

Post-living donor liver transplant biliary strictures: prevalence, predictors, and long-term outcomes in a retrospective study

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Background: Post-liver transplant biliary strictures are a common cause of morbidity among patients who have undergone living donor liver transplantation (LDLT). Limited data are available concerning the response rates to various treatment modalities and the long-term outcomes for these individuals.

Methods: This study was a retrospective analysis of a prospectively collected database, including adult patients aged 18 years or older who underwent LDLT between 2006 and 2022.

Results: Between 2006 and 2022, a total of 3,550 patients underwent liver transplantation. After applying exclusion criteria, 2,956 patients were included in the analysis. During the study period, 344 patients (11.6%) developed biliary strictures. Of these, 77.0% underwent endoscopic retrograde cholangiopancreatography as the primary treatment for biliary strictures, while the remainder received percutaneous transhepatic biliary drainage. Identified risk factors for post-liver transplant biliary strictures included the presence of multiple biliary anastomoses, bile leak, and older donor and recipient ages. The overall graft and patient survival rates were comparable between patients with and without biliary strictures, at both 1 year (93.0% vs. 96.3%) and 5 years (82.3% vs. 79.2%).

Conclusions: Biliary strictures are observed in approximately 11% of recipients following LDLT. While the presence of biliary strictures is associated with increased morbidity, it does not significantly impact patient survival.

Keywords: Liver transplantation; Biliary strictures; Posttransplant complications

HIGHLIGHTS

- In this study, post-living donor liver transplant biliary strictures occurred in 11.6% of cases.
- Multiple biliary anastomoses, bile leak, older donor age, and older recipient age were identified as risk factors for biliary strictures following liver transplantation.
- The presence of biliary strictures does not significantly impact recipient survival following liver transplantation.

INTRODUCTION

Liver transplantation is a lifesaving procedure with excellent outcomes for patients with fulminant liver failure and end-stage liver disease. Advances in surgical techniques, postoperative care, and immunosuppression have led to marked improvements in both graft and patient survival over time. However, biliary complications after surgery remain a key cause of morbidity and mortality among liver transplant recipients, affecting approximately 5% to 35% [1]. Common biliary complications include anastomotic and nonanastomotic biliary strictures, bile leaks, and bilomas. Bile duct stones and casts are also observed in a minority of patients [2]. The incidence of biliary strictures is reported to be between 5% and 25%, with a higher occurrence in cases of living donor liver transplantation (LDLT) compared to deceased donor liver transplantation (DDLT) [1,3]. Several factors contribute to the greater incidence of strictures in LDLT, including smaller bile ducts, multiple and relatively proximal anastomoses, and the risk of bile duct devascularization due to hilar dissection. Biliary strictures typically present within the first 6 to 12 months after transplantation, although presentations on either side of this timeframe are not uncommon [4,5]. These strictures are primarily classified as anastomotic or nonanastomotic. Early anastomotic strictures may be caused by size mismatches between donor and recipient ducts and local edema, while late anastomotic strictures often occur due to ischemic fibrosis. Nonanastomotic strictures result from diffuse ischemic injuries to the bile ducts, which can be due to antibody-mediated rejection, hepatic artery thrombosis (HAT), chronic ductopenic rejection, and ABO-incompatible (ABOi) liver transplant [3,6].

Endoscopic therapy is regarded as the primary therapy for the management of posttransplant biliary strictures. Percutaneous and surgical approaches are required when

endoscopic retrograde cholangiopancreatography (ERCP) is contraindicated or unsuccessful [7,8]. Limited evidence is available concerning the prevalence and long-term outcomes of biliary strictures in LDLT. The present study aimed to examine the incidence and characteristics of biliary strictures in LDLT recipients, along with their impact on long-term graft and patient survival.

Aims and Objectives

The primary objective is to investigate the prevalence of biliary strictures in recipients of LDLT. Secondary objectives are (1) to identify the risk factors associated with biliary strictures in LDLT recipients; and (2) to examine the long-term graft and patient survival outcomes in LDLT recipients who develop biliary strictures.

METHODS

In this retrospective observational study, we analyzed data from a prospectively collected database at Max Super Specialty Hospital in New Delhi, India, a tertiary care facility where over 400 LDLT procedures are performed annually. The study received approval from the relevant Institutional Ethics Committee (TM/MSSH/MHIL/ISC/LIVER & BILIARY SCIENCES/23-72). In accordance with the institutional protocol for retrospective observational studies, the requirement for participant consent was waived.

The study included adult LDLT recipients who underwent surgery between 2006 and 2022. We collected relevant clinical information, including demographic details, blood biochemistry findings, radiological imaging, indications for liver transplantation, preoperative prognostic scores such as the Child-Turcotte-Pugh (CTP) score and the Model For End-Stage Liver Disease (MELD), surgical details, types of vascular and biliary anastomosis, and liver allograft characteristics, including weight, graft-to-recipient weight ratio, and ischemia time. The exclusion criteria included an age under 18 years and a pretransplant diagnosis of primary sclerosing cholangitis (PSC) or PSC overlap syndrome. Additionally, patients who received ABOi allografts and those who underwent retransplantation were excluded from the study.

