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Reoperation etiologies in the initial hospital stay after liver transplantation: a single-center study from Iran

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Background: Liver transplantation (LT) is widely recognized as a life-saving therapy for patients with end-stage liver disease. However, due to certain posttransplant complications, reoperations or endovascular interventions may be necessary to improve patient outcomes. This study was conducted to examine reasons for reoperation during the initial hospital stay following LT and to identify its predictive factors.
Methods: We evaluated the incidence and etiology of reoperation in 133 patients who underwent LT from brain-dead donors over a 9-year period based on our experiences.
Results: A total of 52 reoperations were performed for 29 patients, with 17 patients requiring one reoperation, seven requiring two, three requiring three, one requiring four, and one requiring eight. Four patients underwent liver retransplantation. The most common cause of reoperation was intra-abdominal bleeding. Hypofibrinogenemia was identified as the sole predisposing factor for bleeding. Frequencies of comorbidities such as diabetes mellitus and hypertension did not differ significantly between groups. Among patients who underwent reoperation due to bleeding, the mean plasma fibrinogen level was 180.33±68.21 mg/dL, while among reoperated patients without bleeding, it was 240.62±105.14 mg/dL (P=0.045; standard mean difference, 0.61; 95% confidence interval, 0.19–1.03). The initial hospital stay was significantly longer for the reoperated group (47.5±15.5 days) than for the non-reoperated group (22.5±5.5 days).
Conclusions: Meticulous pretransplant assessment and postoperative care are essential for the early identification of predisposing factors and posttransplant complications. In order to enhance graft and patient outcomes, any complications should be addressed without hesitation, and appropriate intervention or surgery should not be delayed.

Keywords: Liver transplantation; Repeat surgery; Postoperative complications; Etiology

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HIGHLIGHTS

- The most common cause for reoperation after liver transplant was intra-abdominal bleeding.
- Hypofibrinogenemia was identified as the sole predisposing factor for bleeding.
- No statistical differences regarding primary etiology or Model for End-Stage Liver Disease score was identified.

INTRODUCTION

The first liver transplantation (LT) was performed by Thomas E. Starzl in 1963, and it has since become the final treatment option for end-stage liver disease [1-3]. Long-term survival rates have increased significantly since the introduction of cyclosporine [4]. Over the past two decades, approximately 3,500 LTs have been performed on adults at various LT centers across Iran, with 1-year and 5-year survival rates of 85% and 77%, respectively [5].

Four primary types of postoperative complications can result in graft failure: vascular, biliary, parenchymal, and malignant complications [6]. Both early and late complications following LT may necessitate reoperation, which can subsequently impact the overall outcome; such reoperations are typically indicated for intra-abdominal bleeding, intra-abdominal infections, biliary complications, and life-threatening graft vascular complications [7,8]. Among the factors contributing to the need for reoperation, hemorrhage and issues with biliary tract anastomosis are the most prevalent [9]. The aim of this study was to determine the frequency, indications, and predictive factors for reoperations following LT.

METHODS

This study was conducted in compliance with the principles of the Declaration of Helsinki. The study's protocol was reviewed and waived by the Institutional Review Board of Shahid Beheshti University of Medical Sciences. Written informed consent was waived.

In this cross-sectional analytical study, we examined the frequency of and indications for reoperation during the initial hospital stay after LT. Those indications included intra-abdominal bleeding, graft vascular complications, biliary complications, tracheostomy due to respiratory issues, intra-abdominal infections, and wound dehiscence. In total, 133 LT candidates received whole organ grafts from deceased donors, and orthotopic LT was performed on the recipients.

Reoperation is defined as any condition that necessitates the patient's return to the operating room during the same hospital stay. Preoperative data were acquired from the waiting list registry system, while demographic characteristics and clinical information about the patients were extracted from their medical records. Factors such as sex, age, medical comorbidities, history of prior abdominal surgery, pre-LT serum fibrinogen level, platelet count, Model for End-Stage Liver Disease (MELD) score, Child-Pugh classification, hospital stay duration, and ischemic time were included in the analysis to identify potential risk factors for complications requiring reoperation.

