Major Thromboembolic Complications in Liver Transplantation: The Role of Rotational Thromboelastometry and Cryoprecipitate Transfusion

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Background. Although hemorrhage is a major concern during liver transplantation (LT), the risk for thromboembolism is well recognized. Implementation of rotational thromboelastometry (ROTEM) has been associated with the increased use of cryoprecipitate; however, the role of ROTEM-guided transfusion strategy and cryoprecipitate administration in the development of major thromboembolic complications (MTCs) has never been documented. **Methods.** We conducted a study on patients undergoing LT before and after the implementation of ROTEM. We defined MTC as intracardiac thrombus, pulmonary embolism, hepatic artery thrombosis, and ischemic stroke in 30 d after LT. We used a propensity score to match patients during the 2 study periods. **Results.** Among 2330 patients, 119 (4.9%) developed MTC. The implementation of ROTEM was significantly associated with an increase in cryoprecipitate use (1.1 ± 1.1 versus 2.9 ± 2.3 units, $P < 0.001$) and MTC (4.2% versus 9.5%, $P < 0.001$). Further analysis demonstrated that the use of cryoprecipitate was an independent risk factor for MTC (odds ratio 1.1, 95% confidence interval 1.04-1.24, $P = 0.003$). Patients with MTC had significantly lower 1-y survival. **Conclusions.** Our study suggests that the implementation of ROTEM and the use of cryoprecipitate play significant roles in the development of MTC in LT. The benefits and risks of cryoprecipitate transfusion should be carefully evaluated before administration.

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INTRODUCTION

Perioperative hemostasis and transfusion management for patients undergoing liver transplantation (LT) can be complex and challenging. This is, in part, because patients undergoing LT can have significant hemorrhage and less frequently, but potentially devastating thromboembolism.[1,2] Intracardiac thrombosis (ICT) and pulmonary embolism (PE), which occur at a rate of 1%–6%, have an intraoperative mortality up to 45%.[3,4] PE has been reported to be the second most common cause of early postoperative mortality after LT.[5] Hepatic artery thrombosis (HAT) occurs at a rate of 3%–9% and is associated with a high rate of mortality (55%) and retransplantation (80%).[6] Thrombotic and embolic stroke occurs in approximately 2% of LT patients and may contribute to significant postoperative disability and mortality.[7-9]

Rotational thromboelastometry (ROTEM) evaluates the entire process of clot formation and provides useful information on the etiology of coagulopathy.[10] FIBTEM, a ROTEM test assessing the role of fibrin in clot formation, can provide a unique insight into coagulation. Using information obtained by FIBTEM, a normal range has been defined and transfusion algorithms have been proposed.[11] As a result, the introduction of ROTEM is often associated with an institutional change in practice, which is characterized by the increase in the use of fibrinogen (cryoprecipitate or fibrinogen concentrate).[12,13] Although a few studies have shown that an increase in fibrinogen transfusion is accompanied by lower transfusion of other blood products, the ROTEM-derived practice change and the increase in fibrinogen transfusion

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raise some concerns.[14] First, not all increases in the use of fibrinogen are associated with the decrease in transfusion of other blood products. There are some publications suggesting not all fibrinogen transfusions are necessary.[13,15,16] More importantly, increased use of fibrinogen may contribute to the development of hypercoagulability resulting in perioperative thromboembolic complications.[17] Despite these concerns, there are no reports linking ROTEM implementation to thromboembolic complications in LT.

In this study, we aimed to investigate whether ROTEM implementation at our institution was associated with an increased use of cryoprecipitate and if so, whether the increased use of cryoprecipitate was associated with thromboembolic complications.

MATERIALS AND METHODS

After IRB approval (protocol # 17-000740), we performed a retrospective study from a prospectively collected LT database at the University of California at Los Angeles (UCLA). We included adult (age ≥ 18 y) LT patients over 14 y (2004–2017). Patients <18 y old were excluded.

Patients during the study period underwent the standard adult LT management at UCLA, which has been described previously.[18] Patients were evaluated and managed by a multidisciplinary team before LT. Patients were induced with intravenous anesthetics and maintained using a combination of volatile and intravenous anesthetics, and neuromuscular blockers. Patients were monitored with standard American Society of Anesthesiologists monitors, arterial line, central venous catheter, pulmonary artery catheter, and transesophageal echocardiography. Patient received intravenous vasopressors including phenylephrine, norepinephrine, vasopressin, and epinephrine to maintain hemodynamic stability. Vasopressors were administered in continuous infusion or bolus (a large bolus was defined as phenylephrine > 2 mg, norepinephrine 40 μg, and epinephrine > 50 μg). Surgeons performed retrocaval clamping with and without venovenous bypass (VVB), depending on a joint decision made by anesthesiologists and surgeons.

