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Original Research

Factors Affecting Bile Complications After Liver Transplantation: Single-Center Experience

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Abstract

Objectives: In this study, we aimed to investigate the surgical technique and biochemical parameters that affect biliary complications in liver transplants from live and cadaver in our center.

Methods: In this study, 141 patients who underwent liver transplants at Istanbul Yeni Yüzyıl Universty Gaziosmanpaşa Hospital organ transplant center between January 2018 and January 2020 were included in the study. The patients were monitored for 12–24 months. The patients included in the present study were examined retrospectively. Factors that may cause biliary tract complications and treatment modalities for complications were examined.

Results: In this study, liver transplantation from 124 living donors and 17 cadavers was performed. Twenty-three patients were under the age of 18. Only seven of 39 biliary complications were operated on. The rate of finding the right graft in patients with biliary complications was higher ($p<0.05$). There was no statistically significant difference between the groups concerning left, left lateral, and whole graft presence ($p=0.561$, $p=0.172$, and $p=0.057$, respectively). Double biliary anastomosis was to be higher in the biliary complication group, but there was no statistically significant difference ($p=0.086$).

Conclusion: Biliary complications are common, especially in liver transplants taken from the right lobe. Significant patient survival can be achieved with an early diagnosis and an appropriate treatment approach.

Keywords: Biliary complication, ERCP, liver transplantation, risk factors

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Bile duct complications are very common after liver transplantation (LT) and they are the most common surgical problems encountered. In studies, the incidence of bile complications after LT has been reported to be between approximately 2% and 25%.[1,2] Although there is a difference from center to center, the complication rate of bile is relatively higher, especially after right lobe living donor LT (LDLT) and has been reported between 24% and 60%.[3-5] Bile complication rates in deceased donor LT (DDLT) patients are lower than from living donors.[3] Bile duct complications adversely affect patient quality of life. It also brings with it a longer hospital stay and hospital expenses.[6] Conservative approach, percutaneous drain insertion, percutaneous transhepatic cholangiography, endoscopic method, or surgical treatment strategies are used to treat biliary complications.[6] In this study, we

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aimed to present the risk factors affecting biliary complications in liver transplants performed in our center, as well as the treatment options and post-treatment results of complications.

Methods

In this retrospective study, after obtaining Ethics Committee approval dated February 01, 2020 and numbered 2020/43, we included all 141 patients who underwent LT at the organ transplant center of Istanbul Yeni Yüzyıl Universty, Faculty of Medicine, Istanbul, Turkey between January 2018 and January 2020. Patients were recruited for a minimum of 12 months. These patients were studied as groups with and without biliary complications. Recipient age, blood group, gender, etiology, biochemical blood values, height, weight, BMI, model of end-stage liver disease score, child score, and donor age were compared between the two groups as pre-operative parameters. Intraoperative factors were operation time, cold ischemia time (CIT), warm ischemia time (WIT), anhepatic phase, graft type, graft volume weight ratio, and the number of erythrocyte suspension transfusions performed during surgery. Surgically, anastomosis method (interrupted vs. continuous), number of anastomoses (single vs. multiple), suture thickness used (5-0, 6-0, and 7-0), type of suture (PDS vs. prolene), and anastomosis technique (Duct to duct, hepaticojejunostomy, and choledochoduodenostomy) were examined. The bile complication group was examined by dividing it into three groups: Bile leakage, biliary stricture, and both.

Statistical Analysis

The Shapiro–Wilk test was used for assessing whether the variables follow a normal distribution or not. Continuous variables were presented as median (minimum: maximum) and mean±standard deviation values. Categorical variables were reported as n (%). According to the normality test results, independent t-test or Mann–Whitney U tests were used in the comparison between the two groups. Categorical variables were compared between groups using the Pearson Chi-square test or Fisher's exact test. SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp.) was used for statistical analysis and $p<0.05$ was considered statistically significant.

