Research Article

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Liver transplant platelet transfusion predictors

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Preoperative predictors of platelet transfusion in adult patients undergoing liver transplant

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Abstract

Background and Aim: Liver transplantat (LT) is still associated with a significant need for blood product transfusion. This study aimed to identify preoperative factors that can predict the need for platelet transfusion in adults undergoing LT.

Materials and Methods: A retrospective analysis of the database from liver transplant recipients was performed to evaluate the use of platelet transfusion during and after LT. Two groups of recipients were assigned, with or without perioperative platelet transfusion (groups A and B, respectively). Preoperative LT recipient variables such as age, gender, body mass index, pre-transplant laboratory tests, cause of liver transplant, the Model for End-Stage Liver Disease score, and other selected perioperative variables, including surgical data, were compared between the two groups.

Results: Of 150 patients, 70 who received platelet transfusions were included in group A. Regarding the preoperative recipient variables, the two groups showed significant differences in the Model for End-Stage Liver Disease score (p=0.013), pre-transplant platelet count (p<0.001), and international normalized ratio (p<0.001). The results of logistic regression analysis showed that pre-transplant platelet count <50×10^9/L (odds ratio, 0.979; 95% confidence interval [0.969–0.989]; p<0.001), serum creatinine ≥123.76 µmol/L (1.4 mg/dL) (OR, 4.35; 95% CI [1.566–12.097]; p=0.005), international normalized ratio ≥1.5 (OR, 2.771; 95% CI [1.198–6.412]; p=0.017) were identified as predictors for the use of platelet transfusion in LT.

Conclusion: Pre-liver transplant recipients' platelet count, serum creatinine, and international standardized ratio are crucial in predicting platelet utilization during and after LT.

Keywords: Blood transfusion; platelet count; thrombocytopenia; transplants.

Introduction

Transfusion of blood components in liver transplant (LT) is associated with increased patient morbidity, mortality, and costs. Prevention of excessive blood loss and judiciously using blood products are important goals during LT. Indeed, blood transfusion services are an essential part of liver transplant management.

More recently, the coronavirus (COVID-19) pandemic has led to a decline in blood donations and thus the blood supply.[1] As a result, there has been more emphasis on identifying potential predictors of the need for blood transfusion in extensive transfusion-related surgeries such as LT. These predictive capabilities help transfusion services improve preparedness, reduce the wastage of limited resources, and prevent the artificial depletion of this scarce resource due to wastage.

Previous studies have evaluated perioperative variables predicting blood consumption in liver transplants.[2,3] However, significant preoperative LT variables in predicting the need for platelet transfusion are unclear. This issue is also notable in the surgery, as perioperative changes in platelet counts are independent of other blood components.[4] Post-transplant transient thrombocytopenia occurs in most patients early after LT. Platelet counts decrease after the operation and reach nadir levels on postoperative days (POD) 3–6, with a mean platelet reduction of 60%. Then, about two weeks later, the platelet counts return to preoperative levels.[5] This pattern of platelet count changes in liver transplants is similar to the result of our previous study (Fig. 1).[4]

Platelet components intended for a specific patient are no longer available for other medical purposes, which may lead to temporary shortages. The rates of platelet outdating are the highest among blood products and are typical as 10% to 20%.[6]

To our knowledge, there are no published studies on this topic. Our study aimed to identify preoperative factors that can predict platelet component consumption in deceased donor liver transplant (DDLT) recipients.

Materials and Methods

This retrospective study included medical records from 150 consecutive adult patients who underwent LT at our center from April 2019 to December 2021.

As mentioned, thrombocytopenia is common early after LT. During the first postoperative week, a moderate decrease in platelet count (20×10^9/L to 50×10^9/L) occurs in about half of the patients and counts less than 20×10^9/L in about 8% of patients. Then with the restoration of hepatic function, spontaneous recovery of thrombocytopenia usually begins during the second week after LT.[7] However, some postoperative LT variables such as decreased platelet production, hemodilution, platelet con-

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sumption (disseminated intravascular coagulation, sepsis), medications, viral infections, and heparin-induced thrombocytopenia can lead to serious confounding of platelet counts.[5,8,9] Therefore, the inclusion criteria in the present study were adult DDLT cases whose perioperative platelet count changes followed the usual pattern described earlier (Fig. 1).

Exclusion criteria were cases of acute liver failure, split liver transplants, liver re-transplantation, and multi-organ transplants.

The liver transplant procedure was performed using the classic technique, without venovenous bypass or the piggyback technique. The liver grafts were cold-preserved with the University of Wisconsin solution.

