

The effect of thromboelastogram-guided transfusion on postoperative complications and transfusion requirement in the post-reperfusion period in liver transplantation surgery

Gülçin Büyükbezirci¹, Ahmet Topal¹, Resul Yılmaz¹, Feyza Kolsuz Erdem¹, Tefvik Küçükartallar²

¹ Department of Anesthesiology and Reanimation, Necmettin Erbakan University, Meram Faculty of Medicine, Konya, Turkey

² Department of General Surgery, Necmettin Erbakan University, Meram Faculty of Medicine, Konya, Turkey

ORCID ID of the author(s)

GB: 0000-0002-9438-3414
AT: 0000-0001-9832-9741
RY: 0000-0002-5527-2893
FKE: 0000-0003-4250-236X
TK: 0000-0002-6326-4623

Corresponding Author

Gülçin Büyükbezirci
Necmettin Erbakan University, Meram Faculty of Medicine, Department of Anesthesiology and Reanimation, Hocacihan Neighborhood, Abdulhamid Han Street, Selçuklu, Konya, Turkey
E-mail: drgulcin81@gmail.com

Ethics Committee Approval

The study was approved by the Non-Pharmaceutical and Non-Medical Device Research Ethics Committee of Necmettin Erbakan University, Date: 06/01/2023, Number: 2023-4101.

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Published

2023 January 29

Copyright © 2023 The Author(s)

Published by JOSAM

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND 4.0) where it is permissible to download, share, remix, transform, and build upon the work provided it is properly cited. The work cannot be used commercially without permission from the journal.



Abstract

Background/Aim: Liver transplantation surgery is one of the most common abdominal surgeries requiring blood transfusion. Coagulation parameters vary during the perioperative period because of the patient profile. Blood transfusion management should be carefully controlled to avoid causing dysfunction in the newly transplanted organ. Various laboratory parameters are used to achieve this. This study aimed to investigate the effect of transfusion managed by conventional coagulation tests or thromboelastogram (TEG) on blood product consumption and postoperative outcomes in the post-reperfusion period.

Methods: The records of 90 recipients who underwent transplantation between January 1, 2012, and November 30, 2022, were retrospectively analyzed. Twenty patients who were administered blood transfusion under TEG guidance in the post-reperfusion period constituted the case group, while 20 patients non-consecutive randomly selected among other patients who were administered blood transfusion with conventional coagulation tests constituted the control group. In conclusion, 40 patients were included in this retrospective case-control study. We retrospectively analyzed demographic data, surgical data, perioperative laboratory parameters, intraoperative total and post-reperfusion blood and blood product transfusions, TEG parameters, and postoperative complications.

Results: No difference was found between the groups regarding demographic data, etiological factors, surgical data, and preoperative laboratory parameters ($P>0.05$). There was a significant decrease in the amount of fresh frozen plasma (FFP) transfused in the case group compared to the control group in the intraoperative total and post-reperfusion period ($P=0.011$, $P=0.003$). There was no difference between the groups regarding other blood product transfusions and postoperative complications ($P>0.05$). Regarding the effects of intraoperative total and post-reperfusion blood and blood products on ventilator stay, intensive care unit stay, length of stay (LOS), hepatic artery thrombosis, graft rejection, postoperative kidney damage, and first 28-day mortality, only a weak negative correlation was found between intraoperative total and postreperfusion fibrinogen use and LOS ($r=-0.325/P=0.041$, $r=-0.354/P=0.025$).

Conclusion: TEG-guided transfusion in the post-reperfusion period reduced total blood product consumption. Besides, the increase in the use of fibrin has led to a decrease in LOS. However, using TEG has no significant effect on postoperative mortality and morbidity. TEG and an objective assessment of patient clinical status may be an ideal guide for transfusion strategy.

Keywords: liver, transplantation, thromboelastography, blood transfusion

Introduction

Thanks to the advancements in surgical techniques, anesthesia management, and graft preservation in liver transplantation, transplantation can be terminated with a minimal requirement for transfusions [1]. However, transfusion requirements in transplant surgery remain highly variable, and there is no universal consensus regarding transfusion thresholds [2]. Different factors determine the need for blood transfusions, such as perioperative anemia, coagulation disorders, decreased platelet counts, and surgical complications. Besides, the procoagulant and anticoagulant components of the coagulation cascade are affected to varying degrees in patients with liver failure. For this reason, bedside, rapid-result, and comprehensive viscoelastic tests should be used in liver transplantation surgery rather than conventional coagulation tests, which provide information about certain steps of the coagulation cascade [3]. Although it is generally believed that viscoelastic tests will reduce the amount of transfusion and thus the risk of postoperative complications, the dynamic and multifactorial process in liver transplant patients makes it mandatory to manage transfusion not only with laboratory tests but also with the clinical status of the patient.

