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Intraoperative Thromboelastometry as a Predictor of Blood Transfusion Requirements during Adult Living Donor Liver Transplantation

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ABSTRACT

Background: Blood transfusion contributes to the correction of hemostasis impairment and perioperative bleeding. **Objective:** To evaluate the ROTEM variables before the operation to predict the blood transfusion requirements in liver transplant patients. **Study Design:** A prospective observational study. **Settings:** This study was carried out at Department of Anesthesia and Hepatobiliary Unit, Shaikh Zayed Hospital, Lahore Pakistan. **Duration:** From 1st July 2022 to 31st December 2022. **Methods:** A total of 100 consecutive patients undergoing liver transplants were included in the study. Thromboelastometry was performed on all patients and quality control was done by ROTROL N on alternate days. Additionally, EXTEM and INTEM were also performed on the days the system was used. When transfusion was needed, fresh frozen plasma (10m/kg), cryoprecipitate (1unit/10kg body weight), and platelets (6 single donor units) were given. A 24% hematocrit was maintained by transfusing packed red blood cells. Blood loss during the procedure was evaluated by applying modified Gross formula. **Results:** Variables including EXTEM clotting time (95% CI: 1.015-1.264), Maximum clot formation (0.764-0.985), INTEM clotting time (0.897-0.990), Clot formation time (0.955-0.989), and Maximum clot formation (0.416-0.845) were independent predictors of red blood cell transfusion with FIBTEM Maximum clot formation (0.9-1.039) being the dependent predictor. EXTEM clotting time (0.912-0.990), Clot formation time (0.9-1.076), and FIBTEM Maximum clot formation (0.109-0.889) were independent predictors while EXTEM angle α (0.899-2.445) and INTEM variables were dependent predictors of plasma transfusion. In the case of platelet transfusion, EXTEM (1.048-2.131) and INTEM maximum clot firmness (0.299-0.795) were independent predictors. All the thromboelastometric variables in cryoprecipitate transfusion were independent predictors. **Conclusion:** Thromboelastometry is an efficient method for the prediction of intraoperative bleeding and transfusion requirements during a liver transplant.

Keywords: *Liver transplant, Thromboelastometry, Blood transfusion, Blood coagulation.*

INTRODUCTION

Blood transfusion is a common practice during liver transplants but its methods vary in the literature.[1,2] It is important to mention that chronic liver failure patients present normal viscoelastic testing profiles even with low platelet count and high international normalized ratio. This indicates that these patients can maintain hemostasis and may have a successful surgery without transfusion. But this balance is not stable and can immediately lead to bleeding or thrombosis.[3,4] Therefore, it is critical to predict the loss of blood during the operation and the need for transfusion to ensure the availability of blood and required treatment in case of bleeding. This will be helpful to anesthetists as they would be able to determine

beforehand the patient requirement and the precautionary methods needed during the operation. It would also be a cost-effective approach as a calculated amount of blood will be prepared for each patient and the excess blood will be reserved for patients as high risk. Several studies have been conducted to determine the factors that predict the intraoperative outcomes in patients and ways to identify them.[5-7]

Still, the management of coagulation and transfusion techniques during liver transplants is a field that requires work. The risk of intraoperative bleeding can be predicted by monitoring the body's hemostatic reaction perioperatively during surgery to find out the causes of bleeding and treat it timely.[8]

Currently, used coagulation tests are ineffective and can't be relied upon in a perioperative setting as it takes too long to get their results back and hemostatic changes can't be highlighted in late-stage liver disease. In comparison to traditional methods, thromboelastometry is not only faster and more detailed but also provides a clinical assessment of coagulation status as indicated by research.[9,10] The purpose of this study was to evaluate the ROTEM variables before the operation to predict the blood transfusion requirements in liver transplant patients.

METHODS

A prospective observational study was conducted in the This study was carried out at Department of Anaesthesia and Hepatobiliary Unit, Shaikh Zayed Hospital Lahore from August 2017 to August 2019. A total of 100 consecutive patients undergoing liver transplants were included in the study. Patients who experienced severe bleeding during surgery due to vascular injury were not included in the study. All the patients provided their written consent to become a part of the study. The study design and methodology were approved by the ethical committee of the hospital.

