fresh frozen plasma; ROTEM, rotational thromboelastometry.

Table 1 Comparison of baseline characteristics between hypocoagulable and normo-/hypercoagulable ROTEM groups

Characteristics	Hypocoagulable ROTEM ($n = 6$)	Normo-/hypercoagulable ROTEM ($n = 18$)	*p*-Value
Age (y)	37 (20–54)	56 (20–71)	0.083
Male sex	5 (83.3%)	11 (61.1%)	0.31
Indications for therapeutic endoscopy (*n*)			
EHBO with cholangitis	1	4	
EHBO without cholangitis	0	5	
Gastric ulcer	1	2	
Cholangiocarcinoma	0	2	
Mallory–Weiss tear	1	2	
Walled-off necrosis pancreas	0	2	
Others[a]	3	1	
Procedures (*n*)			
Combination endotherapy for ulcer bleed	4	5	
ERCP + biliary sphincterotomy	1	9	
ERCP + biliary sphincterotomy + EUS + FNA	0	1	
EUS + FNA	0	1	
EUS + cystogastrostomy	0	2	
POEM	1	0	
Laboratory results			
Hemoglobin (g/L)	75.5 (27–176)	101.5 (55–136)	0.15
Platelet count (10^9/L)	120 (26–200)	220 (11.6–580)	0.04[b]
Thrombocytopenia (platelet count $< 50 \times 10^9$/L)	1 (16.7%)	1 (5.55%)	0.39
INR	2.16 (1.18–10)	1.535 (0.93–2.72)	0.27
INR > 1.4	4 (66.7%)	12 (66.7%)	1.0
aPTT (s)	53.7 (41.2–120)	42.4 (33.9–62.7)	0.04[b]
aPTT > 40.4 (s)	6 (100%)	11 (61.1%)	0.13
Fibrinogen (g/L)	1.96 (0.44–5.13)	3.21 (1.53–6.63)	0.11
Fibrinogen < 1.5 g/L	2 (33.4%)	0	0.05

Abbreviations: aPPT, activated partial thromboplastin time; EHBO, extrahepatic biliary obstruction; ERCP, endoscopic retrograde cholangiopan-creatography; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; INR, international normalized ratio; POEM, peroral endoscopic myotomy; ROTEM, rotational thromboelastometry.
Note: Data are presented as *n* (%) or median (range).
[a]Others: Achalasia cardia, rectal stercoral ulcer bleed, colonic diverticular bleed, postsphincterotomy bleed.
[b]Statistically significant.

Our study is a first of its kind trying to analyze the benefit of a similar strategy in those patients without liver disease but with derangement of the screening coagulation tests for whom therapeutic endoscopy is being considered.

Giles et al[18] reported that abnormal PT and aPTT tests do not predict bleeding risk in children undergoing endoscopic procedures. Deranged aPTT may indicate underlying factor deficiency which may or may not influence the overall coagulation cascade (e.g., factor XII deficiency). So, ROTEM is an excellent point-of-care test which will inform about the overall coagulation status.

In our study, we noted that significantly less amount of FFP was needed when a ROTEM-based transfusion strategy was followed. The 30-day bleeding and mortality rates did not increase in those who had restricted transfusion based on this strategy. Such an approach could reduce blood product utilization, time, cost, and potential transfusion-related adverse reactions without increasing the risk of bleeding or death.

Limitations of this study include its retrospective nature, small sample size, and being confined to single tertiary care center. Clinician discretion in deciding blood product transfusion based on ROTEM results is another limitation. Some patients with normo-/hypercoagulable ROTEM also received transfusions as they belonged to some departments where ROTEM-based transfusion strategy was not implemented.

Table 2 Comparison of blood products transfused and outcomes between hypocoagulable ROTEM group and normo-/hypercoagulable ROTEM group

Variable	Hypocoagulable ROTEM ($n = 6$)	Normo-/hypercoagulable ROTEM ($n = 18$)	p-Value
No. of patients transfused with FFP	4 (66.7%)	5 (27.8%)	0.08
Total amount of FFP infused (L)	9	4.5	
Median FFP (L) infused/patient	2 (1.75–3.25)	1 (0.75–1)	0.04[a]
No. of patients transfused with platelets	2 (33.4%)	1 (5.56%)	0.07
Total amount of random donor platelet pools infused (U)	15	4	
Median pooled platelets (U) infused/patient	7.5 (2–13)	4	0.33
No. of patients transfused with cryoprecipitate	2	0	
Total amount of cryoprecipitate infused (U)	17	0	
Median cryoprecipitate (U) infused/patient	8.5 (7–10)	0	
No. of patients transfused with packed cells	4 (66.7%)	3 (16.67%)	0.019[a]
Total amounts of packed cells transfused	23	6	
Median RBCs transfused (packs) per patient	6 (3–8)	2	0.03[a]
FFP transfusion only	2 (33.4%)	5 (27.8%)	0.79
Platelet transfusion only	0	1	
FFP, platelets, and cryoprecipitate transfusions	2 (33.4%)	0	
Outcome			
30-d bleeding	2 (33.3%)	0	0.05
30-d mortality	1 (16.7%)	0 (0)	0.25
Lost to follow-up	0	4	

Abbreviations: FFP, fresh frozen plasma; RBC, red blood cell; ROTEM, rotational thromboelastometry.
Note: Data are presented as n (%) or median (range).
[a]Statistically significant.

Instead, transfusions were administered on the basis of the abnormal screening coagulation test results. There is a need for large multicenter prospective studies to validate the results of ROTEM-based transfusion strategy which we have utilized in our study.

Conclusion

For centers pursing the policy of coagulation-based screening prior to interventional endoscopic procedures, the use of ROTEM as point-of-care test can help reduce blood component usage in patients without liver disease who have deranged screening coagulation parameters without any increased risk of 30-day bleeding and mortality.

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