All patients received standard induction anesthesia with fentanyl (1–2 µg/kg), propofol (0.5–2 mg/kg), and muscle relaxants with either succinylcholine or cisatracurium. Anesthesia was maintained with isoflurane in low to moderate concentrations (0.5–1.0 minimum alveolar concentration) and bolus cisatracurium. A remifentanil infusion (0.05–0.3 µg/kg/min) and bolus fentanyl were administered throughout LT based on the patient's hemodynamic responses. Continuous intraoperative monitoring and blood sampling were enabled using a radial arterial line and a central venous catheter. Intravenous fluids contained 1–2% albumin in saline solution. To reduce bleeding during LT, restrictive fluid management techniques were used before the anhepatic phase of surgery. Excessive metabolic acidosis (base excess <-6.0) was treated with sodium bicarbonate. Body core temperature was maintained using a whole body-sized warm blanket. Methylprednisolone was administered to all patients before reperfusion. Inotropes and vasopressors were used at the anesthetist's discretion in response to the patient's hemodynamic status. At the end of the operation, all patients underwent endotracheal tube extubation in the operating room.

Management of Perioperative Transfusion of Blood Components

The need for intraoperative blood transfusion was determined using hemoglobin levels based on serial arterial blood gas testing and bleeding evaluation at different surgery stages. In this study, hemoglobin levels below 8 g/dL or ongoing bleeding were the thresholds for packed red blood cell (PRBC) transfusions. Intraoperative clinical coagulopathy correction was performed under the guidance of rotational thromboelastometry (ROTEM@ TEM International GmbH, Munich, Germany) for administering fresh frozen plasma, fibrinogen concentrate, prothrombin complex concentrate, and antithrombin concentrate.

During surgery, complete blood count (CBC) tests were performed at the discretion of the anesthetist, also routinely 10 minutes after liver reperfusion. Platelet transfusion was recommended for clinically significant bleeding when the intraoperative platelet count was less than the preoperative value.

Postoperative clinical coagulopathy with platelet counts less than 20×10^9/L was the threshold for the platelet transfusion.

The patients were divided: into those with or without perioperative platelet transfusion. Perioperative recipient variables collected for analysis included: age, sex, and body mass index; causes of liver transplants, Model for End-Stage Liver Disease score; pretransplant hemoglobin, platelet count, international normalized ratio, serum bilirubin, serum creatinine; the presence of portal vein thrombosis, ascites, accompanying systemic disease, as well as the technique of surgery, arterial pH at the end of the surgery, and surgical time.

Statistical Analysis

Results are expressed as number (%) for categorical variables and mean±SD or median (range) for continuous variables. The chi-square test was used for qualitative variables. Comparison of continuous variables between the two groups was performed using the independent samples t-test, and the Mann-Whitney test in the case of normal and non-normal distribution data, respectively. Multivariate analysis using a logistic regression model identified the variables that could predict platelet transfusion in LT. P-value <0.05 was considered statistically significant. All statistical analyses were performed with the use of SPSS version 16 software.

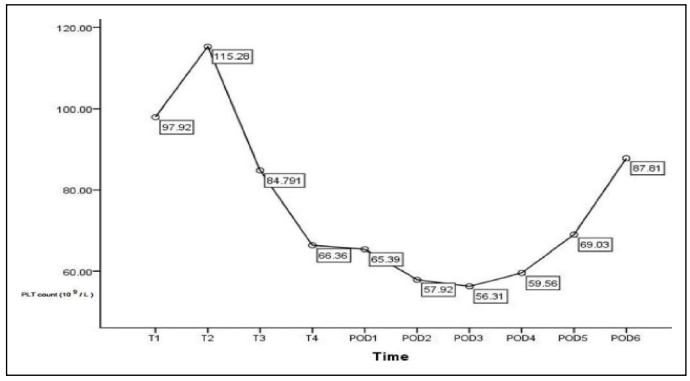

Figure 1. Typical pattern of perioperative platelet count changes as an inclusion criteria for liver transplant recipients.

Ethics Committee Approval

The research followed the Declaration of Helsinki principles. The Ethics Committee approved this retrospective study (Reference number: IR.MUMS.MEDICAL.REC.1399.193) and waived the need for written informed consent.

Results

This retrospective observational study included 150 patients undergoing deceased donor LT. Of these, 70 patients were in the platelet transfusion group. (Group A). The mean age of the patients was 46 years, and men were predominant (68%). The most common blood group type among the recipients was O positive. The main cause of LT in our study was hepatitis B virus cirrhosis (30%). Most patients (56.7%) had Child-Pugh-Turcotte class C. The overall MELD score was 20 points. Table 1 shows the demographic characteristics of the two groups.

In our study MELD score (p=0.013), INR (p<0.001), and platelet transfusions (p<0.001) were significantly higher in Group A. Total bloodless surgery was 5(3.3%) cases, all in group B. The median number of transfused platelets in group A was 9 (Min: 2, Max: 28). Table 2 shows laboratory and intraoperative data in the two groups.