All recipients and donors provided written informed consent for surgery following a detailed explanation of the planned procedure. The liver transplant program at our institute adheres strictly to the 2008 Declaration of Is-

tanbul on organ transplantation. All donors were at least 18 years old and were biologically related to their respective recipients. Donor selection at our center is governed by a rigorous stepwise process that includes a preoperative clinical assessment conducted by a hepatologist, transplant surgeon, psychiatrist, and anesthesiologist. The laboratory assessment encompasses liver function tests, complete blood count, kidney function tests, viral serologies, and other biochemical analyses. For donors, imaging includes computed tomography (CT) volumetry, CT angiography, and magnetic resonance cholangiopancreatography (MRCP). Liver biopsy is selectively performed in candidates with deranged liver function tests and high potential for a steatotic graft.

Donor Procedure in Liver Transplant Surgery

Modified right lobe graft

The most frequently used graft was the modified right lobe graft. The procedure began with dissection of the right triangular ligament to mobilize the right lobe, followed by caval dissection, portal dissection, cholecystectomy, and dissection of the hilar plate. A cholangiogram was conducted after placing a marking stitch at the proposed site of duct division. Following complete transection and a second cholangiogram, ductal division was performed. The duct was then sutured using 6-0 polydioxanone suture (PDS). A final cholangiogram was performed to confirm the absence of leak or stricture.

Left lobe graft

For a left lobe graft, the initial dissection involved mobilizing the left triangular ligament, looping the left hepatic vein, and dissecting the Arantius' ligament. Portal dissection was performed to encircle the left portal vein, the left hepatic artery, and the segment 4 artery. Vascular strictures were divided in the following sequence: artery, portal vein, and left hepatic vein. The duct was sutured with PDS 6-0 suture material. A cholangiogram was performed to confirm the absence of leak or stricture.

Recipient biliary anastomosis procedure

Most of the biliary anastomoses were duct-to-duct. At our center, Roux-en-Y hepaticojejunostomy is employed in cases of pediatric biliary atresia, PSC, and retransplantation. The decision to perform one versus multiple anastomoses was based on the allograft's biliary anatomy. No recipient received a T-tube or stent placement during surgery. A check cholangiogram was performed to exclude

any leaks or strictures. If a leak or stricture was detected, the anastomosis was either revised or converted to Roux-en-Y hepaticojejunostomy.

Diagnosis of biliary complications and management after liver transplantation

During the postoperative period, patients were managed according to the standard protocol. Triple drug immunosuppression, which included calcineurin inhibitors, mycophenolate, and steroids, was administered to recipients. In most cases, steroids were discontinued after 3 months following a gradual tapering process. After discharge from the hospital, patients underwent routine follow-up in the outpatient department. Regular blood investigations were conducted, including complete blood count, liver function tests, kidney function tests, and measurement of tacrolimus trough levels.

Bile leak was diagnosed in patients who exhibited bile in their abdominal drains and/or significant intrabdominal bile collection on ultrasound or magnetic resonance imaging, necessitating percutaneous intervention or ERCP. Patients with deranged liver biochemistry, with or without symptoms of jaundice, pruritus, or fever, underwent MRCP. Biliary stricture on MRCP was characterized by an area of narrowing with dilated intrahepatic biliary radicles. Strictures were further categorized as anastomotic or nonanastomotic based on their location relative to the site of anastomosis. ERCP was the primary treatment of choice for biliary strictures in most cases. Percutaneous transhepatic biliary drainage (PTBD) was considered as the initial therapy in cases involving multiple ductal anastomoses and anticipated difficulties in cannulating the desired bile duct. ERCP was performed using an Olympus 190 duodenoscope (Olympus Corporation). A cholangiogram was initially conducted to map the biliary anatomy and locate the stricture. Tight strictures were dilated using biliary balloons or Soehendra biliary dilators (Cook Medical). The procedure was concluded with the placement of either a 7-Fr or a 10-Fr plastic stent. All patients were administered intravenous antibiotics prior to the procedure and were transitioned to oral antibiotics upon discharge. Patients were discharged after 24 hours if no complications were present. Stent exchange was scheduled at 3-month intervals. At follow-up visits, patients were monitored at regular intervals through clinical assessments, physical examinations, and liver biochemistry tests.

Regarding ERCP, success was defined as the resolution of stricture on cholangiogram or MRCP during

post-ERCP follow-up. ERCP failure was characterized by either of the following criteria: (1) failure of stricture resolution after 2 years on the stent exchange schedule; and (2) assessment of the need for PTBD or surgery (hepaticojejunostomy) at any point during the follow-up period.

Statistical Analysis

Statistical analyses were performed using SPSS ver. 29 (IBM Corp.) and MedCalc Statistical Software ver. 22.021 (MedCalc Software Ltd.). The normality of data distribution was assessed with the Shapiro-Wilk test. For continuous data, the Student t-test was used to compare parametric data and the Mann-Whitney U-test for non-parametric data. Categorical data were compared using the chi-square test or the Fisher exact test. Variables that yielded a P-value of less than 0.10 in univariate analysis were included in the multivariate logistic regression analysis. Kaplan-Meier curves were generated to illustrate the survival probability of the groups, with the log-rank test employed for comparison. A P-value less than 0.05 was considered to indicate statistical significance.