The most significant changes in the coagulation cascade in liver transplantation occur between the end of the anhepatic phase and the post-reperfusion period when the new organ anastomosis is performed [4]. In our clinic, thromboelastogram (TEG) is routinely studied in all patients, particularly post-reperfusion. In patients for whom TEG cannot be studied for various reasons, transfusion is administered under the guidance of conventional coagulation tests. The clinical evaluation of clot formation is one of the most important parameters in making a transfusion decision, along with laboratory parameters. In this context, we retrospectively analyzed the prospectively collected data of liver transplantation patients received in our clinic in the last decade and conducted a case-control study. In this way, we planned to compare the effect of transfusion guided by TEG or conventional coagulation tests on postoperative complications and transfusion volume. It is hypothesized that TEG-guided transfusion will reduce the amount of transfusion and thus the postoperative mortality and morbidity.

Materials and methods

The study was designed as a retrospective case-control study in a university hospital in line with the principles stated in the Declaration of Helsinki, with the decision of Necmettin Erbakan University Non-Pharmaceutical and Non-Medical Device Research Ethics Committee (Decision No: 2023/4101). File records of recipients who underwent liver transplantation between January 1, 2012, and November 30, 2022, were retrospectively reviewed. Recipients under 18 years old who had liver transplants again within 30 days after the first transplantation, who had combined liver and kidney transplantation, who died intraoperatively, and whose file records were insufficient were excluded from the study. Twenty recipients whose blood transfusion was administered under TEG guidance after the reperfusion period of the surgery constituted the case group. Among the recipients whose transfusion was

managed with conventional coagulation tests, 20 recipients selected by non-consecutive random method constituted the control group.

In our faculty, liver transplantation is performed under a special procedure with the same surgical and anesthesia team. All recipients are monitored by electrocardiogram, pulse oximetry, invasive and noninvasive arterial pressure measurement, neuromuscular monitoring, and bispectral index measurement. Anesthesia induction is achieved by administering propofol (1–2 mg/kg), fentanyl (1 mcg/kg), and rocuronium (0.5 mg/kg). After endotracheal intubation, anesthesia was maintained with desflurane inhalation and remifentanyl infusion (0.05–0.4 mcg/kg/min) in a 50% air-50% O₂ mixture with a bispectral index between 40 and 60%. Lung ventilation is provided with a tidal volume of 5–6 mL/kg and a respiratory rate of 10–14/min, keeping the end-tidal CO₂ value in the 35–45 mmHg range. Positive end-expiratory pressure was maintained at 5 mmHg.

Ultimately, recipients are anesthetized, and internal jugular vein catheterization is performed under ultrasonography guidance. During the surgery, the recipients are warmed with a warming blanket, and their body temperature is monitored. The target mean arterial pressure during transplantation is 65 mmHg and above. Hemodynamic disorders are treated with fluid therapy and vasoactive drugs (norepinephrine 0.01–0.05 mcg/kg/min). Crystalloids, colloids, and albumin infusions are used in fluid therapy. Patients receive erythrocyte suspension (ES) transfusions to maintain hemoglobin (Hb) between 8 and 9 g/dL and to maintain O₂ supply.

Preoperative hemogram, biochemistry, international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen values were studied for all recipients. In surgery, TEG or conventional coagulation tests are routinely performed in the first hour after reperfusion, depending on the suitability of the conditions (availability of consumables). TEG or conventional coagulation tests can be performed in case of severe bleeding at other stages of transplantation. In patients undergoing TEG, 2 units of fresh frozen plasma (FFP) are administered when the R time ≥ 11 min, while 1 unit of apheresis platelet suspension (PS) is administered when the MA < 30 mm, and 2 g of fibrinogen concentrate or 4 units of cryoprecipitate when the alpha angle < 55 . In patients undergoing conventional coagulation tests, 2 units of FFP are transfused when INR > 2 or aPTT > 30 , 2 g of fibrinogen concentrate or 4 units of cryoprecipitate when fibrinogen < 120 g/dL, and 1 unit of apheresis PS when platelets $< 30,000 \times 10^3/\mu\text{L}$. If microvascular leakage occurs, tranexamic acid (10–15 mg/kg) is administered despite transfusions in the post-reperfusion period. Clinical signs of surgical bleeding are not ignored when transfusing blood products, and the process is managed in correlation with the surgical team. After surgery, patients are transferred to the reanimation unit for postoperative care.

Thrombelastography analysis was conducted using TEG_5000, version 4.2 (Haemoscope Corporation, Niles, IL, USA). One milliliter of complete blood was taken from the citrated tube and transferred to a kaolin tube. The complete blood was gently mixed for full contact with the kaolin. An automatic pipette transferred 340 μL of the mixture to the test bath. To

antagonize citrate, 20 µl calcium chloride is added to the test bath with an automatic pipette, and the test is started.

