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Can preoperative thrombocytopenia be a risk indicator for emergency surgery due to liver transplant complications?

Karaciğer nakli komplikasyonlarına bağlı acil cerrahide preoperatif trombositopeni bir risk göstergesi olabilir mi?

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ABSTRACT

Aim: This study aimed to investigate the effect of preoperative thrombocytopenia and other risk factors on the need for emergency surgery due to complications following living donor liver transplantation (LDLT), and to evaluate the impact of emergency surgery on patient survival.

Materials and Methods: The data of 270 patients who underwent LDLT for end-stage liver disease between July 2021 and October 2023 were analyzed retrospectively. Patients were divided into two groups: those requiring postoperative emergency surgery and those who did not. Preoperative demographic findings, etiology, comorbidities, Model for End-Stage Liver Disease (MELD) scores, and laboratory parameters (including platelet counts and INR) were compared between the groups.

Results: Postoperative emergency surgery was required in 31 (11%) patients. The most common indications were portal vein thrombosis, intra-abdominal bleeding, and hepatic vein thrombosis. The mean preoperative platelet count was significantly lower (p=0.027) and INR was significantly higher (p=0.047) in the emergency surgery group compared to the non-emergency group. A platelet cut-off value of 81,000/mm³ was identified for predicting reoperation. There was no statistically significant difference between the groups regarding comorbidities or decompensation findings. Emergency surgical intervention significantly shortened patient survival (p<0.001).

Conclusions: Preoperative thrombocytopenia, particularly values below 81,000/mm³, and elevated INR are significant risk indicators for postoperative complications requiring emergency surgery in LDLT recipients. The need for emergency surgery is associated with poor survival outcomes; therefore, high-risk patients should be monitored closely.

Keywords: Liver transplantation, thrombocytopenia, postoperative complications, reoperation, survival rate

ÖZ

Amaç: *Bu çalışma, canlı vericili karaciğer nakli (LDLT) sonrası gelişen komplikasyonlara bağlı acil cerrahi gereksiniminde preoperatif trombositopeni ve diğer risk faktörlerinin etkisini araştırmayı ve acil cerrahinin hasta sağkalımı üzerindeki etkisini değerlendirmeyi amaçlamıştır.*

Gereç ve Yöntem: *Temmuz 2021 ile Ekim 2023 tarihleri arasında son dönem karaciğer hastalığı nedeniyle LDLT uygulanan 270 hastanın verileri retrospektif olarak incelendi. Hastalar postoperatif acil cerrahi gerektirenler ve gerektirmeyenler olmak üzere iki gruba ayrıldı. Gruplar arasında preoperatif demografik bulgular, etyoloji, komorbiditeler, Son Dönem Karaciğer Hastalığı Modeli (MELD) skorları ve laboratuvar parametreleri (trombosit sayıları ve INR dahil) karşılaştırıldı.*

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Bulgular: *Postoperatif acil cerrahi 31 (%11) hastada gerekli görüldü. En sık endikasyonlar portal ven trombozu, karın içi kanama ve hepatik ven trombozu idi. Acil cerrahi grubunda preoperatif trombosit sayısı, cerrahi uygulanmayan gruba göre anlamlı derecede düşük (p=0,027) ve INR anlamlı derecede yüksek (p=0,047) saptandı. Yeniden ameliyatı öngörmede trombosit için kestirim değeri 81.000/mm³ olarak belirlendi. Komorbiditeler veya dekompansasyon bulguları açısından gruplar arasında istatistiksel olarak anlamlı fark izlenmedi. Acil cerrahi müdahalesi hasta sağkalımını anlamlı ölçüde kısalttı (p<0,001).*

Sonuç: *LDLT alıcılarında preoperatif trombositopeni (özellikle 81.000/mm³ altındaki değerler) ve yüksek INR, acil cerrahi gerektiren postoperatif komplikasyonlar için önemli risk göstergeleridir. Acil cerrahi gereksinimi kötü sağkalım sonuçları ile ilişkilidir; bu nedenle yüksek riskli hastalar yakından izlenmelidir.*

Anahtar Sözcükler: *Karaciğer nakli, trombositopeni, postoperatif komplikasyonlar, reoperasyon, sağkalım oranı*