ROTEM was analyzed in a 4-chamber ROTEM device (Munich, Germany). Blood samples for ROTEM were usually collected at 2 time points: after induction of general anesthesia and after reperfusion of the liver graft. The samples were analyzed by the UCLA Department of Pathology and Laboratory Medicine. LT anesthesiologists were required to complete yearly training on ROTEM interpretation, and perform routine ROTEM tracing reviews. Quantitative coagulation tests, including partial thromboplastin time, prothrombin time/international normalized ratio (INR), platelet count, and fibrinogen level, were also obtained, usually in conjunction with ROTEM testing. Upon the patient's arrival to the operating room, 12 units of red blood cells (RBCs) and 12 units of fresh–frozen plasma (FFP) in refrigerated coolers were brought to the room. Platelets and cryoprecipitate were only prepared by the hospital blood bank and delivered to the operating room as requested by anesthesiologists. Fibrinogen concentrate was not available during the study period at our institution. RBC and FFP were transfused via a heated rapid transfusing device through a central line. Cryoprecipitate and platelets were administered through a nonheated line.

Transfusion management was guided by the surgical field assessment, laboratory values, and ROTEM values. Transfusion of cryoprecipitate was guided by clinical bleeding and fibrinogen levels in the study cohort before implementation of ROTEM and by clinical bleeding, fibrinogen levels, and ROTEM values in the study cohort after ROTEM implementation. Blood product transfusion followed a previously published algorithm.[11] Cryoprecipitate was indicated: if EXTEM maximum clot firmness (MCF) <35 mm and FIBTEM MCF <8 mm; if EXTEM MCF <45 mm and FIBTEM MCF <8 mm and clinical bleeding; or if EXTEM MCF <55 mm and FIBTEM MCF <16 mm and persistent bleeding.

After completion of surgery, patients were transferred to the intensive care unit for multidisciplinary postoperative care. We defined major thromboembolic complications (MTCs) as ICT, PE, HAT, and cerebral thrombotic or embolic stroke during LT surgery or within 30 d after LT. ICT and PE were diagnosed by intraoperative echocardiography. HAT was diagnosed radiographically by CT, ultrasound, or surgical examination during exploratory laparotomy. Thrombotic or embolic stroke was defined by radiographically or neurological imaging evidence of ischemic stroke in the central nervous system. We divided the study into 2 periods: period 1 (January 2004 to July 2015) when ROTEM was not available and period 2 (August 2015 to Nov 2017) after ROTEM was implemented at our institution (Figure 1).

We used SPSS for statistical analyses. For univariate analysis, we used an independent sample t-test to analyze continuous variables, and chi-square test to analyze categorical variables. Preoperative and intraoperative variables of patients between patients in periods 1 and 2 were compared. The selected variables that were significant in univariate analysis or were considered as significant for studied outcome were used to generate propensity scores to match patients in periods 1 and 2. We used the closest propensity scores and a 1:1 ratio for matching. After obtaining the postmatched dataset, we then compared preoperative and intraoperative variables of patients between the 2 periods. We used a multivariate logistic regression model to identify independent risks and odds ratios for MTC. We used the Kaplan–Meier analysis to compare survival for patients with and without MTC. Cox survival analysis was used to identify hazard risk for 1-y mortality after LT.

RESULTS

Our study included 2330 adult LT patients. In this study, the mean age was 54.0 (±11.3) y and the mean model for end-stage liver disease model (MELD)-Na score was 36.0 (±11.4). Thirty-six percent of patients were female, 36.3% had viral hepatitis cirrhosis, 25.0% had alcoholic cirrhosis, and 8% had nonalcoholic steatohepatitis (NASH). Preoperatively, 16.8% of patients required vasopressors, 23.4% required pretransplant mechanical ventilation, and 38.6% required hemodialysis. A total of 2002 patients underwent LT in period 1 and 328 patients in period 2.