In accordance with this protocol, the data scanned from the files of liver transplant recipients included gender, age, body mass index (BMI), model for end-stage liver disease (MELD) score, cause of liver failure, previous abdominal surgery, hypertension, diabetes, preoperative kidney injury, encephalopathy, upper gastrointestinal (GI) bleeding, portal vein thrombosis (PVT), portopulmonary hypertension, presence of ascites, preoperative creatinine, Na, K, albumin, bilirubin, Hb, INR, aPTT, platelet, fibrinogen values, post reperfusion Hb, platelet, fibrinogen, INR, aPTT values, intraoperative total fluid loss, amount of diuresis, amount of administered crystalloid, colloid and albumin, amount of ES, PS, fibrinogen, FFP, cryoprecipitate transfused intraoperatively and after reperfusion, surgical duration-related data, presence of reperfusion syndrome, whether the donor is alive or cadaver, presence of postoperative complications (kidney damage, hepatic artery thrombosis, graft rejection, mortality in the first 28 days), LOS, and TEG parameters.

The primary outcome measure was the difference in intraoperative transfused blood and blood products, and the secondary outcome measure was the difference in the development of postoperative complications.

Statistical analysis

The data obtained in this study were analyzed using the SPSS 23.0 package program. Descriptive statistical values of all measurements are presented. Shapiro-Wilk’s test was conducted when analyzing the normality of the scores between the groups since n<30. Because of the normality test, it was determined that the values between the groups did not show normal distribution at P<0.05. Hence, the Mann-Whitney U test was used to analyze the groups' differences. The chi-square test was used to examine intergroup dependence in categorical data. When analyzing the difference and dependency between the groups, P<0.05 was considered the significance level, and it was considered that there was a significant difference between the groups when P<0.05 and there was no significant difference between the groups when P>0.05.

Results

The records of 90 recipients who underwent transplantation between January 1, 2012, and November 30, 2022, were retrospectively analyzed within the scope of the study. As a result of the final cohort formed by inclusion and exclusion criteria, 40 recipients were included in the study. The flow diagram of the study is given in Figure 1.

When the causes of liver failure were analyzed, the etiologic factors of the recipients were: cryptogenic in ten (25%), autoimmune in eight (20%), primary sclerosing cholangitis in five (12.5%), hepatocellular carcinoma in 14 (35%), and intoxication in three (7.5%). The preoperative characteristics are given in Table 1.

When the preoperative laboratory parameters of the recipients were analyzed, no significant difference was found between the two groups (Table 2).

The mean duration of surgery was 494 min, and the mean anhepatic phase duration was 77.17 min. It was determined

that reperfusion syndrome developed in four (20%) patients in the case group and six (30%) patients in the control group. The distribution of intraoperative and surgical data between the groups is presented in Table 3.

Figure 1: Flow diagram of the study.

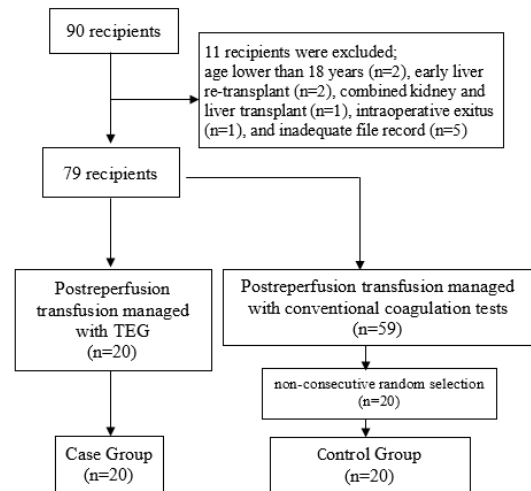


Table 1: Preoperative recipient characteristics (mean[SD], n [%]).

	Case group (n=20)	Control group (n=20)	P-value
Age (year)	43.10(14.05)	45.35(12.89)	0.583
Gender (M/F)	12 (60%) / 8 (40%)	9 (45%) / 11 (55%)	0.342
BMI (kg/m ²)	26.01(2.76)	26.35(3.61)	0.718
MELD Score	21.90(8.52)	17.55(8.57)	0.086
Previous abdominal surgery	0 (0%)	2 (10%)	0.487
Preoperative kidney injury	5 (25%)	4 (20%)	1.000
Preoperative hypertension	4 (20%)	4 (20%)	1.000
Preoperative diabetes mellitus	4 (20%)	2 (10%)	0.661
Preoperative encephalopathy	10 (50%)	7 (35%)	0.337
Preoperative upper GIS bleeding	3 (15%)	3 (15%)	1.000
Preoperative PVT	2 (10%)	0 (0%)	0.487
Preoperative pulmonary Hypertension	2 (10%)	1 (5%)	1.000
Presence of preoperative ascites	1 (5%)	3 (15%)	0.605

SD: standard deviation, M: Male, F: Female, BMI: Body mass index, MELD: Model for end-stage liver disease, GIS: Gastrointestinal system, PVT: Portal vein thrombosis

Table 2: Preoperative recipient laboratory parameters (mean[SD]).