INTRODUCTION

Postoperative emergency surgery rate in organ transplant patients reaches 18% and mortality rate increases up to 5.5% with increasing morbidity. Postoperative complications after living donor liver transplantation, which may be predisposed by preoperative factors, may lead to emergency surgical interventions (1, 2). Decompensation findings and severity, comorbidities, preoperative blood biochemistry parameters including MELD score and changes in blood cell count may affect post-transplant success (3). Platelet values, especially important in terms of bleeding diathesis, inflammation and tissue nutrition, should be carefully examined as a factor of postoperative complications (3–5). Intraabdominal bleeding, hepatic artery thrombosis, portal and hepatic vein thrombosis, severe bile leakage, evisceration, gastrointestinal perforation is common posttransplant complications requiring emergency surgery (6–8). Thrombocytopenia may be a risk factor for these complications (3, 9). In our study, we examined the effect of preoperative comorbidities, decompensation findings, laboratory parameters and thrombocytopenia on postoperative complications requiring emergency surgery. We also examined the effect of this postoperative emergency surgery on mortality and survival.

MATERIALS and METHODS

This single-center retrospective study was conducted at a tertiary university hospital in Istanbul, which has an experienced transplantation center performing an average of 120 living donor liver transplants per year. Collected LT database was retrospectively reviewed. Two hundred and seventy patients who underwent living-donor liver transplantation (LDLT) for end stage liver cirrhosis between July 2021 and October 2023 were included in the study. No cases were included from any other center. The single-center design provided homogeneity in terms of surgical team, operative techniques, anesthesia protocols, intensive care management, and postoperative immunosuppressive therapy standards**.** Because the study was designed retrospectively, no written informed consent form was obtained from patients. All procedures were conducted in accordance with the ethical standards of the committees concerned with human experimentation (institutional and national) and the 1964 Declaration of Helsinki and its later editions. This study was approved by the University Human Experiments Ethics Committee with an ethics committee with 2023/143 decision number on date 11/15/2023.

We also examined the effect of this postoperative emergency surgery on mortality and survival. Reasons for emergency postoperative surgery were portal vein thrombosis, hepatic vein thrombosis, intra-abdominal bleeding, ileus, colonic perforation, evisceration, and wound abscess, cerebral shunt due to increased intracranial pressure (ICP) syndrome, coagulopathy and nephrectomy due to graft dysfunction.

Age, gender, body mass index (BMI), Model for End-Stage Liver Disease (MELD) and Child scores, transfusion of blood products (erythrocytes, other plasma products), anhepatic phase, duration of cold ischemia, operation time, graft-to-recipient weight ratio (G.R.W.R.) values, postoperative intensive care unit and total hospital stay, and etiologies of the patients who underwent emergency surgery and those who did not need emergency surgery were expressed as ratios.

Patients were statistically compared in terms of preoperative INR, platelet, sodium (Na), albumin, total protein, total bilirubin and creatinine values. Also, ascites, esophageal variceal bleeding (EVB), hepatic encephalopathy (HE), spontaneous bacterial peritonitis (SBP) and comorbidities such as diabetes mellitus (DM), hypertension (HT) and coronary artery disease (CAD) were statistically compared. In addition, we examined whether there was a statistical difference in mortality and patient survival between patients in need of postoperative emergency surgical intervention and those who did not.

Blood Product Transfusion Protocol

Perioperative blood product transfusion was performed according to clinical indications. The target hemoglobin was >7–8 g/dL, and platelet count was >50,000/mm³ (in the presence of surgical intervention) or >20,000/mm³ (in the absence of bleeding). The use of fresh frozen plasma (FFP) was restricted due to the risk of post-liver transplant hypercoagulability and vascular thrombosis. FFP was used only for coagulopathy correction in the presence of active bleeding or prior to invasive procedures. Since it is known that INR spontaneously corrects with the onset of new liver function, routine FFP replacement was not performed.