Cryoprecipitate transfusion during LT in each year over 14 y is shown in Figure 1. Mean units of cryoprecipitate used during LT were consistently about 1 unit in each year from 2004 until 2015 when we started a trial of ROTEM. When we initiated ROTEM in August 2015, the use of cryoprecipitate increased significantly with mean cryoprecipitate

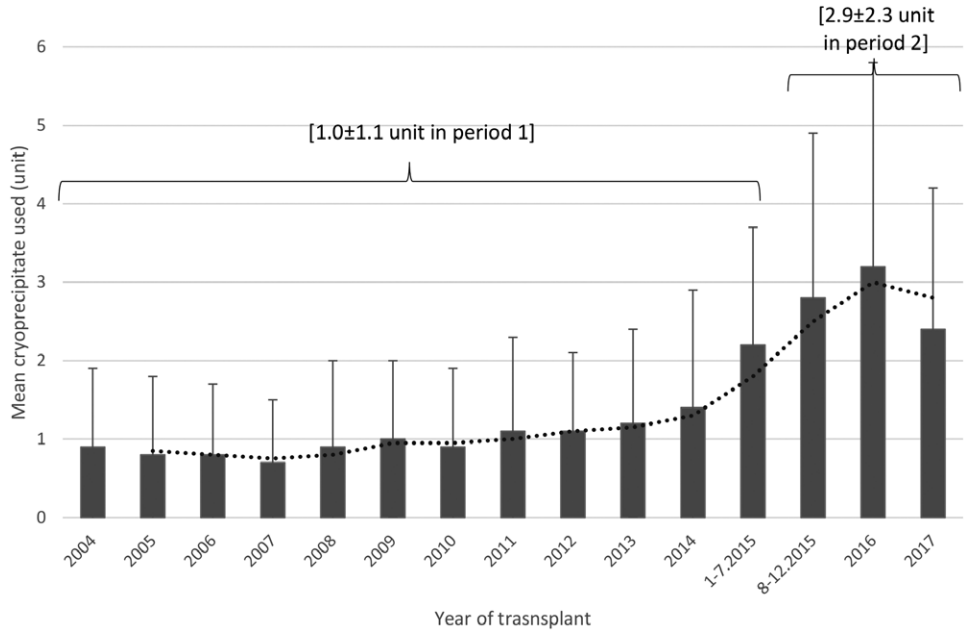

FIGURE 1. The cryoprecipitate use during liver over 14 y.

use of 2.9 ± 2.3 units during LT in period 2 ($P < 0.001$, Figure 1). Multivariate logistic regression showed that patients in period 2 had a 10-fold odds of receiving ≥3 units of cryoprecipitate during LT compared with those in period 1 after controlling baseline fibrinogen concentration, intraoperative RBC, and platelet transfusion (odds ratio 10.9, 95% confidence interval [CI] 7.7-15.6, $P < 0.001$). Comparison of transfusion requirements between the 2 periods for other blood products found that RBC was increased from 19.0 ± 17.1 to 24.1 ± 21.5 units ($P < 0.001$) and platelets from 1.3 ± 1.2 to 1.5 ± 1.3 units ($P = 0.012$). Transfusion of FFP was not significantly different (22.9 ± 18.4 versus 24.7 ± 21.7 units, $P = 0.194$) between periods 1 and 2.

During the entire study period, 115 patients developed MTC with the overall incidence of MTC being 4.9%. Four patients had 2 events, 1 patient had both ICT/PE and HAT, 1 patient had both HAT and stroke, and 2 patients had both ICT/PE and stroke. When the incidence of MTC was compared between the 2 periods, the incidence of MTC in period 2 was more than double (4.2% versus 9.5%, $P < 0.001$) (Figure 2). The incidence of all MTC events including ICT/PE, HAT, and stroke was significantly higher in period 2 compared to period 1 (Figure 2).