The multivariate analysis examined seven variables: gender and age of the recipients, operative time, Model for End-Stage Liver Disease (MELD) score, preoperative platelet count, SCr, and INR. It revealed that the last three variables were significant in predicting intra-post LT platelet consumption in liver transplant patients.

As shown in Table 3, platelet component utilization in LT was 4.3-fold higher when the preoperative recipient's SCr was >1.4 mg/dl and 2.7–fold higher when INR was >1.5. In addition, the odds ratio for the pre-transplant platelet count $<50\times10^9$/L was 0.979; with a 95% confidence interval [CI], 0.969–0.989.

Therefore, the preoperative platelet count, SCr, and INR of LT recipients were the factors independently associated with the transfusion requirements of platelet components.

Table 1. Demographic and preoperative laboratory data in groups with and without platelets transfusion

Preoperative variable	Group A (n=70) with platelets transfusion	Group B (n=80) without platelets transfusion	p
Age, years	44.3 (17.1)	47.3 (15.1)	0.286*
Male (%)	44 (62.9)	58 (72.5)	0.207$
Body mass index, kg/m^2	24.7 (4.8)	24.8 (6.4)	0.865**
Blood group, n (%)			0.071$
A	14 (9.3)	31 (20.7)	
B	23 (15.4)	17 (11.3)	
O	26 (17.3)	27 (18)	
AB	7 (4.7)	5 (3.3)	
Cause of LT, n (%)			0.167$
HBV	20 (28.6)	24 (30)	
HCV	7 (10)	3 (3.8)	
Cryptogenic	18 (25.7)	16 (20)	
AIH	13 (18.6)	12 (15)	
NASH	3 (4.3)	2 (2.5)	
Others	9 (12.9)	23 (28.8)	
MELD score, n (%)	21.04 (5.7)	18.7 (5.2)	0.013**
<16	6 (8.6)	18 (22.5)	
≥16	64 (91.4)	62 (77.5)	
CPT class, n (%)			0.061$
A	4 (5.7)	0 (0)	
B	25 (35.7)	36 (45)	
C	41 (58.6)	44 (55)	
Accompanying systemic disease, n (%)			0.313$
Hypertension	1 (1.4)	3 (3.7)	
Hepatorenal syndrome	5 (7.1)	2 (2.5)	
Severe hepatic encephalopathy	7 (10)	6 (7.5)	
Varix bleeding	18 (25.7)	13 (16.2)	
Ascites (L)	3.8±2.4	3.2±2.3	
Hemoglobin, g/dL	11.5 (1.8)	11.0 (1.8)	0.104**
Platelet count X 10^9/L, n (%)	61.9 (44.8)	119.7 (82.0)	<0.001$
<50 X 10^9/L	36 (51.4)	4 (5.0)	
≥50 X 10^9/L	34 (48.6)	76 (95)	
INR, n (%)	2.0 (1.3)	1.5 (0.5)	<0.001$
<1.5	15 (21.4)	46 (57.5)	
≥1.5	55 (78.6)	34 (42.5)	
Total bilirubin (µmol/L), n (%)	90.6 (107.7)	112.8 (145.3)	0.457*
Serum creatinine (µmol/L), n (%)	109.6 (52.1)	93.7 (46.8)	0.079*
<123.76 µmol/L	49 (70)	66 (82.5)	
≥123.76 µmol/L	21 (30)	14 (17.5)	
Serum albumin (g/L), n (%)			0.381$
<3.3 (g/L)	51 (34)	53 (35.5)	
≥3.3 (g/L)	19 (12.7)	18 (18)	

*: Mann-Whitney test; **: Independent sample t-test; $: Chi Square test. LT: Liver transplant; HBV: Hepatitis B virus; HCV: Hepatitis C virus; AIH: Autoimmune hepatitis; NASH: Non-alcoholic steatohepatitis; MELD: Model for end-stage liver disease; CPT: Child-pugh turcotte. Data were reported using mean (standard deviation) for quantitative variables and frequency (percentage) for qualitative variables.

Discussion

Previous studies have reported perioperative predictors of blood component transfusions. Although, the present study mainly focused on preoperative predictors of platelet transfusions.

Our study demonstrated that preoperative LT factors predicting platelet transfusion in LT included the recipient's platelet count, SCr, and INR.