	Case group (n=20)	Control group (n=20)	P-value
Creatinine (mg/dL)	0.85(0.47)	0.74(0.37)	0.398
Na (mmol/L)	135.30(5.38)	137.55(6.60)	0.142
K (mmol/L)	4.06(0.50)	4.28(0.80)	0.718
Albumin (g/dL)	2.98(0.62)	3.32(0.66)	0.114
Bilirubin (mg/dL)	6.50(7.68)	7.19(6.77)	0.698
Hemoglobin (g/dL)	10.53(1.60)	10.32(2.80)	0.547
Platelet (x10 ³ /uL)	95.15(29.88)	100.85(56.50)	0.678
Fibrinogen (mg/dL)	152.15(35.14)	158.30(31.46)	0.692
INR	1.97(0.83)	2.21(1.47)	0.968
aPTT (seconds)	40.76(9.51)	40.37(10.75)	0.602

SD: standard deviation, Na: Sodium, K: Potassium, INR: International normalized ratio, aPTT: Active partial thromboplastin time

Table 3: Intraoperative and surgical data (mean[SD], n [%]).

	Case group (n=20)	Control group (n=20)	P-value
Dissection time (min)	174.85(69.95)	213.75(108.31)	0.277
Anhepatic phase duration (min)	82.10(18.83)	72.25(17.88)	0.149
Warm ischemia time (min)	82.60(18.58)	84.50(18.13)	0.543
Total surgery time (min)	463.25(108.91)	524.75(166.42)	0.253
Reperfusion syndrome (n%)	4 (20%)	6 (30%)	0.465
Intraoperative total fluid loss (ml)	2445.00(1127.409)	2652.50(2061.84)	0.678
Intraoperative total diuresis (ml)	474.00(158.73)	707.75(402.40)	0.060
Intraoperatively administered crystalloid (ml)	5160.00(1595.19)	5500.00(1577.14)	0.698
Intraoperatively administered colloid (ml)	1140.00(839.42)	1350.00(650.91)	0.068

SD: standard deviation

When TEG values were analyzed in the first hour after reperfusion in the case group, it was determined that the mean R time was 11.50 min, K time was 8.67 min, MA value was 41.49 mm, G value was 4.07 dyne/cm², LY 30 was 0.31%, and alpha angle was 41.24 degrees. When intraoperative total and

postreperfusion blood and blood product transfusions were analyzed, it was found that there was no significant difference in ES, PS, fibrinogen concentrate, and cryoprecipitate transfusions, whereas FFP concentration transfusion was significantly lower in the case group ($P=0.011$, $P=0.003$). Intraoperative total and post-reperfusion blood and blood product transfusion rates are shown in Table 4 and Table 5.

Table 4: Intraoperative total blood and blood product transfusion (mean[SD]).

	Case group (n=20)	Control group (n=20)	P-value
Erythrocyte suspension (unit)	2.30(1.72)	2.05(2.44)	0.314
Fresh frozen plasma (unit)	1.20(1.64)	2.75(1.94)	0.011*
Platelet suspension (unit)	0.25(0.44)	0.05(0.22)	0.289
Fibrinogen concentrate (gr)	1.10(1.21)	0.40(0.82)	0.096
Cryoprecipitate (unit)	0.80(1.64)	1.40(2.35)	0.565
Albumin (mL)	200.00(107.61)	170.00(103.11)	0.265

SD: standard deviation, * $P<0.05$

Table 5: Post-reperfusion laboratory parameters and blood and blood product transfusions (mean[SD]).

	Case group (n=20)	Control group (n=20)	P-value
Hemoglobin (g/dL)	8.62(1.20)	9.11(1.82)	0.495
Platelet ($\times 10^3$ /uL)	95.85(47.78)	81.45(32.59)	0.301
Fibrinogen (mg/dL)	117.30(49.69)	114.85(25.99)	0.947
INR	3.17(1.33)	3.54(1.38)	0.314
aPTT (seconds)	54.56(13.31)	72.49(32.04)	0.127
ES (unit)	0.90(0.72)	0.60(0.88)	0.157
FFP (unit)	0.60(0.94)	1.65(0.75)	0.003*
TS (unit)	0.25(0.44)	0.00(0.00)	0.183
Fibrinogen Concentrate (gr)	0.90(1.02)	0.40(0.82)	0.183
Cryoprecipitate (unit)	1.00(1.78)	1.20(1.88)	0.799

SD: standard deviation, INR: International normalized ratio, aPTT: Active partial thromboplastin time, ES: Erythrocyte suspension, FDP: Fresh frozen plasma, PS: Platelet suspension, * $P<0.05$

It was determined that 26 (65%) transplanted livers were obtained from cadavers and 14 (35%) from living donors. No significant difference was found between the groups regarding cadaver and living donor ratios ($P>0.05$). Similarly, there was no significant difference in postoperative outcomes of transplantations performed from cadavers or living donors ($P>0.05$). Besides, there was no difference between the groups in the postoperative complications that developed in the recipients (Table 6).