Results

In our study, 141 LT patients (124 LDLT, 17 DDLT) were followed over a 1-year period. Twenty-three patients were under the age of 18. Pre-operative parameters between groups are given in Table 1.

Accordingly, there were the most A Rh (+) positive patients in both groups. The mean age of the biliary complication group was 53 years old (min: 1, max: 69) and the normal group was 47 years old (min: 1, max: 70). While the number of females/males in the biliary complication group was 10/29, it was 33/69 in the normal group. The most common etiological reasons were hepatitis B and hepatocellular carcinoma in both groups. Other features between groups are shown in Table 2. There was no statistically significant difference in comparisons of variables made between the groups ($p>0.05$). Intraoperative factors between the groups are shown in Table 2. There was a statistically significant difference between the groups regarding graft types ($p=0.047$). In subgroup analysis, the rate of right graft presence was higher in patients with bile complications ($p=0.005$). There was no statistically significant difference between the groups regarding left, left lateral, and whole graft presence ($p=0.561$, $p=0.172$, and $p=0.057$, respectively).

There was no statistically significant difference in comparisons of other variables made between the groups ($p>0.05$). Surgical factors among the groups are given in Table 3.

There was no statistically significant difference in comparisons of variables made between groups ($p>0.05$). Double biliary anastomosis was higher in the biliary complication group, but there was no statistically significant difference ($p=0.086$). The treatment modalities of the biliary complication group are given in Table 4. As can be seen from the table, only seven of 39 bile complications were operated on. Other cases were treated using methods such as percutaneous drainage, Percutan Transhepatic Cholangioghrapy (PTC), and Endoscopic Retrograde CholangioPancreaticography (ERCP).

Discussion

LT is the best treatment for selected patients with liver failure and end-stage liver disease. While bile complication rates are between 5% and 15% in DDLT, it can be seen as high as 38% in LDLT.[6-9] In our study, there were 39/141 bile complications. There were 18 bile leaks (12.4%), 14 stenosis (9.6%), and seven bile leaks and stenosis (4.6%) complications. The complication rate was 27.6% which was compatible with the other series. Risk factors for biliary complications include ischemia during dissection in the donor bile duct; the non-dominant blood flow of the right hepatic artery, hepatic artery thrombosis, cytomegalovirus (CMV) infection, anastomosis tension, and bile duct diameter are < 4 mm and multiple bile anastomoses. In our study, the rate of the right graft presence was higher in patients with bile complications ($p=0.005$). There was no statistically

Table 1. Pre-operative parameters between groups

	Biliary complication group	Normal group	p
Blood Group			
0	11 (28.21%)	34 (33.33%)	0.904[a]
A	15 (38.46%)	39 (38.24%)	
B	8 (20.51%)	18 (17.65%)	
AB	5 (12.82%)	11 (10.78%)	
Recipient age (year)	53 (1:69)	47 (1:70)	0.139[b]
Gender			
Female	10 (25.64%)	33 (32.35%)	0.439c
Male	29 (74.36%)	69 (67.65%)	
MELD score	14 (2:29)	17 (8:37)	0.071[b]
Child-Pugh- score	8 (5:13)	8 (5:13)	0.107[b]
HB (g/dl)	11.10 (5.60:16.60)	10.65 (6.20:16.50)	0.355[b]
AST	59 (26:559)	55 (14:637)	0.575[b]
ALT	42 (11:564)	37.50 (6:484)	0.612[b]
T.BIL	1.70 (0.30:38)	2 (0.10:49)	0.491[b]
D.BIL	0.90 (0.20:30)	1.10 (0:46)	0.455[b]
Albumin	3.20 (2.30:4.70)	3.40 (2.20:4.80)	0.326[b]
PT	14 (10:40)	15 (11:39)	0.375[b]
INR	1.30 (0.80:3.60)	1.30 (0.90:3.50)	0.549[b]
AFP	4.20 (0.70:400)	3.45 (0.70:655)	0.802[b]
Height (cm)	165 (73:185)	165 (58:192)	0.298[b]
Weight (kg)	74 (8:128)	67 (0.70:126)	0.093[b]
BMI (kg/m^2)	26.33±6.05	23.92±7.03	0.061[b]
Donor Age (y)	33 (20:63)	34 (16:77)	0.594[b]
Etiology			
Hepatit B/D	4 (10.26%)	10 (9.80%)	>0.99[a]
Hepatit C	0	3 (2.94%)	0.561[a]
HCC	13 (33.33%)	21 (20.59%)	0.114[c]
Alcohol	2 (5.13%)	8 (7.84%)	0.727[a]
Cryptogenic	3 (7.69%)	10 (9.80%)	>0.99[a]
NASH	2 (5.13%)	8 (7.84%)	0.727[a]
PBS/PSC	1 (2.56%)	3 (2.94%)	>0.99[a]
Other	14 (35.90%)	39 (38.24%)	0.798[c]