Data Analyses

Data analyses were conducted using IBM SPSS ver. 20 (IBM Corp.) and SAS ver. 9.1 (SAS Institute). A P-value of ≤0.05 was considered to indicate statistical significance. Quantitative data were expressed as mean±standard deviation (SD), while categorical variables were displayed as frequency (percentage) when appropriate. The associations between various characteristics were evaluated using the chi-square test or t-test and were accompanied by 95% confidence intervals (CIs).

RESULTS

Of the 133 patients, 29 patients (21.8%) required reoperation, and 52 reoperations were performed. Specifically, 17 patients (12.8%) underwent one reoperation, 7 patients (5.2%) underwent two reoperations, 3 patients (2.2%) underwent three, 1 patient (0.7%) underwent four, and 1 patient (0.7%) underwent eight. The most common indication for reoperation was intra-abdominal bleeding (n=21, 15.8%), followed by tracheostomy (n=13, 9.7%), peritoneal collection (n=5, 3.7%), liver retransplantation (n=4, 3.0%), hepatic artery thrombosis (n=2, 1.5%), biliary complications (n=2, 1.5%), duodenal perforation (n=2, 1.5%), portal vein thrombosis (n=1, 0.7%), thoracotomy (n=1, 0.7%), and wound infection (n=1, 0.7%) (Table 1).

In this study, 45.1% (n=60) of the patients were male,

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Table 1. Reoperation frequency and etiologies

Variable	Reoperation
Total patients	133
Any etiology	29 (21.8)
Single reoperation	17 (12.8)
Multiple reoperation	12 (9.0)
Specific etiology	
Intra-abdominal bleeding	21 (15.8)
Tracheostomy	13 (9.7)
Peritoneal collection	5 (3.7)
Liver retransplantation	4 (3.0)
Hepatic artery thrombosis	2 (1.5)
Biliary complication	2 (1.5)
Duodenal perforation	2 (1.5)
Portal vein thrombosis	1 (0.7)
Thoracotomy	1 (0.7)
Wound infection	1 (0.7)

Values are presented as number (%).

Table 2. Comparison of characteristics between reoperated and non-reoperated groups

Characteristic	Reoperated group	Non-reoperated group	P-value
Age (yr)	40.5±12.5	38.7±12.2	0.49
Male sex	17 (28.3)	43 (71.7)	0.09
Primary etiology			
Cryptogenic cirrhosis	13 (44.8)	30 (28.8)	0.08
Primary sclerosing cholangitis	6 (20.7)	30 (28.8)	0.04
Autoimmune hepatitis	8 (27.6)	26 (25.0)	0.76
Other	2 (6.9)	18 (17.4)	-
Child-Pugh classification			
Class A	0	1 (1.0)	0.15
Class B	4 (13.8)	15 (14.4)	0.09
Class C	25 (86.2)	88 (84.7)	0.02
MELD score	26.66±5.78	24.75±5.46	0.06
Comorbidity			
Diabetes mellitus	4 (13.7)	7 (6.7)	>0.05
Arterial hypertension	1 (3.4)	4 (3.8)	>0.05
Operation			
Cholecystectomy	1 (3.4)	7 (6.7)	>0.05
TAH-BSO	1 (3.4)	4 (3.8)	>0.05
Umbilical hernia	1 (3.4)	2 (1.9)	>0.05
Appendicitis	0	4 (3.8)	>0.05
Other[a)]	0	4 (1.0)	>0.05

Values are presented as mean±standard deviation or number (%).
MELD, Model for End-Stage Liver Disease; TAH-BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy.
[a)]Colectomy, splenectomy, segmental intestinal resection, and hiatal hernia.

with a mean age of 40.5±12.5 years in the reoperated group and 38.7±12.2 years in the non-reoperated group. No statistically significant differences were observed between the two groups regarding the primary etiology of LT, Child-Pugh classification, MELD score, and comorbidities, including diabetes mellitus and hypertension (P>0.05) (Table 2).