Table 6: Postoperative complication development (mean[SD], n[%]).

	Case group (n=20)	Control group (n=20)	P-value
Postoperative kidney injury	10(50%)	8(40%)	0.525
Hepatic artery thrombosis	5(25%)	3(15%)	0.695
Graft rejection	8(40%)	7(35%)	0.744
Length of stay on the ventilator (days)	1.90(3.54)	2.75(4.55)	0.547
Duration of icu stay (days)	5.60(4.51)	6.10(6.61)	0.678
Length of hospital stay (days)	15.65(11.44)	15.95(6.79)	0.620
First 28 days of mortality	8(40%)	7(35%)	0.744

SD: standard deviation

Regarding the effects of intraoperative total and post-reperfusion blood and blood products on ventilator stay, intensive care unit stay, LOS, hepatic artery thrombosis, graft rejection, postoperative kidney damage, and first 28-day mortality, only a weak negative correlation was found between intraoperative total and postreperfusion fibrinogen use and LOS ($r=-0.325/P=0.041$, $r=-0.354/P=0.025$).

Discussion

In this retrospective case-control study, we investigated the effect of TEG or conventional coagulation tests on the number of transfused blood products and postoperative complications in the post-reperfusion period of liver transplantation. According to the results of the study, it was found that the amount of transfused FFP decreased when TEG was used. However, there was no change in the number of other

blood products. There was no difference between the two groups regarding the development of postoperative complications, but the LOS decreased with increasing fibrinogen use.

Simultaneous changes in the procoagulant, anticoagulant, and fibrinolytic system in end-stage liver failure cause a process in which the coagulation system is rebalanced globally. This new balance may cause bleeding in patients and increase the tendency to hepatic artery thrombosis and portal vein thrombosis [5]. In addition to changes in the coagulation system, the presence of systemic infection, portal hypertension, and renal dysfunction also increase the risk of bleeding [6]. Apart from these changes that make it difficult to manage the coagulation system, each stage of the liver transplant operation also causes variations in coagulation and poses serious challenges to patient blood management. Hypercoagulability often occurs at the onset of surgery, whereas progressive fibrinolysis is seen in the anhepatic phase. Coagulation gradually improves in 1 h after reperfusion of the liver allograft [7]. However, due to increased demand for a limited donor supply, the use of high-risk donors has increased recently, including advanced-age donors, significant steatosis, post-mortem donations, and infections. This leads to delayed allograft function and the risk of severe perioperative bleeding in critically ill recipients [8]. Therefore, in these patients, coagulation should be closely monitored, and any bleeding episodes should be accurately recognized.

Conventional coagulation tests are insufficient to predict bleeding in patients with liver failure [9]. TEG and rotational thromboelastometry are increasingly used to guide transfusions in liver transplant patients [10]. Current evidence on the use of TEG in liver transplantation suggests that using TEG rather than conventional coagulation tests results in fewer blood product transfusions without increased mortality or complications. TEG was first used in liver transplantation by Kang et al. [7], and a 33% reduction in transfusion volume was achieved. Wang et al. [11] compared two different TEG protocols in their study. While fewer FFP transfusions were performed in the strict protocol group (R time>15 min or MA of <40 mm), there was no difference in mortality. De Pietri et al. [12] randomized 60 liver transplant patients to a TEG-based transfusion protocol and significantly reduced the transfusion. De Pietri also found that TEG use had no adverse effect on 30-day and 6-months survival [13]. Perioperative TEG values also have potential value in predicting outcomes of liver transplantations. Zahr Eldeen et al. [14] reported that preoperative TEG values could predict early hepatic artery thrombosis. Contrary to common literature, Gaspari et al. [15] reported that TEG use did not reduce blood product consumption. The most important difference of this study from the other studies is that since they used kaolin TEG, they kept the threshold values considerably lower than the literature, specifically for MA and alpha angle. We also use kaolin TEG in the clinic and apply thresholds similar to this study. However, the most important difference of this study from our study is that they methodologically developed a scoring method and formed their cohort according to this scoring rather than randomly. Although there was no statistical difference in our study regarding demographic and surgical data, this difference in methodology may have caused

the difference in study results. Our study found that using TEG decreased blood product transfusion, in line with the general literature. We found that 91 blood and blood product units were used in the case group and 180 units in the control group. There was a significant difference in terms of TDP use, with significantly less TDP use in the case group. Meanwhile, we detected no significant difference between the groups regarding mortality and morbidity.