In the present study, the recipient's preoperative Plt counts and INR were important hematological factors predicting the need for platelet

Table 2. Clinical and laboratory data during and after liver transplant in the groups with and without platelet transfusion

Variable	Group A (n=70) with platelets transfusion	Group B (n=80) without platelets transfusion	p
Warm ischemia, time, min	52.3 (11.1)	50.3 (14.0)	0.352**
Cold ischemia, time, min	188.8 (74.7)	173.3 (48.1)	0.129**
Surgical, time, min	376.5 (74.6)	353.4 (74.7)	0.060**
Piggyback LT technique, n (%)	35 (50)	30 (62.5%)	0.123$
PVT yes, n (%)	20 (28.6)	18 (22.5%)	0.394$
Blood loss, mL	3128.57 (1427.36)	2085.31 (1070.05)	<0.001*
Intra-op PRBC (units)	3.51 (2.01)	2.40 (1.54)	0.001*
Intra-op FFP (units)	3.87 (2.34)	3.01 (1.85)	0.033*
Intra-op Cryo (units)	1.38 (1.44)	1.02 (1.52)	0.059*
Intra-op Fibrinogen concentrate (g)	1.0 (0.85)	0.56 (0.80)	0.001*
Last arterial pH	7.33±0.05	7.35±0.04	0.120**
Post-op PRBCs (units)	2.98 (2.09)	1.15 (1.55)	<0.001*
Post-op FFP (units)	2.37 (2.50)	0.5750 (1.29)	<0.001*
Post-op Cryo (units)	0.30 (1.04)	0.12 (0.66)	0.213*
ICU length of stay (days)	7.05 (2.86)	6.01 (2.05)	0.031*
Total Platelet transfusion, mean (min–max) unit	9 (2–28)	0 (0–0)	<0.001

*: Mann-Whitney test; **: Independent sample t-test; $: Chi Square test. LT: Liver transplant; PRBC: Packed red blood cell; ICU: Intensive care unit. Data were reported using mean (standard deviation) for quantitative variabes and frequency (percentage) for qualitative.

transfusion in LT. However, the study by De Santis and colleagues[10] reported that LT recipients with lower preoperative platelet counts (<100,000/L) than those with higher counts required more PRBC (p=0.01) and FFP units (p=0.037) transfusion but not platelet component (p=0.82). These conflicting results may be due to inconsistent coagulation management and platelet transfusion thresholds. Improvements in anesthetic care and advances in knowledge of hemostatic disorders associated with liver transplantation have led to changes in transfusion requirements. It is controversial whether altered coagulation tests are associated with increased blood loss during LT, especially because prothrombin time and activated partial thromboplastin time can disclose only alteration on the procoagulant aspect of coagulation, and not anticoagulant and fibrinolysis.

However, in terms of INR, our findings are similar to those of previous studies.[10] As in the retrospective survey of Cywinski et al.,[11] higher INR and lower platelet counts before LT proved to be highly statistically significant predictors of higher intraoperative use of blood products.

Moreover, in our results, the other predictor of platelet transfusion was pre-LT recipients SCr. Many previous studies have also shown this result. Mangus et al.[12] have reported that higher preoperative serum creatinine is associated with increased blood loss and probably increased requirements for blood components. Modanlou and colleagues[13] included that recipients with a pre-LT SCr greater than 1.3 mg/dL were about four times more likely to require a perioperative PRBC transfusion. In addition, plasma and PLT transfusions correlated well with the number of RBC units used.

Several studies have shown that the MELD score predicts blood loss and is an important determinant of blood component consumption during LT.[14,15] Conflicting results have also been reported.[10,16] Hence, the relationship between the MELD score and the need for blood transfusion in LT is controversial.

Table 3. Final logistic regression model to predict platelet consumption in 150 primary liver transplants

Variable	p	OR (95% CI, lower–upper)
Preoperative platelet count <50 X 10^9/L	<0.001	0.979 (0.969–0.989)
Preoperative SCr ≥123.76 µmol/L, (1.4 mg/dl)	0.005	4.35 (1.566–12.097)
Preoperative INR ≥1.5	0.017	2.771 (1.198–6.412)

SCr: Serum creatinine; INR: International normalized ratio. OR: Odd ratios; CI: Confidence interval.

Interestingly, there was a significant difference in the MELD score between the two groups of our study. However, this variable was insignificant for predicting preoperative LT platelet consumption in the final logistic regression model. The effect of pathophysiological diversity associated with underlying liver disease, surgical factors, and the consequence of cardiovascular instability may be potential factors affecting transfusion in LT. Blood transfusion requirement in LT seems multifactorial and may be independent of the preoperative MELD score.

The main limitation of our study was the retrospective nature of this study.

Conclusion

Our study showed that the predictors of perioperative LT platelet transfusion were; the recipient's preoperative platelet count, SCr, and INR.

Ethics Committee Approval: The Mashhad University Clinical Research Ethics Committee granted approval for this study (date: 24.06.2020, number: IR.MUMS.MEDICAL.REC.1399.193).

Author Contributions: Concept – SM; Design – SM; Supervision – SM, MT; Materials – SM, RT; Data Collection and/or Processing – SM, RT; Analysis and/or Interpretation – MT; Literature Search – SM; Writing – SM; Critical Reviews – MT.

Conflict of Interest: The authors have no conflict of interest to declare.

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