RESULTS

A total of 3,550 patients underwent liver transplantation between August 2006 and December 2022. After exclud-

ing pediatric cases, deceased donor transplants, PSC, PSC overlap, ABOi transplants, and retransplantations, 2,956 adult recipients were analyzed for biliary complications. Of these, 209 (7.1%) experienced bile leak in the early postoperative period. Among the patients with biliary leaks, 51 (24.4%) experienced in-hospital mortality, 54 (25.8%) developed biliary strictures, and 104 (49.7%) did not develop strictures during follow-up. Of the 2,747 patients without biliary leak in the immediate postoperative period, 296 (10.7%) died in the hospital, 290 (10.5%) developed biliary strictures, and 2,161 (78.6%) did not develop strictures. Patients who developed biliary strictures, whether after biliary leak or not, were categorized into the stricture group. Those who did not develop biliary stricture, regardless of whether it followed biliary leak, were placed in the no-stricture group (Fig. 1).

During the study period, biliary strictures were observed in 344 cases, accounting for 11.6% of the total. The median age of patients with strictures was significantly higher than that of those without strictures (50 vs. 49 years, $P=0.044$). Additionally, median MELD (21 vs. 18, $P<0.001$) and CTP scores (11 vs. 10, $P=0.0008$) were significantly higher in the stricture group. The proportions of diabetes mellitus and hypertension were also significantly higher among recipients with strictures. In both groups, the liver donors were predominantly male. Donors in the stricture group exhibited a significantly higher median age (32 vs. 30 years, $P=0.011$). Graft weight, graft-to-re-

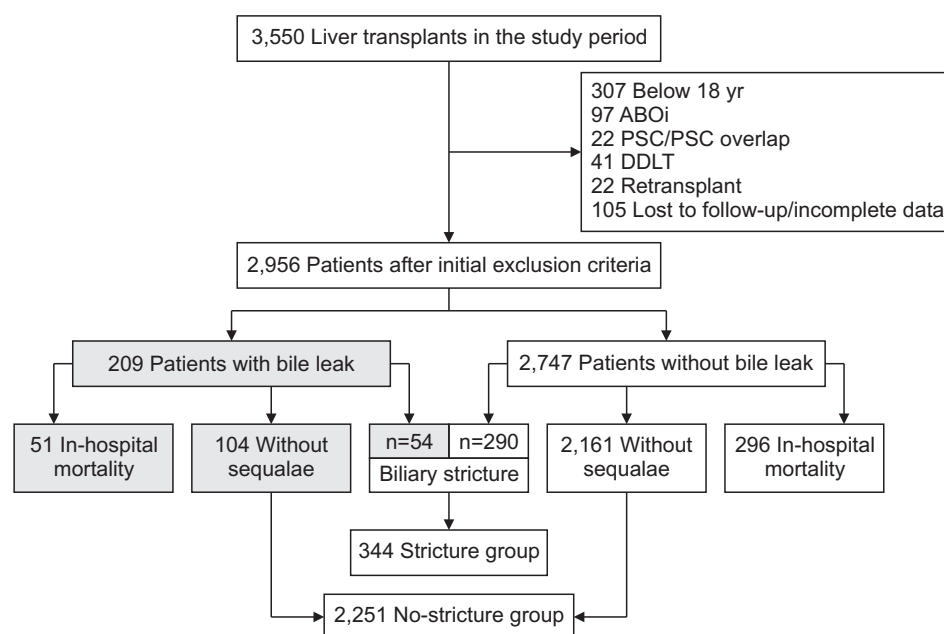


Fig. 1. Flowchart of patient selection. Fourteen patients were excluded for analysis with incomplete information from the no-stricture group. ABOi, ABO-incompatible; PSC, primary sclerosing cholangitis; DDLT, deceased donor liver transplantation.

Table 1. Comparison of clinical and demographic profiles between groups

Parameter	No biliary stricture (n=2,251)	Biliary stricture (n=344)	P-value
Recipient			
Age (yr)	49 (41–55)	50 (42–56)	0.044*
Male sex	1,845 (82)	293 (85.2)	0.145
MELD	18 (14–23)	21 (15–27)	<0.001*
CTP	10 (8–12)	11 (9–12)	<0.001*
Comorbidities			
Diabetes mellitus	528 (23.5)	107 (31.1)	0.003*
Hypertension	167 (7.4)	40 (11.6)	0.007*
Pulmonary tuberculosis	57 (2.5)	10 (2.9)	0.853
Donor			
Age (yr)	30 (23–39)	32 (24–41)	0.011*
Male sex	1,250 (55.5)	194 (56.4)	0.539
Graft			
Graft weight (g)	749 (660–840)	738 (650–820)	0.124
<650 g	508 (22.6)	86 (25.0)	0.317
≥650 g	1,743 (77.4)	258 (75.0)	-
GRWR	1.04 (0.86–1.23)	1.00 (0.82–1.20)	0.095
CIT	103 (77–132)	105 (74–136)	0.737
WIT	36 (30–45)	35 (29–41)	0.671
Donor hepatectomy			0.340
Open	2,153 (95.7)	326 (94.8)	
Laparoscopic	62 (2.7)	14 (4.1)	
Robotic	36 (1.6)	4 (1.2)	
Type of graft			0.038*
Extended right lobe ^{a)}	251 (11.2)	21 (6.1)	
Left lobe	36 (1.6)	9 (2.6)	
Modified right lobe	1,893 (84.1)	300 (87.2)	
Right posterior sector	24 (1.1)	5 (1.5)	
Standard right lobe	47 (2.1)	9 (2.6)	
Type of anastomosis			0.396
Duct-to-duct	2,069 (91.9)	320 (93)	
Hepaticojejunostomy	46 (2.1)	8 (2.3)	
Both duct-to-duct and hepaticojejunostomy	71 (3.2)	16 (4.7)	
No. of anastomoses	1.2±0.4	1.3±0.5	<0.001*

Values are presented as median (range), number (%), or mean±standard deviation.