Preoperative Vascular Evaluation

All patients underwent comprehensive vascular imaging as part of our standard pre-transplant evaluation protocol. A portal triphasic computed tomography (arterial, portal venous, and late venous phases) was performed for all patients. Portal vein, hepatic veins, and hepatic artery flow patterns were systematically evaluated using Doppler ultrasonography. Magnetic resonance angiography was performed in selected cases for anatomical detailing. Patients with detected preoperative portal vein thrombosis were excluded from the study as they required different surgical techniques (thrombectomy, jump graft) that could independently affect postoperative outcomes. A limited number of patients with preoperative hepatic vein thrombosis (Budd-Chiari syndrome) were included.

Postoperative Management and Anticoagulation Protocol

A standard postoperative management protocol was applied to all patients. Immunosuppression consisted of tacrolimus (target trough level 8–12 ng/mL), mycophenolate mofetil, and tapered steroids. This protocol was regulated considering the risk of hepatic artery and portal vein thrombosis. The anticoagulation strategy was managed with particular caution. In the absence of active bleeding, low molecular weight heparin (enoxaparin) was initiated in the postoperative period once the INR value dropped below 2. Low-dose aspirin (100 mg/day) was added on postoperative day 7 in patients whose platelet count rose above 50,000/mm³.

Statistical analysis

Nominal and ordinal parameters were described with frequency analysis, whereas scale parameters were described with means and standard deviations. Chi-Square Test and Chi-Square Likelihood tests were used for differences between categorical parameters. Kolmogorov-Smirnov test was used for normality of scale parameters. Mann-Whitney U test was used for difference analysis since distributions were non-normal. Spearman's rho correlation and Cox Regression tests were used for relational analysis. SPSS 17.0 for Windows was used at 95% Confidence Interval.

RESULTS

Early Postoperative Causes of Emergency Surgery

The number of patients undergoing postoperative emergency surgery was 31, 11% of all patients. Hepatic artery thrombosis was not observed in any patient. The reasons for emergency surgical intervention due to complications were PVT (28%), HVT (16%), bile leakage (9%), intraabdominal bleeding (26%), ileus (6%), colonic perforation (3%), evisceration and wound infection (6%), cerebral shunt due to increased intracranial pressure (3%), and graft nephrectomy due to kidney graft dysfunction in a combined liver-kidney transplant patient (3%).

Preoperative Demographic Findings and Etiology

When the data of 270 patients included in the study were examined, the mean age of the group undergoing postoperative emergency surgery (n = 31) was 34.4 ± 24.1 years, while the mean age of the group not requiring emergency surgery (n = 239) was 49.1 ± 18.5 years. The MELD score, indicating the severity of liver failure, was found to

be numerically higher in the emergency surgery group (23.0 ± 16.3) compared to the non-emergency group (15.8 ± 6.6) (Table-1). When evaluated in terms of etiological factors, the most common causes in patients undergoing emergency surgery were observed as cryptogenic cirrhosis (21%), hepatocellular carcinoma (16%), and biliary atresia (15%), respectively (Table-2). No marked difference was observed between the groups in terms of gender distribution and Body Mass Index (BMI) (Table-1).

Perioperative Graft Factors, Findings Related to Follow-up and Hospitalization Periods

When operative process and graft factors were evaluated, similar results were obtained between the groups with and without emergency surgery in terms of anhepatic phase, cold ischemia time, and operation time (Table-1). The mean graft-to-recipient weight ratio (GRWR) was 1.29 ± 0.78 in the emergency surgery group and 1.10 ± 0.33 in the non-surgical group (Table-1). In postoperative follow-up periods, the duration of intensive care unit stay for patients requiring emergency surgery (5.1 ± 4.05 days) was longer compared to the other group (2.4 ± 2.07 days). Similarly, the total length of hospital stay was found to be higher in the emergency surgery group (17.5 ± 13.3 days) compared to the group without surgery (14.3 ± 5.8 days) (Table-1).

In the postoperative period (after the initial LDLT and before potential reoperation), routine blood product transfusion was not performed in either group. Blood products were administered only in the presence of clinical indications (active bleeding, severe anemia, or coagulopathy correction prior to invasive procedures). Patients requiring emergency surgery received blood product support according to their needs during the preoperative preparation phase for reoperation, the intraoperative period, and the post-reoperation period.