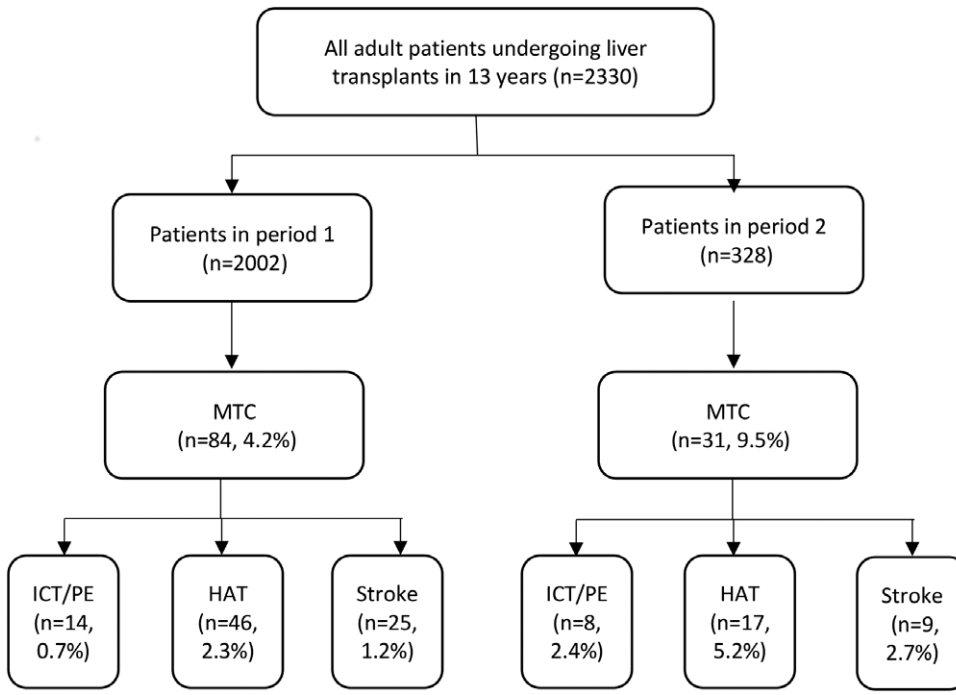

FIGURE 2. MTCs in the 2 periods. MTC, major thromboembolic complication.

TABLE 1.

Comparison of preoperative and intraoperative variables between the two periods using data before and after propensity match

	Before propensity match			After propensity match		
Variables	**Period 1 (n = 2002)**	**Period 2 (n = 328)**	**P**	**Period 1 (n = 326)**	**Period 2 (n = 326)**	**P**
Age (y)	54.0 ± 11.3	54.3 ± 11.5	0.663	53.6 ± 11.6	54 ± 11.5	0.450
Weight (kg)	80.1 ± 19.7	81.7 ± 23.3	0.247	83.0 ± 20.1	81.8 ± 23.4	0.492
Height (cm)	169.4 ± 10.6	168.6 ± 10.5	0.212	169.6 ± 11.0	168.6 ± 10.5	0.277
MELD-Na	25.2 ± 11.4	30.5 ± 10.5	<0.001	30.6 ± 11.0	30.5 ± 10.5	0.901
Encephalopathy	44.0	56.6	<0.001	56.1	56.6	0.891
Intubation	23.5	22.4	0.690	30.5	29.8	0.857
Hypertension	30.5	28.8	0.557	30.0	28.8	0.737
Coronary artery disease	8.0	12.5	0.012	9.9	12.5	0.319
Preoperative dialysis	36.6	52.5	<0.001	50.3	52.3	0.609
Diabetes mellitus	26.2	32.6	0.024	32.0	32.6	0.867
Gastroesophageal bleeding	33.9	42.3	0.006	40.5	42.7	0.570
Hepatitis C	31.0	22.0	0.004	23.0	22.2	0.823
Hepatitis B	6.6	4.7	0.257	5.5	4.8	0.683
Nonalcoholic steatohepatitis	6.4	17.4	<0.001	18.4	17.5	0.759
Baseline platelet counts	69.8 ± 51.3	68.7 ± 56.8	0.750	71.0 ± 56.2	68.8 ± 57.0	0.624
Baseline INR	1.8 ± 0.6	2.0 ± 0.7	<0.001	2.0 ± 0.8	2.0 ± 0.7	0.885
Baseline fibrinogen	170.0 ± 86.1	149.3 ± 92.8	0.001	153.6 ± 82.0	149.3 ± 92.8	0.552
Postreperfusion syndrome	15.8	20.8	0.040	19.1	20.8	0.626
Cold ischemia time (min)	410.2 ± 147.8	471.4 ± 150.8	<0.001	468.1 ± 156.3	471.3 ± 151.0	0.802
Warm ischemia time (min)	43.7 ± 11.8	52.2 ± 15.5	<0.001	49.9 ± 15.3	52.2 ± 15.6	0.068
Surgical time (min)	324.6 ± 72.5	336.6 ± 60.9	0.001	343.9 ± 84.0	336.7 ± 61.0	0.216
Intraoperative venovenous bypass	34.9	49.7	<0.001	50.3	49.7	0.876
Intraoperative dialysis	11.3	24.0	<0.001	23.6	24.0	0.913

Postreperfusion syndrome is defined as by a decrease in mean artery pressure by 30% for at least 1 min during the first 5 min after portal reperfusion.
MELD-Na, model for end-stage liver disease-sodium.