MELD, Model for End-Stage Liver Disease; CTP, Child-Turcotte-Pugh score; GRWR, graft-to-recipient weight ratio; CIT, cold ischemic time; WIT, warm ischemic time.

^{a)}Represents the row/column proportions that differed on Z-test.

*P<0.05.

Table 2. Comparison of postoperative parameters between groups

Parameter	No biliary stricture (n=2,251)	Biliary stricture (n=344)	P-value
Bleeding	28 (1.2)	13 (3.8)	<0.001*
MHV block	13 (0.6)	3 (0.9)	0.518
Bile leak	104 (4.6)	54 (15.7)	<0.001*
PVT	18 (0.8)	5 (1.5)	0.231
HAT	19 (0.8)	0	0.086
ICU stay (day)	10 (8–14)	14 (10–21)	<0.001*
Hospital stay (day)	21 (19–27)	26 (21–36)	<0.001*
OS (mo)	187 (151–187)	195 (109–195)	0.411

Values are presented as number (%) or median (interquartile range).

MHV, middle hepatic vein; PVT, portal vein thrombosis; HAT, hepatic artery thrombosis; ICU, intensive care unit; OS, overall survival.

*P<0.05.

recipient weight ratios, and ischemic times did not differ significantly between the two groups. The use of extended right lobes was significantly less common in the stricture group (6.1% vs. 11.2%, P=0.038). Most patients in the study underwent duct-to-duct biliary anastomosis, and the type of biliary anastomosis was similar between groups. However, the mean number of anastomoses was significantly higher among those with strictures, at 1.3 versus 1.2 (P<0.001) (Tables 1 and 2).

The rates of postoperative complications such as bleeding (3.8% vs. 1.2%, P<0.001) and bile leak (15.7% vs. 4.6%, P<0.001) were significantly higher among patients with strictures. Other complications, including HAT, middle hepatic vein obstruction, and portal vein thrombosis, were comparable between the two groups. Additionally, the median duration of stay in the intensive care unit (14 vs. 10 days, P<0.001) and the overall hospital stay (26 vs. 21 days, P<0.001) were significantly longer in the stricture group.

Over a median follow-up period of 11 months (interquartile range, 5–24 months), nearly four-fifths of the patients with strictures, specifically 265 (77.0%), underwent ERCP as the primary modality to alleviate this condition (Fig. 2). PTBD was the primary therapy for 73 patients (21.2%). ERCP was successful in 175 (66.0%) of the cases, with a mean of 1.89 sessions per patient. Cholangitis was the most common ERCP-related complication, occurring in 20 patients (7.6%). Post-ERCP pancreatitis developed in seven patients (2.7%), and two patients experienced ERCP-related perforation. Fourteen patients (15.9%) with failed ERCP underwent hepaticojejunostomy. In contrast,

only one patient who initially received PTBD was treated with hepaticojejunostomy (Fig. 2).

Death Due to Biliary Complications

Of the 344 patients with biliary stricture, 16 (4.6%) died from complications related to this condition or associated interventions. Thirteen patients died due to complications of cholangitis, while one patient each died from ERCP-related papillotomy bleed, pancreatitis, and perforation.

Open Versus Minimally Invasive Donor Hepatectomy

In the no-stricture group, 2,153 patients (95.7%) underwent open donor surgery. Laparoscopic donor surgery was performed in 62 patients (2.7%), while robotic donor surgery was carried out in 36 patients (1.6%). Of the 344 patients with biliary stricture, 326 (94.7%) underwent open donor hepatectomy, while 14 patients (4.1%) received laparoscopic donor surgery. Only four patients (1.1%) under-

went robotic donor surgery in this study, since the robotic program at our center primarily gained momentum after 2022.

In multiple logistic regression analysis, factors such as older donor and recipient age, higher MELD score, bile leak, and multiple biliary anastomoses were identified as predictors of biliary strictures in transplant recipients. During a median follow-up period of 55 months (inter-quartile range, 22–81 months) among 2,595 patients, 520 patients (20.0%) were lost to follow-up, and 398 patients (15.3%) died—64 from the stricture group and 334 from the no-stricture group. The median survival times were similar between groups (195 months for patients with strictures vs. 187 months for those without, $P=0.411$) (Table 3, Fig. 3). In the logistic regression analysis assessing risk factors for bile leak in recipients, a higher MELD score, the presence of multiple biliary anastomoses, and the use of hepaticojejunostomy for biliary reconstruction