Perioperative transfusions are associated with worse postoperative outcomes [16]. Significant differences are observed in transfusion practices among anesthesiologists due to the transplantation process. Depending on coagulopathy and portal hypertension, blood product transfusion may be required during the dissection phase [17]. Deepening of coagulopathy in the anhepatic phase, particularly delayed graft function or worsening graft failure shortly after reperfusion, may also increase the need for transfusion. Similar to other recommendations, The Liver Intensive Care Group of Europe (LICAGE) recommends avoiding blood transfusion in the absence of clinically significant bleeding associated with coagulopathy [18]. Although the use of viscoelastic tests for targeted treatment of coagulopathy in liver transplantation is included in the European Society of Anesthesia (ESA) guidelines, a consensus is needed for cut-off values to guide optimal transfusion in practice [19]. The success of conservative transfusion policies in transplant recipients who tolerate very low platelet counts in the absence of active bleeding is remarkable [20]. Platelet transfusion was found to be an independent risk factor for worse outcomes in liver transplantation [21]. Hence, platelet transfusion is recommended in the presence of clinically significant bleeding supported by viscoelastic tests. Similarly, we used MA values of <30 in the case group and $<30,000$ in the control group as threshold values, although much higher values have been determined in the literature. We did not encounter any problems in bleeding control, and no correlation between platelet transfusion with postoperative complications was detected.

Due to the dynamic process of transplantation surgery, the correlation of viscoelastic tests with conventional coagulation tests in different phases of surgery is also different. Coagulopathy, which deepens gradually in other phases, improves with the onset of allograft function, typically by the end of the first hour [7]. Yoon et al. [22] compared conventional laboratory tests with TEG values at various stages of liver transplantation and found that TEG and conventional coagulation tests showed a good correlation in the dissection and post-reperfusion phases, whereas TEG was more advantageous in the anhepatic phase. In our clinic, we perform blood product transfusion after reperfusion by supporting clinical indicators with laboratory parameters, especially because it also shows the function of the allograft and may affect postoperative graft function. We found that the amount of FFP was significantly lower in the TEG-guided case group, but there was no difference in the transfusion of other blood products. Although not statistically significant, this may be due to higher fibrinogen use in the case group. Besides, although we did not observe any correlation between conventional test values and TEG values, we can state that there is less correlation between INR and aPTT values and R time compared to other parameters. Another factor

in these results may be that our MELD scores were lower than 25 in both groups, and the patients did not have an increased transfusion risk.

Increased infection rates and hepatic artery thrombosis after liver transplantation have been associated with ES transfusion [23]. While still provider- and institution-dependent, some guidelines suggest that morbidity and mortality will be reduced when more liberal transfusion strategies are applied to patients with cardiac comorbidities, targeting a hemoglobin of ≥ 9 g/dL. Likewise, the World Health Organization also recommends restrictive transfusion strategies in critically ill patients that have been shown to have no detrimental effect on outcomes [24]. Many studies have argued for a threshold Hb concentration of 7 g/dL for transfusion and a Hb threshold value between 8–9 g/dL in those with a higher risk of side effects of anemia [25]. Optimizing cardiac output, ventilation, and oxygenation helps improve tolerance to lower Hb concentrations. In our clinic, we optimized all factors affecting oxygen delivery in transplantation and determined the Hb threshold value for ES transfusion as 8–9 g/dL. In the study, we transfused an average of 2 units of ES in both case and control groups. We believe that these values are quite low for transplantation surgery. Moreover, intraoperative total and post-reperfusion transfused ES were not correlated with postoperative complications. We consider strategies such as restrictive fluid therapy in the dissection phase, low Hb threshold values we determined for ES transfusion, avoiding prophylactic treatment for all blood products, and transfusing only in the case of clinically active bleeding supported by laboratory values that affect these results.

Most fibrinogen is synthesized in the liver, and its half-life is shortened in chronic liver failure [26]. When hemodilution or massive bleeding occurs, fibrinogen is the first factor to reach critical levels [27]. A fibrinogen concentration below 150 mg/dL increases hemorrhagic tendency; therefore, signs of fibrinogen deficiency on viscoelastic tests should suggest that fibrinogen transfusion may be necessary [19]. In their observational study, noval-Padillo et al. [28] found that ES, FFP, and PS transfusion decreased by 50%, and transfusion-free transplantation rates increased from 3.5% to 20% in patients receiving fibrinogen. A study on fibrinogen and FFP in surgical and trauma patients concluded that fibrinogen levels were generally associated with improved outcome measures, whereas FFP caused serious side effects [29]. In our study, it was found that fibrinogen values decreased in both groups in the post-reperfusion period. Although the amount of fibrinogen given intraoperatively (total and after reperfusion) was higher in the case group than in the control group, the difference was insignificant. Regarding the effect on postoperative complications, there was a negative correlation between fibrinogen use and LOS.