Data are expressed as n (%), median (minimum: maximum) and mean±standard deviation. aFisher's Exact test, bMann–Whitney U test, cPearson Chi-Square test, dIndependent samples t-test; (MELD- Model for End-Stage Liver Disease, HB-Hemoglobin, ALT- Alanine aminotransferase, AST- Aspartate aminotransferase, T.BIL- Total bilirubin, D.BIL- Direct bilirubin, PT- Prothrombin time, INR- International normalized ratio, AFP- Alpha-Fetoprotein, BMI- Body mass index, HCC- Hepatocellular carcinoma, NASH- Nonalcoholic steatohepatitis, PBS/PSC- Primary Biliary Cirrhosis / Primary Sclerosing Cholangitis).

significant difference between the groups regarding left, left lateral, and whole graft presence (p=0.561, p=0.172, and p=0.057, respectively). At the same time, double biliary anastomosis and anastomosis technique were higher in the biliary complication group, but there was no statistically significant difference (p=0.086 and p=0.073). Arıkan et al. also reported that the number of bile ducts did not affect biliary complication rates.[9] Perhaps, as the number of cases increases, this value, which is close to the statistical limit, may be statistically meaningful. Sakamoto et al. found in their study that difficult hepatectomy and operative time are independent risk factors for bile leakage.[10] In our study, the findings showed that operative time did not significantly increase bile complications. Apart from this, no difference was found between the anastomosis type, suture type, and anastomosis technique between the groups. Percutaneous drainage, PTC, ERCP, and reoperation are the main treatment modalities for bile complications. The success rate of ERCP in the treatment of biliary strictures is reported to be 75%.[11] In our study, 32 patients (82%) improved with non-surgical treatment methods. As in other bile ducts, ERCP and PTC are used for diagnostic

Table 2. Intraoperative factors between groups

	Biliary complication group (n=39)	Normal group (n=102)	p
Operation time (hour)	6 (4:9)	6 (2:11)	0.371[b]
CIT (minute)	38 (18:680)	42 (13:585)	0.505[b]
WIT (minute)	35 (18:68)	34 (23:102)	0.859[b]
AHF (minute)	54 (32:210)	55 (31:198)	0.836[b]
Graft Type			
R	34 (87.18%)	64 (62.75%)	0.047[a]
L	0	3 (2.94%)	
LLS	3 (7.69%)	17 (16.67%)	
W	2 (5.13%)	18 (17.65%)	
GBWR	1.20 (0.80:3.20)	1.30 (0.80:4.50)	0.232[b]
ES given	3 (0:10)	2.50 (0:22)	0.717[b]

Data are expressed as n (%), median (minimum: maximum) and mean±standard deviation. [a]Fisher's Exact test, [b]Mann–Whitney U test (CIT-Cold Ischemia Time, WIT- warm ischemia time, AHF- Acute Hepatic Failure, R-Right lobe, L- Left lobe, LLS- left lateral segment, W- Whole, GBWR- graft to body weight ratio, ES Trans- erythrocyte suspension).