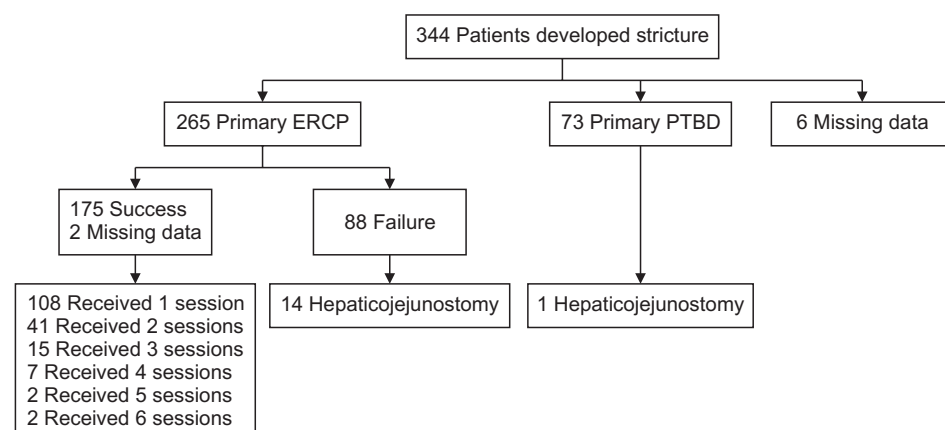


Fig. 2. Management of patients with strictures. ERCP, endoscopic retrograde cholangiopancreatography; PTBD, percutaneous transhepatic biliary drainage.

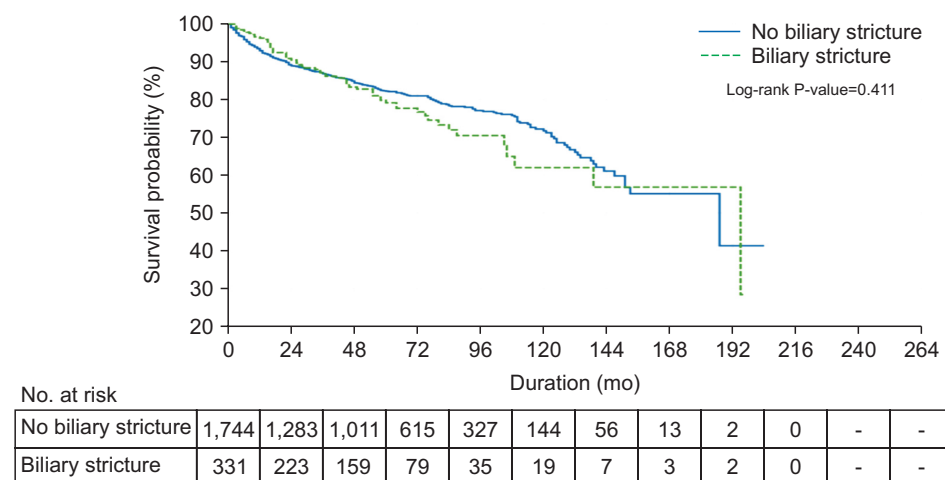


Fig. 3. Comparison of overall survival between patients with and without biliary strictures.

Table 3. Univariate and multivariate logistic regression analyses for biliary stricture

Variable	Univariate		Multivariate	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age	1.01 (0.99–1.02)	0.055	1.01 (1.00–1.02)	0.012*
Donor age	1.01 (1.00–1.02)	0.005*	1.01 (1.00–1.03)	0.001*
CTP	1.09 (1.03–1.16)	0.001*	0.98 (0.91–1.06)	0.789
MELD	1.03 (1.02–1.05)	<0.001*	1.03 (1.01–1.05)	<0.001*
Graft weight	0.99 (0.99–1.00)	0.094	0.99 (0.99–1.00)	0.145
GRWR	0.63 (0.40–1.00)	0.054	0.79 (0.43–1.44)	0.446
CIT	0.99 (0.99–1.00)	0.609	-	-
WIT	0.99 (0.98–1.00)	0.110	-	-
Donor hepatectomy				
Open	1 [Reference]			
Laparoscopic	1.49 (0.82–2.70)	0.180	-	-
Robotic	0.73 (0.26–2.08)	0.564	-	-
No. of biliary anastomoses	1.97 (1.57–2.48)	<0.001*	1.79 (1.40–2.29)	<0.001*
Duct-to-duct	1 [Reference]			
Hepaticojejunostomy	1.12 (0.52–2.40)	0.762	-	-
Both duct-to-duct and hepaticojejunostomy	1.45 (0.83–2.53)	0.183	-	-
Bile leak	3.99 (2.80–5.68)	<0.001*	3.76 (2.52–5.61)	<0.001*

CI, confidence interval; CTP, Child-Turcotte-Pugh; MELD, Model for End-Stage Liver Disease; GRWR, graft-to-recipient weight ratio; CIT, cold ischemic time; WIT, warm ischemic time.

*P<0.05.