Table-1. Statistical Results of Emergency Surgery According to Preoperative Demographic Variables, Peripherative Graft Findings, Hospital Stay, Mortality, Survival

Variable	Emergent Surgery (n = 31)	No Emergent Surgery (n = 239)	p Value
Gender			
Male (%)	11.9	88.1	p > 0.05
Female (%)	10.9	89.1	
Age (years) mean ± SD (CI)	34.4 ± 24.1 (25.3–43.4)	49.1 ± 18.5 (46.7–51.5)	p > 0.05
BMI (kg/m²) mean ± SD (CI)	25.8 ± 7.06 (22.6–28.9)	26.8 ± 5.4 (26.9–27.5)	p > 0.05
MELD score mean ± SD (CI)	23.0 ± 16.3 (13.8–18.9)	15.8 ± 6.6 (14.9–16.7)	p > 0.05
Child–Pugh class (%)			
A	5.3	94.7	
B	10.3	89.7	p > 0.05
C	12.8	87.2	
Peripherative blood product transfusion (%)			
Erythrocyte transfusion	16.7	83.3	
Other plasma products	0	100	p > 0.05
None	9.7	90.3	
Anhepatic phase (min) mean ± SD (CI)	88.7 ± 33.2 (73.5–103.8)	90.1 ± 34.9 (84.9–95.3)	p > 0.05
Cold ischemia time (min) mean ± SD (CI)	66.8 ± 27.6 (54.2–79.4)	63.9 ± 35.0 (58.6–69.1)	p > 0.05
Operation time (min) mean ± SD (CI)	481.4 ± 79.4 (437–525)	464.6 ± 78.4 (450–478)	p > 0.05
Graft-to-recipient weight ratio (GRWR) mean ± SD (CI)	1.29 ± 0.78 (0.93–1.64)	1.10 ± 0.33 (1.05–1.14)	p > 0.05
ICU stay (days) mean ± SD (CI)	5.1 ± 4.05 (3.5–6.7)	2.4 ± 2.07 (2.1–2.7)	p < 0.05
Hospital stay (days) mean ± SD (CI)	17.5 ± 13.3 (12.1–22.9)	14.3 ± 5.8 (13.6–15.1)	p > 0.05

Differences were considered statistically significant at p < 0.05

Values for categorical variables are row percentages, i.e. the proportion of patients within each category who did and did not require emergency surgery (row total = 100%). Group sizes for blood product transfusion: erythrocyte transfusion n = 42, other plasma products n = 4, no transfusion n = 176.

Table-2. Statistical Analysis of Patients in Need of Emergency Surgery According to Etiologies

Etiology %	Emergent Surgery	No Emergent Surgery	Total (n:270)
HBV	10	14	14
HBV + HDV	–	3	2
HCC	16	13	13
Ethanol	–	5	5
NASH	10	13	13
Cryptogenic	21	26	23
Autoimmune hepatitis	6	7	8
Primary biliary cirrhosis	–	2	1
Primary sclerosing cholangitis	3	1	1
HCV	3	3	3
Secondary biliary cirrhosis	–	1	1
Budd–Chiari syndrome	–	2	1
Caroli disease	6	1	2
PFIC	3	1	2
Biliary atresia	15	3	4
Other genetic disorders*	7	5	5

Abbreviations: HBV: Hepatitis B virus; HDV: Hepatitis D virus; HCV: Hepatitis C virus; HCC: Hepatocellular carcinoma; PFIC: Progressive familial intrahepatic cholestasis.
*Other genetic disorders include Wilson disease, Alagille syndrome, sarcoidosis, and scleroderma.
Values are column percentages within each group (emergent surgery n = 31; no emergent surgery n = 239; total n = 270), rounded to the nearest integer.

Statistical findings of preoperative decompensation findings and comorbidities

There was no statistically significant difference between patients who underwent emergency surgery and those who did not in terms of comorbidities such as ascites (p=0.066), EVB (p=0.059), HE (p=0.567), SBP (p=0.607); DM (p=0.875), HT (p=0.061), CAD (p=0.969), which are preoperative decompensation findings.