Table 3. Surgical factors among the groups

	Biliary complication group (n=39)	Normal group (n=102)	p
Anastomosis type			
Duct to Duct	35 (89.74%)	76 (74.51%)	0.167[a]
Hepaticojejunal	4 (10.26%)	24 (23.53%)	
Choledocoduodenal	0	2 (1.96%)	
Anastomosis number			
One	22 (56.41%)	73 (71.57%)	0.086[c]
Two	17 (43.59%)	29 (28.43%)	
Anastomosis technique			
One by one	37 (94.87%)	85 (83.33%)	0.073[c]
Continuous	2 (5.13%)	17 (16.67%)	
Suture size number			
5-0	0	2 (1.96%)	>0.99[a]
6-0	38 (97.44%)	98 (96.08%)	
7-0	1 (2.56%)	2 (1.96%)	
Suture type			
Prolen	25 (64.10%)	68 (66.67%)	0.774[c]
PDS	14 (35.90%)	34 (33.33%)	

Data are expressed as n (%). [a]Fisher's Exact test, [c]Pearson Chi-square test; (PDS- Polydioxanone).

and therapeutic purposes in these patients.[12,13] Sixteen patients were treated with ERCP alone and ten patients with ERCP and PTC. Four patients improved with only percutaneous drainage and antibiotic treatment. Four patients were treated with PTC alone. Four patients were operated on due to bile leakage. Two for early leakage (primary repair and hepaticojejunostomy were performed) and two for hepaticojejunostomy. Two patients underwent surgery due to stenosis (hepaticojejunostomy and Whipple). The first is a pediatric patient, because the internal-external catheter cannot be inserted with the PTC. The other, an adult patient, was caused by bleeding, perforation, and penetration of the ERCP catheter into the tissue while performing ERCP due to stenosis in the post-operative 1st month. In this case, total pancreaticoduodenectomy was performed due to duodenal and pancreatic necrosis and widespread bleeding. One patient with leak and stenosis was operated on. He also had hepaticojejunostomy. In our 39 patients

Table 4. The treatment modalities of the biliary complication group

n=39	Leak (n=18)	Stenosis (n=14)	Mikst (n=7)
Percutaneous drainage	4	0	0
PTC	1	2	1
ERCP	8	6	2
PTC and ERCP	3	4	3
Operation	4	2	1

PTC- Percutaneous Transhepatic Cholangiography; ERCP- Endoscopic Retrograde Cholangiopancreatography.

with biliary complications, four patient mortalities were observed during 12–24 months of follow-up (10%). In the non-complicated group, mortality was observed in 16 of 102 patients during 12–24 months of follow-up (15%). Patients' survival of both groups after 24 months was similar (90% vs. 85%).

The drawbacks of our study are that it is retrospective, single center and the number of patients is relatively small, we can't check ischemia, non-dominant flow in the right hepatic artery, hepatic artery thrombosis, anastomotic tension, CMV infection, and all other risk factors. However, keeping the patients' data regularly and the experience of the transplant team over 10 years are the positive aspects of this study.

Conclusion

Biliary complications are the most common problems after LT. They progress with a lengthy hospital stay and hospital expenses. The rate of finding the right graft in patients with biliary complications was higher. The vast majority of patients were successfully treatment with ERCP and PTC. In our study, anastomosis number and anastomosis technique CIT, WIT, AHF are not statically meaningful. We think that they will be significant with the increase in the number of patients.

Highlight Key Points

Bile duct complications are an important cause of morbidity after LT and may be a risk factor for bile complications after liver right lobe transplantation.

Management of bile complications after LT requires a multidisciplinary approach.

Disclosures

Ethics Committee Approval: Approval for this study, dated 01 February 2020 and numbered 2020/43, was obtained from the ethics committee of Istanbul Yeni Yüzyıl University.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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