Table 4. Univariate and multivariate logistic regression analyses for bile leak

Variable	Univariate		Multivariate	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age	1.00 (0.98–1.01)	0.962	-	-
Donor age	1.00 (0.98–1.01)	0.810	-	-
CTP	1.13 (1.05–1.22)	<0.001*	1.06 (0.97–1.17)	0.182
MELD	1.03 (1.01–1.05)	<0.001*	1.02 (1.00–1.04)	0.042*
Graft weight	1.00 (0.99–1.00)	0.405	-	-
GRWR	1.09 (0.60–2.00)	0.766	-	-
CIT	0.99 (0.99–1.00)	0.574	-	-
WIT	0.99 (0.99–1.00)	0.922	-	-
No. of biliary anastomoses	2.16 (1.63–2.86)	<0.001*	2.47 (1.82–3.35)	<0.001*
Duct-to-duct	1 [Reference]			
Hepaticojejunostomy	2.06 (0.96–4.40)	0.060	3.15 (1.37–7.24)	0.007*
Both duct-to-duct and hepaticojejunostomy	1.74 (0.91–3.32)	0.091	1.08 (0.53–2.21)	0.816

CI, confidence interval; CTP, Child-Turcotte-Pugh; MELD, Model for End-Stage Liver Disease; GRWR, graft-to-recipient weight ratio; CIT, cold ischemic time; WIT, warm ischemic time.

*P<0.05.

were associated with increased risk (Table 4).

DISCUSSION

In this retrospective study, the overall rate of biliary stricture in adult recipients of LDLT was 11.45%. ERCP served as the first-line treatment for most of these patients and was successful in approximately 66% of cases. The median time for the development of strictures was 11 months posttransplant. Cholangitis was the most common complication following ERCP, occurring in 7.6% of cases, while post-ERCP pancreatitis was observed in 2.7%. The 1-year and 3-year survival rates for patients with biliary strictures were 94.1% and 84.9%, respectively.

Patients treated with LDLT have a higher incidence of biliary strictures compared to those receiving organs from deceased donors, for several reasons. In LDLT, the graft ducts tend to be smaller, and multiple anastomoses may be present since the biliary anastomosis is often more proximal. Additionally, devascularization of the bile duct due to hilar dissection and injuries at the cut surface of the bile duct contribute to the increased risk [2,8–10]. There is a scarcity of large-scale studies on biliary complications in LDLT recipients [1,2,8]. Wadhawan et al. [8] previously reported on biliary outcomes after liver transplant in 338 patients, noting a biliary stricture rate of 13.3%. More recently, Gad et al. [11] identified a 22% incidence of biliary strictures [11]. Other studies have indicated a stricture rate ranging from 15% to 25% among LDLT recipients [2,12–14]. The overall biliary stricture rate in our study was 11.6%, which is low relative to most published studies. Over time, advancements in surgical techniques have led to a reduced rate of biliary strictures at our center. A combination of refined surgical procedures, the surgeons' accumulated experience, and other factors likely contributed to the lower incidence of biliary strictures. Our institute represents one of the largest LDLT centers in India and Asia, with decades of experience and surgical expertise.

In addition to bile leak, our study revealed that advanced donor and recipient age, higher MELD score, and multiple biliary anastomoses were associated with an increased risk of biliary strictures in liver transplant recipients. Previous studies have reported these factors as contributing to the risk of anastomotic biliary strictures after LDLT. Wadhawan et al. [8] demonstrated that the

presence of multiple biliary anastomoses was a risk factor for posttransplant biliary strictures. In another study by Akamatsu et al. [2], bile leak and living donor status were identified as risk factors for biliary strictures. Other research has indicated that a high MELD score, prolonged cold and warm ischemia times, advanced donor and recipient age, and conventional biliary anastomosis are risk factors for biliary stricture in liver transplant recipients [2]. The surgical technique used for biliary anastomosis can also influence the rate of biliary complications. Duct-to-duct anastomosis may be performed using continuous absorbable sutures, interrupted nonabsorbable sutures, or a mixed technique. However, previous studies have not demonstrated any significant difference in outcomes with different techniques [15–17]. At our center, biliary anastomosis is typically performed in a duct-to-duct manner when feasible, using 7-0 PDS sutures. Prior to 2023, the posterior layer was completed continuously, while the anterior layer was done in an interrupted fashion. However, since 2023, both layers have been established using an interrupted technique.

Minimally invasive donor hepatic resection in LDLT, including both laparoscopic and robotic techniques, provides better cosmetic outcomes and facilitates the early recovery of living donors. However, the adoption of these methods is not yet widespread, and research on their long-term outcomes is limited. In the present study, minimally invasive donor surgery was not identified as a risk factor for biliary strictures in liver transplant recipients. Song et al. [18] reported on 295 patients who underwent laparoscopic donor hepatectomy, demonstrating outcomes comparable to those of open donor surgery [18–21]. Notably, only a small number of patients in our study underwent minimally invasive surgery, and more robust evidence from larger studies is required.

In a recent study by Taniai et al. [22], ABO incompatibility was the only identified risk factor for biliary strictures. However, the study had a small sample size, including only 26 patients. ABOi liver transplantation is recognized as a risk factor for nonanastomotic diffuse biliary strictures [22]. Nonanastomotic strictures were not observed in our study, as we excluded patients with ABOi liver transplantation and PSC. The exclusion of these patients may have contributed to the lower overall incidence of biliary stricture in our study.