Preoperative laboratory findings

There was no statistical difference in sodium (Na) (p=0.120), albumin (p=0.093), total protein (p=0.405), total bilirubin (p=0.147), creatinine (p=0.406) between patients who underwent emergency surgery and those who did not. However, INR was statistically higher (p=0.047) and platelets were lower (p=0.027) in patients who underwent emergency surgery (Table-3). The ROC curve for PLT in estimating reoperation was constructed, and the area under the curve was 0.641 (95% CI = 0.531 to 0.751, P < 0.021). The cut-off value of PLT was 81.0 (10^3/ml) with a sensitivity of 60.9% and a specificity of 60.3% (Figure-1).

Although the mean MELD score was numerically higher in the emergency surgery group (23.0 ± 16.3) compared to the non-emergency group (15.8 ± 6.6), this difference was not statistically significant (p>0.05). Furthermore, ROC curve analysis for the MELD score did not identify a significant cut-off value for predicting emergency surgery (p=0.652).

Table-3. Statistical Analysis of Patients in Need of Emergency Surgery According to Preoperative Decompensation Findings, Comorbidities and Laboratory Parameters

Preoperative Variables	Emergent Surgery (n =	No Emergent Surgery (n	*p* value
Ascites (%)			
Yes	13.1	5.2	0.066
No	86.9	94.8	
Esophageal variceal bleeding (EVB) (%)			
Yes	3.6	12.6	0.059
No	96.4	87.4	

Hepatic encephalopathy (HE) (%)			
Yes	12.0	9.5	0.567
No	88.0	90.5	
Spontaneous bacterial peritonitis (SBP) (%)			
Yes	16.7	10.2	0.607
No	83.3	89.8	
Diabetes mellitus (DM) (%)			
Yes	9.8	10.6	0.875
No	90.2	89.4	
Hypertension (HTN) (%)			
Yes	0	12.0	0.061
No	100	88.0	
Coronary artery disease (CAD) (%)			
Yes	10.0	10.4	0.969
No	90.0	89.6	
INR mean ± SD (CI)	1.7 ± 0.6 (1.4–1.9)	1.4 ± 0.48 (1.4–1.5)	**0.047**
Platelet (×10³/mm³) mean ± SD (CI)	86.7 ± 64.7 (58.7–114.7)	119.1 ± 90.0 (106.5–131.7)	**0.027**
Sodium (mmol/L) mean ± SD (CI)	134.4 ± 5.4 (132.1–136.8)	136.3 ± 4.3 (135.7–136.9)	0.120
Albumin (g/dL) mean ± SD (CI)	2.8 ± 0.65 (2.5–3.1)	3.1 ± 0.72 (3.0–3.2)	0.093
Total protein (g/dL) mean ± SD (CI)	6.6 ± 1.07 (6.1–7.07)	6.8 ± 0.85 (6.6–6.9)	0.405
Total bilirubin (mg/dL) mean ± SD (CI)	4.21 ± 3.67 (2.6–5.8)	4.43 ± 6.71 (3.5–5.3)	0.147
Creatinine (mg/dL) mean ± SD (CI)	0.87 ± 0.61 (0.69–1.13)	0.88 ± 0.69 (0.78–0.98)	0.406

Abbreviations: EVB: Esophageal variceal bleeding; HE: Hepatic encephalopathy; SBP: Spontaneous bacterial peritonitis; DM: Diabetes mellitus; HTN: Hypertension; CAD: Coronary artery disease. All laboratory parameters presented in the table were obtained from routine preoperative blood samples collected immediately before the surgical procedure.

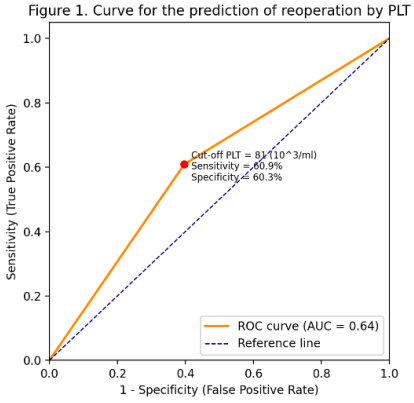

Figure-1. Curve for the prediction of reoperation by PLT

Mortality and Patient Survival Statistical Findings

The mean follow-up time of patients who underwent emergency surgery due to complications was 11.3 months (range: 6.8-15.8), and the mean survival time of patients who did not need reoperation was 23 months (range: 21.8-24.3). Emergency surgical intervention statistically shortened survival (p<0.001).