Limitations

Our study had some limitations. First, the data set was obtained retrospectively. This may lead to biases in the objectivity of the results. The second is that the number of cases was small, and we randomly selected the control group by non-consecutive sampling. Our results could have been much more objective if we had used a scoring method in which different factors were standardized when selecting the control group.

Furthermore, the small number of cases decreased the power of statistical analyses. Although TEG is a real-time test, it is also a test that gives instant results. Thus, the coagulation cascade should be evaluated more frequently in a dynamic process such as liver transplantation. If repeated sequential TEG measurements had been studied in each phase of surgery, the effect on transfusion rates might have been much different. Similarly, if TEG studies could be continued in the postoperative period, the effect of the strategy applied, particularly in the post-reperfusion period, on postoperative complications could be evaluated more accurately.

Conclusion

In conclusion, TEG-guided transfusion decreased total blood product consumption in the post-reperfusion period. Besides, the increase in the use of fibrin has led to a decrease in LOS. The use of TEG has no significant effect on mortality and morbidity. Although there is still a need to establish thresholds for transfusion, using TEG combined with an objective assessment of patient clinical status may be an ideal guide for transfusion strategy.

References

- Mallett SV. Clinical Utility of Viscoelastic Tests of Coagulation (TEG/ROTEM) in Patients with Liver Disease and during Liver Transplantation. *Semin Thromb Hemost.* 2015 Jul;41(5):527-37. doi: 10.1055/s-0035-1550434.
- Lopez-Plaza I. Transfusion guidelines and liver transplantation: time for consensus. *Liver Transpl.* 2007 Dec;13(12):1630-2. doi: 10.1002/lt.21225.
- Buliarca A, Horhat A, Mocan T, Craciun R, Procopet B, Sparchez Z. Viscoelastic tests in liver disease: where do we stand now? *World J Gastroenterol.* 2021 Jun 21;27(23):3290-302. doi: 10.3748/wjg.v27.i23.3290.
- Thai C, Oben C, Wagener G. Coagulation, hemostasis, and transfusion during liver transplantation. *Best Pract Res Clin Anaesthesiol.* 2020 Mar;34(1):79-87. doi: 10.1016/j.bpa.2020.03.002.
- Dalal A. Anesthesia for liver transplantation. *Transplant Rev (Orlando).* 2016 Jan;30(1):51-60. doi: 10.1016/j.trre.2015.05.003.
- O'Leary JG, Greenberg CS, Patton HM, Caldwell SH. AGA Clinical Practice Update: Coagulation in Cirrhosis. *Gastroenterology.* 2019 Jul;157(1):34-43.e1. doi: 10.1053/j.gastro.2019.03.070.
- Kang YG, Martin DJ, Marquez J, Lewis JH, Bontempo FA, Shaw BW Jr, et al. Intraoperative changes in blood coagulation and thromboelastographic monitoring in liver transplantation. *Anesth Analg.* 1985 Sep;64(9):888-96.
- O'Mahony CA, Goss JA. The future of liver transplantation. *Tex Heart Inst J.* 2012;39(6):874-5.
- Caldwell SH, Hoffman M, Lisman T, Macik BG, Northup PG, Reddy KR, et al. Coagulation in Liver Disease Group. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management. *Hepatology.* 2006 Oct;44(4):1039-46. doi: 10.1002/hep.21303.
- Stravitz RT, Lisman T, Luketic VA, Sterling RK, Puri P, Fuchs M, et al. Minimal effects of acute liver injury/acute liver failure on hemostasis as assessed by thromboelastography. *J Hepatol.* 2012 Jan;56(1):129-36. doi: 10.1016/j.jhep.2011.04.020.
- Wang SC, Lin HT, Chang KY, Mandell MS, Ting CK, Chu YC, et al. Use of higher thromboelastogram transfusion values is not associated with greater blood loss in liver transplant surgery. *Liver Transpl.* 2012 Oct;18(10):1254-8. doi: 10.1002/lt.23494.
- De Pietri L, Bianchini M, Montalti R, De Maria N, Di Maira T, Begliomini B, et al. Thromboelastography-guided blood product use before invasive procedures in cirrhosis with severe coagulopathy: A randomized, controlled trial. *Hepatology.* 2016 Feb;63(2):566-73. doi: 10.1002/hep.28148.
- De Pietri L, Ragusa F, Deleuterio A, Begliomini B, Serra V. Reduced Transfusion During OLT by POC Coagulation Management and TEG Functional Fibrinogen: A Retrospective Observational Study. *Transplant Direct.* 2015 December 15;2(1):e49. doi: 10.1097/TXD.0000000000000559.
- Zahr Eldeen F, Roll GR, Derosas C, Rao R, Khan MS, Gunson BK, et al. Preoperative Thromboelastography as a Sensitive Tool Predicting Those at Risk of Developing Early Hepatic Artery Thrombosis After Adult Liver Transplantation. *Transplantation.* 2016 Nov;100(11):2382-2390. doi: 10.1097/TP.0000000000001395.
- Gaspari R, Teofili L, Aceto P, Valentini CG, Punzo G, Sollazzi L, et al. Thromboelastography does not reduce transfusion requirements in liver transplantation: A propensity score-matched study. *J Clin Anesth.* 2021 May;69:110154. doi: 10.1016/j.jclinane.2020.110154.
- Goldaracena N, Méndez P, Quiñonez E, Devetach G, Koo L, Jeanes C, et al. Liver Transplantation without Perioperative Transfusions Single-Center Experience Showing Better Early Outcome and Shorter Hospital Stay. *J Transplant.* 2013;2013:649209. doi: 10.1155/2013/649209.
- Massicotte L, Lenis S, Thibeault L, Sassine MP, Seal RF, Roy A. Effect of low central venous pressure and phlebotomy on blood product transfusion requirements during liver transplantations. *Liver Transpl.* 2006 Jan;12(1):117-23. doi: 10.1002/lt.20559.
- Biancofiore G, Blasi A, De Boer MT, Franchini M, Hartmann M, Lisman T, et al. Perioperative hemostatic management in the cirrhotic patient: a position paper on behalf of the Liver Intensive Care Group of Europe (LICAGE). *Minerva Anesthesiol.* 2019 Jul;85(7):782-98. doi: 10.23736/S0375-9393.19.13468-2.
- Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol.* 2013 Jun;30(6):270-382. doi: 10.1097/EJA.0b013e32835f4d5b.
- Weeder PD, Porte RJ, Lisman T. Hemostasis in liver disease: implications of new concepts for perioperative management. *Transfus Med Rev.* 2014 Jul;28(3):107-13. doi: 10.1016/j.tmr.2014.03.002.
- de Boer MT, Christensen MC, Asmussen M, van der Hilst CS, Hendriks HG, Slooff MJ, et al. The impact of intraoperative transfusion of platelets and red blood cells on survival after liver transplantation. *Anesth Analg.* 2008 Jan;106(1):32-44. doi: 10.1213/01.ane.0000289638.26666.ed.