ERCP remains the primary modality of choice for the management of biliary strictures. In LDLT, the success rate of ERCP has been reported to be low compared to

DDLT and other forms of benign strictures. Various studies have reported success rates for ERCP in these patients ranging from 40% to 92%. Differences in the definition of ERCP success and variations in technical expertise may account for these disparate results. Akamatsu et al. [2] reported a success rate of 57% in a systematic review [23–25]. In our study, ERCP was successful in 66% of cases, and cholangitis (7.6%) and pancreatitis (2.7%) were the two most frequent complications observed. The reported incidence rates of pancreatitis and cholangitis in liver transplant recipients range from 2.7% to 6.4% and 0.7% to 5.1%, respectively [26–28]. Less common complications include bleeding and perforation, which occurred in 0.8% and 0.4% of cases, respectively, in our study. The use of preprocedural antibiotics and the reduction of immunosuppression during the periprocedural period can help lower the risk of infectious complications. Most patients with nonresolution of strictures following ERCP were successfully managed with a percutaneous approach, and hepaticojejunostomy was performed in selected cases.

Overall, patient and graft survival rates in individuals with biliary strictures were comparable to those in patients without biliary strictures. However, the median hospital stay was longer for patients with biliary strictures, as they experienced a higher incidence of bile leak during the postoperative period.

Bile leak is a major risk factor for the development of biliary strictures. In our study, the incidence of bile leak was 7%; previous studies have reported rates of 2% to 25% [2,6]. Most of our patients improved with conservative treatment alone. Endoscopic intervention was reserved for patients with persistent bile leak beyond 4 to 6 weeks after liver transplantation. Bile leak and strictures largely share reported risk factors, including advanced donor and recipient age, higher CTP score, higher MELD score, prolonged cold and warm ischemia times, and HAT. The presence of smaller and multiple bile ducts may also elevate the risk of bile leak. Additionally, the incidence of bile leak can be influenced by the surgical techniques used for biliary anastomosis reconstruction [1,17,29–32]. In our study, higher MELD score, multiple biliary anastomoses, and the use of hepaticojejunostomy for biliary reconstruction were identified as risk factors for bile leak. Another notable finding from our study was that only 34.1% of patients with bile leak developed biliary strictures. Although bile leak is a known and common cause of biliary stricture, its presence does not invariably lead to stricture formation. Many patients with bile leak who re-

ceived conservative management recovered without any delayed biliary complications.

Our study has several limitations. Most notably, it was retrospective in nature and exclusively included recipients of LDLT. Consequently, the results may not be generalizable to DDLT recipients. Nevertheless, this study represents one of the largest investigations into the incidence and predictors of biliary strictures among LDLT recipients, with a sample of over 2,500 patients.

In conclusion, anastomotic biliary strictures and bile leaks significantly contribute to morbidity in liver transplant recipients. With advancements in surgical techniques, the incidence rate of these biliary complications has significantly decreased. Although postoperative biliary strictures contribute to considerable morbidity, they do not affect patient survival. Effective endoscopic and nonendoscopic treatment modalities are available to manage these complications.

