A comparative study of the biliary outcome in Roux-en-Y hepaticojejunostomy versus duct-to-duct biliary anastomosis in right-lobe living-donor liver transplantation in adults

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Received: 05 September 2022
Revised: 17 September 2022
Accepted: 26 September 2022
Published: 05 April 2023

The Egyptian Journal of Surgery 2023, 41:1395–1404

Background
Recently, liver transplantation settled to be a real breakthrough in surgery as the only curable treatment to deal with fatal liver diseases. Living-donor liver transplantation (LDLT) is the only available option in Egypt owing to the inactive deceased-donor program. Surgeons of recipient's operation should occupy refined surgical skills and experience to reduce the risk of complications. The incidence of biliary complications (BCs) ranges from 5.3 to 40.6%. Leaks occur in 0–21.9%, while strictures occur in 3.7–25.3%. Duct-to-duct anastomosis (D2D) and hepaticojejunostomy (HJ) are the two most common techniques of bile-duct anastomosis in LDLT. D2D is gaining popularity over HJ, because of shorter operative time, fewer septic complications, a better physiologic gastrointestinal function, and rapid recovery, beside easier endoscopic approach to the reconstructed biliary tract.

Patients and methods
The current surgical methodology is a prospective study with nonrandomized convenient sampling that was conducted at Liver Transplantation Unit in Air Forces Specialized Hospital and Nasser Institute for Research and Treatment, Cairo, Egypt, between August 2019 and August 2021. During this study, 40 patients candidate for LDLT were divided into two groups according to type of biliary anastomosis, group A included 20 recipients who had stentless D2D biliary anastomosis compared with group B, including 20 recipients who underwent Roux-en-Y HJ.

Results
A total of 40 recipients were divided into two equal groups according to biliary reconstruction into group A D2D biliary anastomosis, and group B Roux-en-Y HJ. The incidence of biliary-related complications was higher in group A reaching 30%, double that recorded in group B (15%, P=0.262).The incidence of biliary leakage was reversed being doubled in group B 10 versus 5% in group A (P=0.553). After exclusion of seven mortalities (one in group A and six in group B) who did not complete the 6-month follow-up period necessary for complete observation of biliary anastomotic stricture, there was insignificant difference between the two groups. The overall mortality was 17.5% (seven out of 40 recipients), and all died from non-BC-related causes. The only recipient who died from biliary sepsis following endoscopic retrograde cholangiopancreatography and stenting for biliary anastomotic stricture, was included in the results as he died after 5 months from the operation. In a trial to understand the relation between the biliary reconstruction and the complication rate, we found that there was a higher frequency of complications in both 1×1 and 2×2 technique in group A (33% each). In contrast, all that complications happened in group B were in 1×1 technique. In addition, we could not apply the statement that the higher the number of ducts, the higher the rate of complications in the study as two duct grafts represent 66.7% of complications in group A compared with 100% in single-duct graft in group B.

Conclusion
BC is multifactorial, making it impossible to specify a single predictable risk factor to avoid. The advantages of D2D over HJ, especially the beneficial use of endoscopic retrograde cholangiopancreatography in management of complications, are buffered by the higher incidence of BC that is involved with D2D. Therefore, we think that surgeons should master both reconstruction techniques and weight the risk-and-benefit case-by-case.

Keywords:
biliary complications, duct-to-duct biliary anastomosis, living-donor liver transplantation, Roux-en-Y hepaticojejunostomy

Egyptian J Surgery 2023, 41:1396–1404

1110-1121

Introduction

Recently, liver transplantation settled to be a real breakthrough in surgery as the only curable treatment to deal with fatal liver diseases. Living-donor liver transplantation (LDLT) as a treatment for end-stage liver disease (ESLD) is the only available option in Egypt owing to the inactive deceased-donor program [1].

In practice, most of the patients indicated for LDLT do not have the luxury of having an ideal living donor, although we have big families in Egypt. In such cases, an imperfect but acceptable donor's biliary anatomy does not contraindicate donation. Surgeons of recipient's operation should occupy refined surgical skills and experience to reduce the risk of complications.

Most of liver-transplant centers all over the world are still facing biliary stricture complicating LDLT as a relatively common complication. Improvement in surgical techniques, growing experience, better postoperative management, and immunosuppressive therapy have improved the incidence of biliary complications (BCs) over the years [2,3].

The incidence of BC ranges from 5.3 to 40.6%. Leaks occur in 0–21.9%, while strictures occur in 3.7–25.3% [4,5]. Anastomotic strictures represent the majority of strictures after LDLT. The incidence in most of the reports was more than 90% [6].

Duct-to-duct anastomosis (D2D) and hepaticojejunostomy (HJ) are the two most common techniques of bile-duct anastomosis in LDLT. D2D is gaining popularity over HJ, because of shorter operative time, fewer septic complications, that is lower incidence risk of cholangitis, gives the patient a better physiologic gastrointestinal function, and rapid recovery beside easier endoscopic approach to the reconstructed biliary tract if needed in the future [7].