Comparison of patient variables between the 2 periods found that patients in period 2 had higher acuity of liver disease and comorbidities. As shown in Table 1, patients in period 2 had higher MELD-Na scores, a higher percentage of NASH as diagnosis, more encephalopathy and more preoperative hemodialysis, compared with those in period 1. In addition, patients in period 2 had higher baseline INR and lower fibrinogen levels. Intraoperatively, patients in period 2 had a higher percentage of VVB, longer cold ischemia time, warm ischemia time, and surgery time than those in period 1.

Ten variables (age, MELD-Na, steatohepatitis, platelet count, INR, surgery time, use of VVB, cold ischemia time, warm ischemia time, and intraoperative dialysis) were selected in a logistic regression model to generate propensity scores. After matching, there were 326 patients in each period. After matching, patient characteristics, preoperative and intraoperative variables were comparable and significant differences between the 2 periods were eliminated (Table 1).

After matching, there were no significant differences in RBC and platelet transfusions between periods 1 and 2. FFP transfusion was significantly less in period 2 compared with period 1. However, cryoprecipitate use remained significantly increased (2.9 ± 2.6 units for each LT case) in period 2 compared with that in period 1 (1.6 ± 2.3 units, $P < 0.001$) (Table 2).

Postmatch analysis showed MTC was 4.0% in period 1 and 9.5% in period 2 ($P < 0.005$). We then compared patients with and without MTC using the postmatch data. No significant differences were detected regarding preoperative and intraoperative variables except for age, intraoperative RBC, and cryoprecipitate transfusions (Table 3) and pressors. Age was significantly higher in the MTC group than in the non-MTC group. RBC was increased from 24.5 units in patients in the non-MTC group to 32.0 units in patients in the MTC group ($P = 0.030$). A significantly higher number of patients in the MTC group required ≥18 units of RBC transfusion compared with those in the non-MTC group. Cryoprecipitate use was increased from 2.1 units in patients without MTC to 3.6 units in patients with MTC ($P < 0.001$). Both pressor infusion and bolus were significantly higher in the MTC group compared with the non-MTC group (Table 3).

TABLE 2.

Blood products used during transplant between 2 periods using postmatched data

	Period 1 (n = 326)	Period 2 (n = 326)	P
Red blood cells (units)	25.8 ± 21.5	24.1 ± 21.5	0.326
Fresh–frozen plasma (units)	30.3 ± 22.7	24.7 ± 21.7	0.002
Platelets (units)	1.5 ± 1.2	1.5 ± 1.3	0.900
Cryoprecipitate (unit)	1.6 ± 2.3	2.9 ± 2.6	<0.001
Pressor infusion	79.7	96.4	<0.001
Pressor bolus	39.3	48.7	0.021

Multivariable logistic regression revealed that intraoperative cryoprecipitate and RBC transfusion were 2

TABLE 3.

Variables between patients with and without MTC

	Nonthromboembolic group (n = 608)	Thromboembolic group (n = 44)	P
Age	53.7 ± 11.8	57.4 ± 7.1	0.037
Weight (kg)	82.6 ± 21.6	79.3 ± 23.8	0.339
Height (cm)	168.9 ± 10.5	171.1 ± 13.6	0.240
MELD-Na	30.5 ± 10.7	30.8 ± 10.6	0.650
Encephalopathy	56.1	56.6	0.891
Intubation	30.7	22.4	0.021
Hypertension	30.0	28.8	0.737
Coronary artery disease	9.9	12.5	0.319
Preoperative dialysis	50.3	52.5	0.592
Diabetes mellitus	32.0	32.6	0.867
Gastroesophageal bleeding	40.5	42.3	0.659
Hepatitis C	23.0	22.2	0.823
Hepatitis B	5.5	4.8	0.683
Nonalcoholic steatohepatitis	18.4	17.5	0.759
Platelet count	70.8 ± 57.3	57.5 ± 43.1	0.131
INR	2.0 ± 0.7	2.0 ± 0.8	0.966
Postreperfusion syndrome	19.1	20.8	0.626
Cold ischemia time (min)	466.4 ± 149.8	440.3 ± 114.4	0.258
Warm ischemia time (min)	50.1 ± 14.2	51.7 ± 13.6	0.456
Surgery time (min)	340.7 ± 74.3	334.4 ± 61.3	0.583
Venovenous bypass	50.3	49.7	0.876
Red blood cells (units)	24.5 ± 20.7	31.9 ± 29.6	0.030
RBC transfusion groups divided by a median value			
<18 units	46.9	23.6	0.007
≥18 units	53.1	74.4	
Fresh–frozen plasma (units)	27.5 ± 22.1	30.5 ± 26.4	0.391
Cryoprecipitate (unit)	2.1 ± 2.3	3.6 ± 4.6	<0.001
Platelets (units)	1.5 ± 1.3	1.6 ± 1.4	0.633
Intraoperative dialysis	23.6	24.0	0.913
Pressor infusion	79.7	96.4	<0.001
Pressor bolus	39.3	48.7	0.021