ARTICLE INFORMATION

Conflict of Interest

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

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REFERENCES

- Williams ED, Draganov PV. Endoscopic management of biliary strictures after liver transplantation. *World J Gastroenterol* 2009;15:3725–33.
- Akamatsu N, Sugawara Y, Hashimoto D. Biliary reconstruction, its complications and management of biliary complications after adult liver transplantation: a systematic review of the incidence, risk factors and outcome. *Transpl Int* 2011;24:379–92.
- Magro B, Tacelli M, Mazzola A, Conti F, Celsa C. Biliary complications after liver transplantation: current perspectives and future strategies. *Hepatobiliary Surg Nutr* 2021;10:76–92.
- Gastaca M. Biliary complications after orthotopic liver transplantation: a review of incidence and risk factors. *Transplant Proc* 2012;44:1545–9.
- Akhter A, Pfau P, Benson M, Soni A, Gopal D. Endoscopic management of biliary strictures post-liver transplantation. *World J Metaanal* 2019;7:120–8.
- Fasullo M, Patel M, Khanna L, Shah T. Post-transplant biliary complications: advances in pathophysiology, diagnosis, and treatment. *BMJ Open Gastroenterol* 2022;9:e000778.
- Freise CE, Gillespie BW, Koffron AJ, Lok AS, Pruett TL, Emond JC, et al. Recipient morbidity after living and deceased donor liver transplantation: findings from the A2ALL retrospective cohort study. *Am J Transplant* 2008;8:2569–79.
- Wadhawan M, Kumar A, Gupta S, Goyal N, Shandil R, Taneja S, et al. Post-transplant biliary complications: an analysis from a predominantly living donor liver transplant center. *J Gastroenterol Hepatol* 2013;28:1056–60.
- Sharma S, Gurakar A, Jabbour N. Biliary strictures following liver transplantation: past, present and preventive strategies. *Liver Transpl* 2008;14:759–69.
- Wang SF, Huang ZY, Chen XP. Biliary complications after living donor liver transplantation. *Liver Transpl* 2011;17:1127–36.
- Gad EH, Ayoup E, Aziz AM, Ibrahim T, Elhelbawy M, Abd-Elsamee MA, et al. Biliary complications after adult to adult right-lobe living donor liver transplantation (A-ARLLDLT): analysis of 245 cases during 16 years period at a single high centre: a retrospective cohort study. *Ann Med Surg (Lond)* 2022;77:103577.
- Todo S, Furukawa H, Kamiyama T. How to prevent and manage biliary complications in living donor liver transplantation? *J Hepatol* 2005;43:22–7.
- Gondolesi GE, Varotti G, Florman SS, Muñoz L, Fishbein TM, Emre SH, et al. Biliary complications in 96 consecutive right lobe living donor transplant recipients. *Transplantation* 2004;77:1842–8.
- Yazumi S, Yoshimoto T, Hisatsune H, Hasegawa K, Kida M, Tada S, et al. Endoscopic treatment of biliary complications after right-lobe living-donor liver transplantation with duct-to-duct biliary anastomosis. *J Hepatobiliary Pancreat Surg* 2006;13:502–10.
- Seifert L, von Renesse J, Seifert AM, Sturm D, Meisterfeld R, Rahbari NN, et al. Interrupted versus continuous suture technique for biliary-enteric anastomosis: randomized clinical trial. *BJS Open* 2023;7:zrac163.
- Kasahara M, Egawa H, Takada Y, Oike F, Sakamoto S, Kiuchi T, et al. Biliary reconstruction in right lobe living-donor liver transplantation: comparison of different techniques in 321 recipients. *Ann Surg* 2006;243:559–66.
- Liu CL, Lo CM, Chan SC, Fan ST. Safety of duct-to-duct biliary reconstruction in right-lobe live-donor liver transplantation without biliary drainage. *Transplantation* 2004;77:726–32.
- Song JL, Yang J, Wu H, Yan LN, Wen TF, Wei YG, et al. Pure laparoscopic right hepatectomy of living donor is feasible and safe: a preliminary comparative study in China. *Surg Endosc* 2018;32:4614–23.
- Hasegawa H, Takahashi A, Kakeji Y, Ueno H, Eguchi S, Endo I, et al. Surgical outcomes of gastroenterological surgery in Japan: report of the National Clinical Database 2011–2017. *Ann Gastroenterol Surg* 2019;3:426–50.
- Marubashi S, Nagano H. Laparoscopic living-donor hepatectomy: review of its current status. *Ann Gastroenterol Surg* 2021;5:484–93.
- Chen PD, Wu CY, Hu RH, Ho CM, Lee PH, Lai HS, et al. Robotic liver donor right hepatectomy: a pure, minimally invasive approach. *Liver Transpl* 2016;22:1509–18.
- Taniai T, Furukawa K, Haruki K, Yanagaki M, Hamura R, Akaoka M, et al. Multimodal management for refractory biliary stricture after living donor liver transplantation. *Transplant Proc* 2023;55:940–4.

23. Costamagna G, Pandolfi M, Mutignani M, Spada C, Perri V. Long-term results of endoscopic management of postoperative bile duct strictures with increasing numbers of stents. *Gastrointest Endosc* 2001;54:162–8.
24. Morelli J, Mulcahy HE, Willner IR, Cunningham JT, Draganov P. Long-term outcomes for patients with post-liver transplant anastomotic biliary strictures treated by endoscopic stent placement. *Gastrointest Endosc* 2003;58:374–9.
25. Morelli G, Fazel A, Judah J, Pan JJ, Forsmark C, Draganov P. Rapid-sequence endoscopic management of posttransplant anastomotic biliary strictures. *Gastrointest Endosc* 2008;67:879–85.
26. Ambrus RB, Svendsen LB, Hillingsø JG, Hansen ML, Achiam MP. Post-endoscopic retrograde cholangiopancreatography complications in liver transplanted patients, a single-center experience. *Scand J Surg* 2015;104:86–91.
27. Hüsing A, Cicinnati VR, Maschmeier M, Schmidt HH, Wolters HH, Beckebaum S, et al. Complications after endoscopic sphincterotomy in liver transplant recipients: a retrospective single-centre study. *Arab J Gastroenterol* 2015;16:46–9.
28. Lim CH, Shih KL, Wu SS, Fan CS, Yen HH, Su WW, et al. Safety of endoscopic retrograde cholangiopancreatography in liver transplanted patients: a single-center retrospective study. *Adv DigMed* 2020;7:9–13.
29. Sheng R, Sammon JK, Zajko AB, Campbell WL. Bile leak after hepatic transplantation: cholangiographic features, prevalence, and clinical outcome. *Radiology* 1994;192:413–6.
30. Saab S, Martin P, Soliman GY, Machicado GA, Roth BE, Kunder G, et al. Endoscopic management of biliary leaks after T-tube removal in liver transplant recipients: nasobiliary drainage versus biliary stenting. *Liver Transpl* 2000;6:627–32.
31. Park JB, Kwon CH, Choi GS, Chun JM, Jung GO, Kim SJ, et al. Prolonged cold ischemic time is a risk factor for biliary strictures in duct-to-duct biliary reconstruction in living donor liver transplantation. *Transplantation* 2008;86:1536–42.
32. Shah SA, Grant DR, McGilvray ID, Greig PD, Selzner M, Lilly LB, et al. Biliary strictures in 130 consecutive right lobe living donor liver transplant recipients: results of a Western center. *Am J Transplant* 2007;7:161–7.