Thromboelastometry was performed on all patients and quality control was done by ROTROL N on alternate days. Additionally, EXTEM and INTEM were also performed on the days the system was used. Blood samples were taken before the operation, at every stage during the transplant, and also in case of intraoperative bleeding. Thromboelastometry was performed at room temperature within 10 minutes of blood collection. One anesthetist performed all the perioperative analyses and had no part in managing the patients. The anesthetist involved with the management of recipients performed the intraoperative analysis for decision-making during the operation and was blinded to the analysis done by the other anesthetist.

No medication was administered to the patients before the procedure. After standard monitoring by the anesthetist, propofol 2 mg/kg and fentanyl 1.5µg/kg were administered to induce anesthesia, and rocuronium 0.9mg/kg was also administered for Endotracheal intubation. Maintenance of anesthesia was done by sevoflurane in O2 and fentanyl. Electrolytes and pH were checked after every hour. When transfusion was needed, fresh frozen plasma (10m/kg), cryoprecipitate (1unit/10kg body weight), and platelets (6 single donor units) were given. A 24% hematocrit was maintained by transfusing packed red blood cells. If hyperfibrinolysis was detected as a result of thromboelastometry, tranexamic acid (10mg/kg) was administered. Blood loss during the procedure was evaluated by applying modified Gross formula.

All the data were analyzed by SPSS version 17. A p-value less than 0.0.5 was regarded as statistically significant. ROC curve was used to assess the cutoff values for sensitivity and specificity. To assess the factors that appeared distinct in the univariate analysis, multivariate analysis was performed for the calculation of 95% CI and odds ratio.

RESULTS

Out of 100 patients selected for the study, 95 patients were included in the final analysis. 2 were excluded due to vascular injury and 3 of the patients developed a hepatic tumor so they had to be excluded from the study. 68 patients were diagnosed with hepatitis C and the remaining 27 patients suffered from hepatocellular carcinoma along with Hep-C. The average age of the study patients was 45.1 ± 5.5 years and the MELD score was 15.14 ± 3.09. The average time of surgery was 9.09 ± 2.29 hours. The average ratio between graft volume and body weight of patients was 1.01 ± 0.1. Tranexamic acid was given to 5 patients. The intraoperative analysis of patients is shown in Table I. 15% of the patients did not require any type of transfusion, 20% were not transfused packed red blood cells, 35% were not transfused fresh frozen plasma, 85% were not transfused platelets and 62% were not transfused cryoprecipitate.

The results in table 2 show a significant association between packed red blood cells transfusion and the variables analyzed in the thromboelastometry. Variables including EXTEM clotting time, MCF, INTEM clotting time, CFT, and MCF were independent predictors of this transfusion with FIBTEM MCF being the dependent predictor.

Table 1: Intraoperative data

	Mean	Standard deviation	Minimum	Maximum
aPTTs	46.4	13.1	21	93
INR	1.54	0.33	0.8	2.5
Platelet count, mm^{-3}	69.18	28.13	22	148
HB, g/dl	10.10	1.22	7.6	13
HCT, %	31.5	3.3	23	43
Fibrinogen, mg/dl	123.83	52.14	32	298
EXTEM clotting time, s	88.00	42.4	32	226
EXTEM clot formation time, s	291.96	139.92	91	792
INTEM maximum clot firmness, mm	41.75	8.93	26	66
EXTEM ANG α, degree	48.82	11.7	27	76
INTEM clotting time, s	177.08	47.17	98	330
INTEM clot formation time, s	245.2	104.1	81	560
INTEM maximum clot firmness, mm	42.22	6.55	26	61
INTEM ANG α, degree	48.34	12.11	22	76
FIBTEM MCF, mm	8.22	1.45	3	15
Blood loss, ml	3150	995.2	1450	5550
PRBCs, units	3.98	2.9	0	13
FFP, units	3.99	3.90	0	17
Platelets, units	1.4	1.09	0	22
Cryoprecipitate, units	3.2	1.92	0	20

Table 2: Transfusion of Fresh blood plasma, Packed red blood cells, Platelets, and Cryoprecipitate