INR, international normalized ratio; MELD-Na, model for end-stage liver disease-sodium; MTC, major thromboembolic complication; RBC, red blood cell.

independent risk factors for the development of MTC (Table 4). Patients who received 18 or more units of RBC had 2 times higher odds of developing MTC compared with those who received less RBC. The increased use in cryoprecipitate was associated with higher odds of developing MTC. However, the risk was significantly increased when 2 units of cryoprecipitate were administered during LT (MTC occurred at 3.9%–7.5% in the 0–2 unit of cryoprecipitate group versus 10.8% in the 3 or more units group, $P = 0.026$, Figure 3). Because ROTEM data were only available after the ROTEM implementation, the analysis could be performed on patients in period 2. The analysis of FIBTEM showed none of the baseline and postreperfusion values were significantly different between patients with and without MTC (Table 5). Analysis of other EXTEM and INTEM failed to show significant differences between patients with and without MTC (**Table S1,** http://links.lww.com/TP/C22).

TABLE 4.

Multivariate logistic regression model for MTC

	Odds ratio	95% CI	*P*
Cryoprecipitate (unit)	1.138	1.044-1.242	0.003
Red blood cells ≥ 18 units (median)	2.063	1.004-4.240	0.049

MTC, major thromboembolic complication.

The Kaplan–Meier survival analysis showed patients in the MTC group had decreased 1-y survival (70.2%) after LT compared to those in the non-MTC group (85.9%, Log-rank test, $P < 0.001$) (Figure 4). Cox survival analysis showed that MTC was a risk factor for 1-y mortality (hazard ratio 2.17, 95% CI 1.506-3.126, $P < 0.001$). Other risk factors for 1-y mortality included MELD-Na score, pretransplant mechanical ventilation, and intraoperative RBC transfusion (hazard ratios 1.009–1.649, 95% CI 1.004-2.102, all $P < 0.001$).

DISCUSSION

In this large retrospective study of 2330 adult patients, we found that the implementation of ROTEM was associated with increased cryoprecipitate usage and an increased incidence of MTC in LT. We further demonstrated that the increased use of cryoprecipitate was an independent risk factor for MTC. Our study suggests that the implementation of ROTEM and the use of cryoprecipitate may play significant roles in the development of MTC in LT. The benefits and risks of cryoprecipitate transfusion need to be carefully evaluated before administration.

Patients undergoing LT are diverse, many of whom have the underlying conditions that may lead to thromboembolic complications. LT patients, despite having prolonged prothrombin time and clinically apparent bleeding, may have a paradoxically hypercoagulable state, with high procoagulant activity and a decrease in native anticoagulants.[2,19] Patients with cirrhosis may exhibit a "rebalanced hemostatic system," which is characterized by a balance in low levels of procoagulation and anticoagulation factors and a low threshold to develop either hypocoagulopathy or hypercoagulopathy. Systemic hypocoagulopathy may coexist with regional hypercoagulopathy in these patients. Hemodynamic compromise, venous stasis, and disseminated intravascular coagulation may also lead to thromboembolic complications.[20] During massive bleeding and blood resuscitation, a transient hypercoagulable state is possible if transfusion is not well balanced.

Although ROTEM is superior to conventional tests, it has limitations. First, the normal ranges of ROTEM are obtained from individuals without end-stage liver disease and clinical implications of these ranges in the setting of LT are ill-defined. LT patients may have ROTEM values that are often distributed below the normal ranges, similar to the values measured by the conventional tests.[16] A level below the normal range of the conventional tests in LT patients does not mean that transfusion is necessary. We suspect that the same principle would apply in the relationship between ROTEM and transfusion as well. Second, blood and factor transfusion indications based on ROTEM values are not well defined. Although a few retrospective studies have shown a relationship between ROTEM values and transfusion, the optimal ROTEM values that indicates the need for cryoprecipitate to treat clinically bleeding are unknown.[15] Third, some studies suggest that ROTEM can