The history of previous abdominal surgery was assessed among all patients, and no statistically significant difference was found between the two groups (P>0.05). Among the patients who underwent reoperation, 10.2% (n=3) had a history of abdominal surgery, including cholecystectomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy, and umbilical hernia. In contrast, 20.2% (n=21) of the non-reoperated patients had a history of abdominal surgery, with cholecystectomy being the most common surgery at a prevalence of 6.7% (Table 2).

In terms of laboratory data, the platelet count per liter was 99.28±65.73 (mean±SD) in the reoperated group and 118.65±92.78 (mean±SD) in the non-reoperated group, with no significant difference observed between the two. The plasma fibrinogen level was significantly lower among reoperated patients (196.28±85.23 mg/dL) compared to the non-reoperated group (228.75±73.45 mg/dL) (P<0.05; standard mean difference, 0.43; 95% CI, 0.018–0.850). Similarly, when comparing the operated patients with and without bleeding, the mean plasma fibrinogen level was 180.33±68.21 mg/dL in the patients with bleeding and 240.62±105.14 mg/dL in those without bleeding (P=0.045; standard mean difference, 0.61; 95% CI, 0.19–1.03).

Both cold and warm ischemic times were nearly statistically equivalent, with no significant difference observed. The initial hospital stay was notably longer in the reoperated group (47.5±15.5 days) compared to the non-reoperated group (22.5±5.5 days), as shown in Table 3.

DISCUSSION

In patients with end-stage liver disease, LT is a life-saving therapy and yields favorable clinical outcomes [1,2]. However, postoperative complications, such as biliary and vascular issues, may necessitate reoperation proce-

Table 3. Comparison of laboratory data and graft information

Variable	Reoperated group	Non-reoperated group	P-value
Laboratory value			
Platelet count (/L)	99.28±65.73	118.65±92.78	0.72
Plasma fibrinogen level (mg/dL)	196.28±85.23	228.75±73.45	<0.05
Graft information			
Warm ischemic time (min)	48±18	43±12	0.85
Cold ischemic time (hr)	6.1±2.8	6.3±2.9	0.97
Length of first transplantation hospital stay (day)	47.5±15.5	22.5±5.5	0.04

Values are presented as mean±standard deviation.

dures to ensure patient survival [7,8,10,11]. Hemorrhage (67.9%) and biliary tract complications (14.8%) are the most common factors leading to reoperation, and a significant increase in mortality has been observed among patients who undergo these additional procedures [9]. In this study, we examined the prevalence and types of reoperation after LT using a comparison between patients who underwent reoperation and those who did not.

Studies have reported reoperation frequencies after LT to be 29.3% [11] and 17.3% [12]. In our study, the prevalence of reoperation during the initial hospital stay following LT was 21.8%, which aligns with these previous reports. In previous research, up to 29% of patients at an LT center required reoperation; the most common cause was posttransplant intra-abdominal bleeding, which occurred in 17.3% of patients. Consistent with our study, the plasma fibrinogen level before LT was significantly lower in patients who required reoperation compared to those who did not [7]. In other studies, 10.8% [13] and 16.6% [14] of patients required reoperation for bleeding after LT. It has also been concluded that appropriate administration of platelets, antifibrinolytics, fibrinogen, fresh frozen plasma, and other interventions are associated with the management of coagulopathic effects of LT [7,13,14].