	Variables	B	SE	P	OR	95% CI
Packed red blood cells transfusion	β0 26.42					
	EXTEM clotting time	0.125	0.042	<0.05	1.135	1.015-1.264
	EXTEM maximum clot formation	-0.525	0.055	<0.05	0.865	0.764-0.985
	INTEM clotting time	0.042	0.019	<0.05	0.940	0.897-0.990
	INTEM clot formation time	0.017	0.008	<0.05	0.969	0.955-0.989
	INTEM maximum clot formation	-0.508	0.170	<0.01	0.590	0.416-0.845
	FIBTEM maximum clot formation	-0.619	0.008	<0.05	1.015	0.9-1.039
	R^2= 0.60					
Fresh frozen plasma transfusion	β0 13.49					
	EXTEM clotting time	0.039	0.017	<0.05	0.948	0.912-0.990
	EXTEM clot formation time	0.037	0.015	<0.05	1.037	0.9-1.076
	EXTEM ANG α	-0.292	0.246	>0.05	1.486	0.899-2.445
	INTEM clotting time	0.040	0.019	>0.05	1.041	0.991-1.099
	INTEM clot formation time	0.052	0.009	>0.05	0.968	0.607-0.9
	INTEM maximum clot firmness	-0.225	0.128	>0.05	0.788	0.608-1.020
	INTEM ANG α	-0.291	0.231	>0.05	0.669	0.417-1.062
	FIBTEM MCF	-0.939	0.519	<0.05	0.315	0.109-0.889
	R2= 0.81					
Platelet transfusion	β0 9.89					
	EXTEM maximum clot firmness	-0.101	0.179	0.019	1.498	1.048-2.131
	INTEM maximum clot firmness	-0.9	0.237	0.003	0.490	0.299-0.795
	R2= 0.42					
Cryoprecipitate transfusion	β0 28.09					
	FIBTEM MCF	-1.497	0.008	0.001	0.569	0.949-0.982
	EXTEM clot formation time	0.010	0.006	0.010	1.012	0.9-1.025
	EXTEM maximum clot firmness	-0.301	0.055	0.005	0.858	0.755-0.979
	INTEM clotting time	0.015	0.008	0.019	0.978	0.959-0.990
	INTEM clot formation time	0.019	0.009	0.001	0.959	0.939-0.979
	INTEM maximum clot firmness	-0.299	0.080	0.001	0.749	0.429-0.890
	R2= 0.59					

Similarly, these variables were also associated with fresh frozen plasma transfusion. EXTEM clotting time, CFT, and FIBTEM MCF were independent predictors while EXTEM angle α and INTEM were dependent predictors. In the case of platelet transfusion, EXTEM and INTEM maximum clot firmness were independent predictors. All the thromboelastometric variables in cryoprecipitate transfusion were independent predictors. The sensitivity and specificity value of thromboelastometric variables is shown in table 3.

Table 3: The cut-off values, specificity, and sensitivity of thromboelastometric variables

Variables	Cutoff value	Sensitivity	Specificity	AUC	Accuracy	PPV	NPV	p	SE	95% CI
Packed red blood cells										
EXTEM clotting time, s	59	78.6%	62.7%	0.70	75.1%	45.2%	19.4%	<0.01	0.04	0.55-0.75
INTEM clotting time, s	152	78.6%	53.4%	0.69	74.2%	44.4%	19.4%	<0.01	0.04	0.54-0.75
INTEM clot formation time, s	201	70.4%	71.6%	0.69	74.1%	26.2%	27.1%	<0.01	0.05	0.53-0.75
EXTEM maximum clot firmness, mm	41	100%	69.8%	0.80	85.2%	28.4%	0%	<0.01	0.02	0.79-0.83
INTEM maximum clot firmness, mm	41.2	100%	70.4%	0.82	87.0%	27.1%	0%	<0.01	0.02	0.79-0.85
Fresh frozen plasma										
EXTEM clotting time, s	65	76.2%	56.3%	0.69	72.1%	41.0%	21.5%	<0.01	0.04	0.52-0.73
EXTEM clot formation time, s	220	82.1%	77.3%	0.89	89.8%	20.0%	15.0%	<0.01	0.02	0.74-0.85
FIBTEM MCF, mm	8.2	83.6%	73.1%	0.79	79.7%	24.5%	14.7%	<0.01	0.03	0.68-0.79
Cryoprecipitate										
INTEM clotting time, s	176.2	76.4%	64.4%	0.62	66.4%	33.3%	21.1%	<0.01	0.04	0.46-0.66
EXTEM clot formation time, s	235.9	76.4%	55.1%	0.68	73.5%	42.7%	21.1%	<0.01	0.03	0.55-0.79
INTEM clot formation time, s	201.1	76.4%	45.3%	0.65	70.3%	52.1%	21.1%	<0.01	0.04	0.59-0.78
EXTEM maximum clot firmness, mm	34.2	89.5%	51.6%	0.70	77.5%	46.1%	8.3%	<0.01	0.04	0.59-0.81
INTEM maximum clot firmness, mm	35.7	86.3%	62.8%	0.78	79.4%	36.0%	11.4%	<0.01	0.04	0.68-0.80
FIBTEM MCF, mm	7.2	80.1%	82.2%	0.80	84.2%	15.6%	17.6%	<0.01	0.03	0.57-0.89
Platelets										
EXTEM maximum clot firmness, mm	35.6	72.5%	72.1%	0.69	72.1%	65.8%	25.0%	<0.05	0.05	0.54-0.76
INTEM maximum clot firmness, mm	37.4	72.5%	82.2%	0.79	81.1%	15.6%	25.0%	<0.01	0.04	0.69-0.86