DISCUSSION

It is known that platelets are effective in all phases of the process from ischemia-reperfusion injury to full graft compliance after LDLT (3). With this effect on graft regeneration, thrombocytopenia may be a determinant for postoperative complications and mortality/survival (3, 10). The effect of

preoperative thrombocytopenia, which increases these complications and mortality and shortens survival, should be a warning for us before transplantation (11–13). In addition, considering the risk of platelets decreasing up to 60% in the postoperative period in liver transplant recipients, it is obvious that preoperative thrombocytopenia will prepare the ground for postoperative complications and emergency interventions (3, 14). Complications increased by thrombocytopenia and related emergency surgery include bleeding, severe infection and sepsis, and perforations. In different studies, platelet values that increase the complication rate have been statistically analyzed with different cut-off values such as <30,000, <50,000, <100,000 and <150,000. It has been observed to affect mortality and survival especially in studies with platelet values <30,000 and <150,000 (9, 15, 16). However, no significant result was observed in studies evaluating the relationship between preoperative INR and postoperative complications (4, 17). In our study, it was found that the need for emergency surgery increased after transplantation at platelet values <81,000. Similarly, it was observed that elevated INR statistically increased the rate of emergency surgery.

Portal and hepatic vein thrombosis are multifactorial complications. In our study, technical factors (standardized microsurgical anastomosis), graft factors (similar cold ischemia times), and hemodynamic management (standard protocols) were similar between the groups. Notably, there were four patients (1.5%) with preoperative hepatic vein thrombosis (Budd-Chiari syndrome) in our series, and none of these patients developed new vascular thrombosis in the postoperative period; this can be considered an indicator of technical success. However, the lower mean age in the emergency surgery group (34.4 ± 24.1 vs 49.1 ± 18.5) suggests that different pathophysiological mechanisms might play a role in the pediatric age group. In multivariate analysis, even after adjusting for potential confounders such as age, MELD score, and operation time, preoperative platelet count <81,000/mm³ remained an independent risk indicator for thrombosis.

The main causes of coagulopathy in end-stage liver failure patients are splenomegaly-induced thrombocytopenia due to portal hypertension and impaired synthesis of coagulation factors in the liver (elevated INR). After the new liver is transplanted, INR usually returns to normal within the first 24–48 hours as portal hypertension recedes and a normally functioning liver takes over. However, thrombocytopenia improves more slowly because splenomegaly does not regress immediately. This creates a paradox in the early postoperative period: while INR normalizes, platelet counts may remain low, creating a picture that can increase thrombosis risk alongside hypercoagulability. Furthermore, delaying the initiation of anticoagulation in thrombocytopenic patients to reduce bleeding risk may additionally contribute to the thrombosis risk. Within this pathophysiological framework, preoperative thrombocytopenia should be viewed not as a sole causal factor, but as a marker defining a high-risk patient population.

While both elevated MELD scores and decreased platelet counts were observed in the emergency surgery group, our analysis revealed that MELD score itself was not a statistically significant predictor of emergency reoperation (p=0.652). This finding suggests that preoperative thrombocytopenia may represent an independent risk factor that provides additional prognostic value beyond traditional markers of liver disease severity such as MELD score.

Comorbidities have an important place among the factors that may affect emergency surgery after transplantation. When DM, HT and CAD were evaluated, they did not affect the rate of postoperative emergency surgery at a high rate, but some studies have shown a significant effect (18, 19). No effect of these comorbidities was found in our study.

Likewise, as decompensation findings, which are another indicator of the severity of portal hypertension causing thrombocytopenia, occur, postoperative complications and the rate of surgical intervention will increase. In addition to the findings showing an increase in postoperative surgical intervention in the presence of EVB, HE, ascites and SBP, it has also been observed that there is no effect (18, 20). In the light of these heterogeneous results, our study showed that decompensation findings did not affect the rate of emergency surgery after transplantation.

CONCLUSION

While preoperative thrombocytopenia in liver transplant recipients, especially values below 81,000/mm³, is a risk factor for emergency surgical intervention after transplantation, studies with

higher participation will contribute more to this issue.

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