- Yoon JU, Cheon JH, Choi YJ, Byeon GJ, Ahn JH, Choi EJ, et al. The correlation between conventional coagulation tests and thromboelastography in each phase of liver transplantation. *Clin Transplant.* 2019 Mar;33(3):e13478. doi: 10.1111/ctr.13478.
- Dunn LK, Thiele RH, Ma JZ, Sawyer RG, Nemerug EC. Duration of red blood cell storage and outcomes following orthotopic liver transplantation. *Liver Transpl.* 2012 Apr;18(4):475-81. doi: 10.1002/lt.23379.
- Spahn DR, Theusinger OM, Hofmann A. Patient blood management is a win-win: a wake-up call. *Br J Anaesth.* 2012 Jun;108(6):889-92. doi: 10.1093/bja/aes166.
- McIntyre L, Timmouth AT, Fergusson DA. Blood component transfusion in critically ill patients. *Curr Opin Crit Care.* 2013 Aug;19(4):326-33. doi: 10.1097/MCC.0b013e3283632e56.
- Tennent GA, Brennan SO, Stangou AJ, O'Grady J, Hawkins PN, Pepys MB. Human plasma fibrinogen is synthesized in the liver. *Blood.* 2007 Mar 1;109(5):1971-4. doi: 10.1182/blood-2006-08-040956.
- Hartmann M, Szalai C, Saner FH. Hemostasis in liver transplantation: Pathophysiology, monitoring, and treatment. *World J Gastroenterol.* 2016 January 28;22(4):1541-50. doi: 10.3748/wjg.v22.i4.1541.
- Noval-Padillo JA, León-Justel A, Mellado-Miras P, Porras-Lopez F, Villegas-Duque D, Gomez-Bravo MA, et al. Introduction of fibrinogen in the treatment of hemostatic disorders during orthotopic liver transplantation: implications in the use of allogenic blood. *Transplant Proc.* 2010 Oct;42(8):2973-4. doi: 10.1016/j.transproceed.2010.08.011.
- Kozek-Langenecker S, Sørensen B, Hess JR, Spahn DR. Clinical effectiveness of fresh frozen plasma compared with fibrinogen concentrate: a systematic review. *Crit Care.* 2011;15(5):R239. doi: 10.1186/cc10488.

The National Library of Medicine (NLM) citation style guide has been used in this paper.