DISCUSSION

This study was conducted to assess ROTEM variables before the operation to predict the blood transfusion requirements in liver transplant patients. Several studies have been conducted to predict intraoperative transfusion but that was done by conventional coagulation tests, we used the thromboelastometric variables which were way more efficient.[11] A study by Caldwell *et al*[12] also suggested that traditional coagulation tests were not effective enough to get a full analysis of the coagulation process, thus methods like thromboelastometry should be used to carry out such analysis. Similarly, Hass *et al*[13] also indicated that variables that if PT and aPTT did not prove to be effective predictors of intraoperative bleeding or the need for transfusion. Conventional coagulation tests did not receive much appreciation from Reyle-Hahn *et al*[14] and Massicotte *et al*[15] either which showed that these are not a helpful predictor of blood transfusion need during a liver transplant.

In this study, the results prove that thromboelastometry was helpful in predicting the need for blood transfusion and the intraoperative bleeding during a liver transplant. Thromboelastometry has been previously used to predict the need for transfusion during cardiac surgery and this study also suggested that this method may also predict blood loss after the operation. However, Davidson *et al*[16] and Cammerer *et al*[17] negate this conclusion and conclude that thromboelastometry is a good predictor of intraoperative transfusion but is not useful to predict postoperative bleeding after heart surgery. These studies differed from our study with respect to baseline variables. The blood loss in our study was much higher than in these studies i.e 3150ml, while in Davidson *et al*[16] and Cammerer *et al*[17] it was 787 ml and 536 ml respectively. The lesser the blood loss, the less efficient are the thromboelastometry prediction ability. This is proved by Lee *et al*[18] in Davidson *et al*,[16] there was not only a limited number of patients but also only one red blood cell transfusion was done except in 1 patient. While in our study, 80% of patients were transfused packed red blood cells, 65% fresh frozen plasma, 15% platelets, and 38% received cryoprecipitate. An association between the number of patients getting a blood transfusion and the thromboelastometric prediction was shown through the regression coefficient which was lowest for platelet transfusion. In addition, we analyzed coagulopathic patients which led to positive predictive results.

Our study also proved that the number of patients transfused increases the predictive ability of

thromboelastometry. This has been supported by Plotkin *et al*.[19]

The results of our study suggested MCF as an independent predictor of packed red blood cells transfusion with an AUC value of 0.82 and sensitivity and specificity of 100% and 70.4% respectively. The results are supported by Leemann *et al*.[20] and Schöchl *et al*.[21] Similarly, EXTEM and INTEM maximum clot firmness were independent predictors of platelets and cryoprecipitate transfusion, and the AUC values were in agreement with Roullet *et al*[22] and Blasi *et al*.[23] In our study FIBTEM MCF was a strong independent predictor of plasma transfusion, these results were also reported by Rumph *et al*.

CONCLUSION

Thromboelastometry is an efficient method for the prediction of intraoperative bleeding and transfusion requirements during liver transplants.

LIMITATIONS

We could not analyze all the derangement intraoperative factors which affect the intraoperative transfusion requirement as thromboelastometry was not capable of analyzing them. Also, our predictive model did not consider the loss of blood and the need for transfusion due to surgical bleeding.

SUGGESTIONS / RECOMMENDATIONS

It is recommended that further research be carried out using greater sample.

CONFLICT OF INTEREST / DISCLOSURE

None.

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