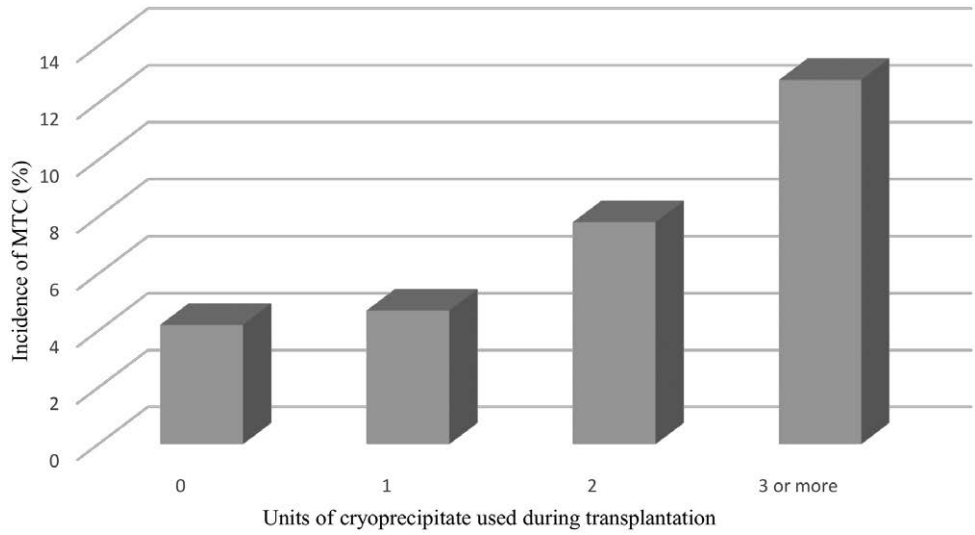

FIGURE 3. Units of cryoprecipitate used in transplantation in relationship with the development of MTC. MTC, major thromboembolic complication.

TABLE 5.

ROTEM (FIBTEM) values in patients with and without MTC

Test time	Test items	Non-MTC (n = 297)	MTC (n = 31)	*P*
Baseline	CT	256.3 ± 448.9	343.7 ± 481.7	0.650
	A10	8.0 ± 5.5	8.4 ± 6.4	0.824
	A20	8.6 ± 5.6	9.5 ± 7.4	0.581
	MCF	8.5 ± 6.1	9.2 ± 6.6	0.676
Postreperfusion	CT	147.0 ± 299.8	252.5 ± 475.5	0.317
	A10	6.7 ± 2.8	6.9 ± 2.4	0.831
	A20	7.6 ± 3.4	8.2 ± 2.3	0.263
	MCF	7.7 ± 4.9	7.9 ± 2.7	0.817

A10, amplitude 10 min after CT; A20, amplitude 20 min after CT; CT, clotting time; MCF, maximum clot firmness; MTC, major thromboembolic complication; ROTEM, rotational thromboelastometry.

be variable and inappropriate for hemostasis assessment in some clinical conditions.[16,21,22] Finally, many studies including this one have shown that ROTEM is associated with the increased use of cryoprecipitate. Even preparation to implement ROTEM (trial before the official usage) is associated with a modest increase between January 2015 and July 2015 in the cryoprecipitate use shown in this study (Figure 1). Because the ROTEM-associated change in transfusion practice is not necessarily benign or beneficial, the optimal ROTEM cutoffs in LT and ROTEM-derived transfusion algorithms need to be carefully evaluated in future studies.

Cryoprecipitate contains concentrated procoagulants including fibrinogen, von-Willebrand factor, factor VIII, and factor XIII.[2] Supraphysiologic levels of procoagulants in cryoprecipitate may lead to thromboembolic complications.[23] In the setting of endothelial dysfunction, cryoprecipitate may contribute to the development of thromboembolic events.[2,24] A previous long-term observational study found cryoprecipitate administration was associated with thromboembolic events.[25] But the majority of the thromboembolic events from this study were deep venous thrombosis, which may be multifactorial in origin. The preparation of cryoprecipitate through freezing and thawing can generate thrombotic particles or clots.[26] Clinically, some believe that cryoprecipitate, because of containing both precoagulant and anticoagulant, is safer regarding the thromboembolic risk compared with other blood products like platelets. Our findings, in contrast to this belief, highlight the importance of the benefits (hemostasis) and risks (cost and thromboembolic complications) assessment before cryoprecipitate administration.

Our findings are limited by the nature of retrospective single-center study. Additionally, this study involved a long period, which was required to accumulate a sufficient number of MTC. Patients in period 2 tended to be more critically ill, with higher MELD-Na score and transfusion requirements, likely owing to changes in allocation policies. However, we used a robust matching method to minimize the selection bias in this study. It is possible that ROTEM implementation was coincident with other events that we were unaware of, which may have influenced the rates of thromboembolic events or transfusions. Because the etiologies of the MTC are not identical, it is possible to introduce bias when combining them together. For example, surgical factors, such as differences in individual surgical technique and other anatomic differences, may play a role in the development of HAT, which is not addressed in this study. However, ICT, PE, HAT, and ischemic stroke are thromboembolic events sharing a common pathophysiology,[2] which forms the basis for 1 group in the study.