Aim

The aim of this study is to compare the biliary outcome between stentless D2D and Roux-en-Y HJ biliary anastomosis in LDLT patients using right-liver graft (RLG).

Patients and methods

The current surgical methodology is a prospective study with nonrandomized convenient sampling that was conducted at Liver Transplantation Unit in Air Forces Specialized Hospital and Nasser Institute for Research and Treatment, Cairo, Egypt, between August 2019 and August 2021. During this study, 40 patients candidate for LDLT were divided into two groups according to type of biliary anastomosis, group A included 20 recipients who had stentless D2D biliary anastomosis compared with group B, including 20 recipients who underwent Roux-en-Y HJ.

Informed consent was obtained from every recipient before recruitment in the study, and after explaining the purpose and procedures. The approval from the ethical committees of both institutes as well as the approval of the supreme committee of organ transplant, MOH, Egypt, was taken case-by-case.

All patients underwent evaluation and preparation for the surgery according to the center protocol. The anatomy of the vessels of the liver and the biliary tract was confirmed using noninvasive contrast-enhanced computed tomography angiography and biliary anatomy was assessed using MRCP.

All patients above 18 years old eligible for LDLT with RLG without middle hepatic vein, fulfilling the criteria of transplantation according to the center protocol and approved by the transplantation multidisciplinary committee, were included.

The primary surgical intention for biliary reconstruction was D2D anastomosis, especially under unfavorable bowel-loop conditions, such as marked edema, peritonitis-induced thickening, for example spontaneous bacterial peritonitis, or shrunken mesentery. HJ was done in all recipients with primary sclerosing cholangitis (PSC), adult biliary atresia, and in some cases, needing multiple-duct anastomoses, common bile-duct (CBD) dilatation (diameter >1.5 cm), or definite injury of the recipient's bile duct because of the dissection during the recipient's hepatectomy, for example during thrombectomy in case of portal vein thrombosis. In addition, if it was impossible to use recipient's bile duct when there was no bleeding at its cut end before the anastomosis or it

was too short for a direct D2D without tension and if the recipient duct opening was smaller than the graft duct opening.

Recipients with previous HJ, left-liver graft as graft regeneration causes stretching and pulling, thereby narrowing the lumen, damaging the duct, and resulting in stricture formation (29), dual graft. Recipient's age below 18 years even with RLG was excluded. Patients that die within less than 3 months of liver transplant or incomplete data were excluded from this study.

Patients with biliary nonanastomotic (ischemic-type) strictures (manifested as hepatic artery thrombosis, recurrence of PSC, or acute or chronic rejection) were also excluded. In addition, selected cases in which a combination of D2D and HJ performed for multiple-donor bile ducts were also excluded.

The recipients' age, sex, blood type, hepatopathy, diagnosis of hepatocellular carcinoma, model for end-stage liver-disease score, Child–Pugh score, BMI, and graft-to-recipient weight ratio (GRWR) were abstracted.

Intraoperatively, variables included the following: cold ischemia time, operative time, number of bile ducts, method of reconstruction, and intraoperative duplex reading were recorded. Postoperatively, the outcome included the following: postoperative duplex reading, morbidity (hepatic artery thrombosis, recurrent portal vein thrombosis), biliary leak or biliary anastomotic stricture (BAS), and mortality.

An anastomotic biliary stricture was suspected once the patient was symptomatic, including itching, fever, and icterus, or when serum alkaline phosphatase levels and GGT were elevated, confirmed with MRCP finding as intrahepatic duct dilatation of 3 mm or more in the presence of considerable extrahepatic biliary narrowing.

Postoperative bile leakage was diagnosed once bile was detected from the wound or the operatively placed drain or drained intra-abdominal collection with total bilirubin level in the fluid more than three times that in the serum.

All interventions were done by a team of surgeons with experience in hepatobiliary and liver-transplant surgery. All authors are surgeons, and all contributed to the study. The last two authors are staff surgeons with special dedication to hepatobiliary surgery and liver transplantation, and have more than 18 years of experience. At least one of them was always present at the interventions. Biliary reconstruction was done by these two surgeons throughout the whole study.

In the recipient surgery, hilar dissection was carefully performed to preserve adequate blood supply where the hepatic arteries of the recipient were ligated at the level of the second-order branches and the bundle, including the extrahepatic biliary tree and the right hepatic artery (RHA), was left en bloc, then the bile duct was sharply divided above the hilar bifurcation. Biliary anastomosis was performed by the transplant surgeon using magnification loop size 6.0, with 6-0 polydioxanone-absorbable suture after completion of vascular anastomosis. Ductoplasty might be performed if the graft had two bile ducts less than 2 mm apart to set them close together as a common orifice using interrupted 6-0 polypropylene suture. Graft bile ducts less than 1 mm in diameter were routinely suture-ligated in the donor operation.