A 2023 study indicated that patients with ascites who exhibited higher fibrinogen levels on postoperative day 1 experienced improved 1- and 2-year survival rates [15]. In our study, the frequency of intra-abdominal bleeding (15.8%) was consistent with other studies and was associated with preoperative coagulopathy and low plasma fibrinogen level, the latter of which was identified as the sole significant factor contributing to bleeding complications after LT. In this context, medical therapy is recommended for patients who are relatively hemodynamically stable. Thrombocytopenia, hypofibrinogenemia, and coagulopathy with elevated international normalized ratio should be managed with infusions of platelets, fibrinogen, and fresh frozen plasma. If the patient does not respond to treatment or experiences ongoing bleeding or hemodynamic instability, surgical exploration should be performed without hesitation during the critical period to enhance graft and patient outcomes.

In our study, the second most common reason for reoperation was tracheostomy (n=13, 9.7%), followed by peritoneal collection (n=5, 3.7%), which included infected biloma and microbial or fungal abscesses. Liver retransplantation was performed in four patients (3.0%), which included two patients who underwent a first reoperation due to hepatic artery thrombosis and two patients with primary liver dysfunction.

In general, vascular complications such as arterial stenosis, arterial thrombosis, aneurysms in the vascular anastomosis, and portal vein thrombosis are important contributors to morbidity and mortality following LT [16-18]. The prevalence of these complications is estimated to be between 5% and 10% in arteries, 1% to 3% in portal veins, and less than 2% in the caval vein [18-22]. In the present study, we observed vascular complications such as hepatic artery thrombosis and portal vein thrombosis with frequencies of 1.5% and 0.7%, respectively.

The incidence of biliary complications, such as biliary leakage, biliary stricture, bilomas, and necrosis of the bile ducts, has been reported to range from 8.2% to 39.0% in various studies. Biliary complications following a liver transplant can substantially increase morbidity and mortality; moreover, the frequency of these complications differs significantly between Roux-en-Y anastomosis and duct-to-duct anastomosis [11,23-25]. The frequency of biliary complications at our center was 1.5% (n=2), and these consisted of biliary leakage in duct-to-duct anastomosis.

At our center, endoscopic retrograde cholangiopancreatography is the initial approach for assessing the ex-

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tent of disruption in patients with bile leakage and duct-to-duct anastomosis, followed by intervention therapy if feasible. For patients with complete disruption, infected biloma, sepsis without the possibility of percutaneous drainage, or Roux-en-Y anastomosis, reoperation is necessary. In the two instances of biliary leakage in the present study, surgical exploration was carried out as a result of complete disruption or biloma, while percutaneous drainage was not feasible or accessible.

In a study examining liver transplant experiences at our center between 2009 and 2017, 116 patients were prioritized for LT based on their MELD scores and Child-Pugh classifications. Sepsis was identified as the most common postoperative complication, while bleeding was the primary cause for reoperation. Notably, patients with lower MELD scores demonstrated better post-LT survival outcomes than those with higher MELD scores [1].

DiNorcia et al. [7] reported that among 1,620 patients undergoing LT, 427 (29%) experienced complications, with bleeding being the most common reoperative complication. Compared to patients who did not require reoperation, those with reoperative complications had higher MELD scores. Reoperative complications were associated with longer hospital stays, increased use of mechanical ventilation, vasopressors, renal replacement therapy, extended warm and cold ischemia times, and higher intraoperative blood transfusion requirements compared to patients who did not require reoperation [7]. However, the association between MELD scores and post-LT survival benefits remains controversial. A systematic review of 37 LT studies revealed that 15 studies found no statistically significant association between MELD scores and post-transplant survival, while 22 studies identified a significant association [26].

Our study presents certain limitations in terms of data collection. Specifically, we did not assess potential confounding factors. Additionally, our sample size, consisting of 29 patients, was inadequate for conducting multivariable analysis based on background characteristics. A thorough evaluation of pretransplant clinical and laboratory findings, including past medical/surgical history, laboratory data, and coagulation profiles, is essential for identifying patients at elevated risk for posttransplant reoperation. Furthermore, meticulous pretransplant assessment and postoperative care are crucial for the early detection of predisposing factors and posttransplant complications. Any complications should be managed promptly, and appropriate interventions or operations must not be delayed to enhance graft and patient outcomes.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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