In conclusion, we found in this large retrospective study that the implementation of ROTEM-guided transfusion was associated with an increase in cryoprecipitate usage and an increased incidence of MTC in LT. Increased use of cryoprecipitate was independently associated with MTC. Patients with MTC experienced significantly decreased 1-y survival. Our study suggests that the implementation of ROTEM and the use of cryoprecipitate play significant roles in the development of MTC in LT. The benefits and risks of cryoprecipitate need to be carefully evaluated before administration. Furthermore, these findings support the judicious use of cryoprecipitate during LT and call for more studies to evaluate the optimal ROTEM-derived transfusion algorithms in LT.

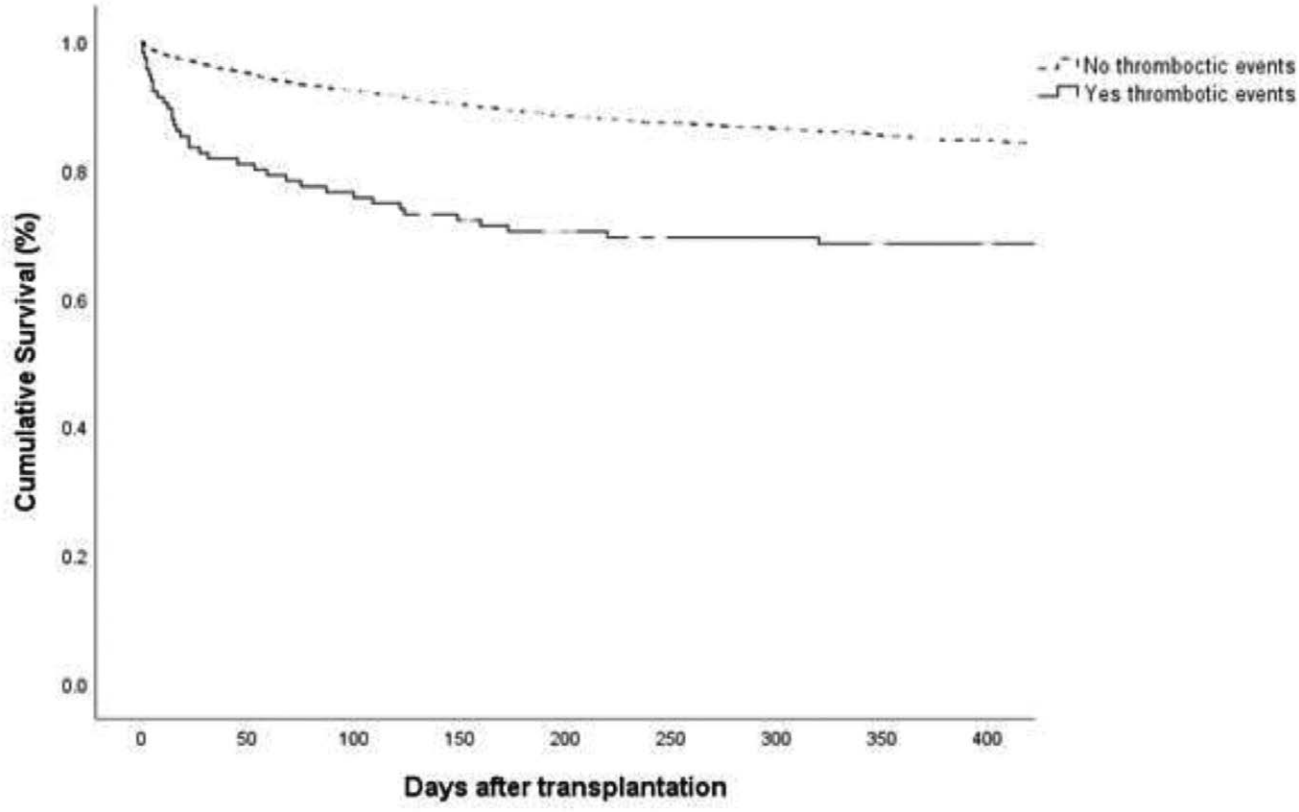

FIGURE 4. Survival curve of patients with and without MTC. MTC, major thromboembolic complication.

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