In the donor surgery, an intraoperative cholangiogram through the cystic duct was performed routinely with fluoroscopy to confirm the biliary anatomy and to guide the bile-duct transection point minimizing the number of graft-duct openings obtained from various donor bile-duct anatomies. The right hepatic ducts were then transected sharply with particular attention to minimize duct dissection and maintain liver tissue around the duct. Parenchymal transection was thereafter performed using the Cavitron Ultrasonic Surgical Aspirator (CUSA system 200; Valleylab Inc., Boulder, Colorado, USA) and bipolar electrocautery without inflow interruption. At the end of the operation, the bile-leakage test, white test was performed through the cystic duct using Vitalipid N Adult solution (Fresenius Kabi, Egypt) to detect any leakage from the bile duct or the cut surface.

In group A: stentless D2D anastomosis was done by end-to-end anastomosis using interrupted 6-0 polydioxanone sutures with knots outside the lumen. The primary intension during arterial reconstruction was to use left hepatic artery in arterial reconstruction. In case of RHA used, the recipient bile duct was dissected out to obtain enough length, taking care to preserve the blood supply to the duct by avoiding removal of the connective tissue between the CBD and the RHA and guaranteed by the good mucosal color and arterial bleeding from the cutting stump. If a second biliary anastomosis was needed, right and left branches of the recipient's CBD were used. We did not use cystic duct in biliary reconstruction, so, if the recipient biliary duct was unsuitable for two anastomoses, HJ was used instead.

While in group B: the jejunum was divided about 20 cm from the Treitz's ligament and the distal limb was elevated to the hilum of the graft using the retrocolic route. The side-to-side enteroentrostomy was done 60 cm distal to the cut end using a linear GIA-75 stapler (Ethicon, Cornelia, Georgia, USA) over which a second hemostatic layer was taken by 4-0 polydioxanone suture. The ostia through which the stapler was introduced was closed extramucosally by 4-0 polydioxanone suture in two layers.

The proximal limb was anastomosed end-to-side to the elevated distal limb. A small orifice was made in the Roux-en-Y limb close to the proximal end and mucosal eversion was done via four 6-0 polydioxanone sutures, then anastomosis was done by 6-0 polydioxanone suture with knots outside the lumen and no stents were used. If a second biliary anastomosis was needed, two separate orifices were used. In selected case, HJ was performed even when ductoplasty was done.

All patients were followed up for at least 6 months, during the hospital stay, daily laboratory and radiological assessment was done during the first 2 weeks and then twice weekly until discharge. After discharge, follow-up was scheduled once weekly for the first 3 months, then once monthly for the following 3 months, and then every 3 months afterward. Patients were asked every visit postoperatively for abdominal ultrasound and duplex together with routine laboratory data and immunosuppressive drug level. Follow-up contrast-enhanced computed tomography with angiography was done only if necessary and as a part of the complete workup 12 months after LDLT, or based on the patient's condition.

MRCP was done if there is intrahepatic biliary-radicle dilatation by ultrasound, itching even with normal bilirubin, and consistent rise in alkaline phosphatase and GGT. BCs were managed either by endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangioplasty (PTC) or both after case-by-case discussion with the multidisciplinary committee of the Liver Transplantation Unit.

As liver biopsy is an invasive procedure with possible complications, it is only requested if needed to exclude other causes of jaundice, such as graft rejection (acute or chronic), recurrence of primary hepatopathy, or drug-induced cholestasis.

The primary treatment of BAS consisted of a PTC for all patients with HJ. A PTC or an ERCP or a combination of both procedures were utilized as indicated for patients with D2D anastomosis. Surgical revision was indicated when these modalities failed.

Statistical analysis

Recorded data were analyzed using the Statistical Package for Social Sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as mean±SD and ranges. Data were explored for normality using Kolmogorov–Smirnov and Shapiro–Wilk test.

The following tests were done:

(1) Independent-samples *t* test of significance was used when comparing between two means and Mann–Whitney *U* test: for two-group comparisons in nonparametric data.
(2) The comparison between groups with qualitative data was done by using χ^2 test.
(3) Kaplan–Meier survival analysis: is a descriptive procedure for examining the distribution of time-to-event variables.
(4) Log-rank test to compare time-to-event variables by levels of a factor variable.
(5) The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *P* value was considered significant as the following:
(6) *P* value
    (a) *P* value less than or equal to 0.05 was considered significant.
    (b) *P* value less than or equal to 0.001 was considered as highly significant.
    (c) *P* value more than 0.05 was considered insignificant.

Results

We started our LDLT program in 2015. Between August 2019 and the end of August 2021, we had performed 212 LDLTs, comprising 151 adult cases and 58 pediatric cases and three dual-graft transplants. All patients finished at least 6 months of follow-up.

The two groups were comparable in age (Table 1) with the mean±SD in group A and group B that was 54.55 ± 13.43 compared with 48.90 ± 18.15, respectively. Table 1 shows that sex distribution was comparable in each of group A, 17 (85%) male patients and three (15%) female patients compared with group B, 12 (60%) male patients and eight (40%) female patients, there was no statistically significant difference between the groups regarding age and sex with *P* value of 0.270 and 0.077, respectively.

While there is no statistically significant difference between groups (Table 1) according to weight (kg),

Table 1 Comparison between duct-to-duct group and hepaticojejunostomy group according to baseline characteristics

Baseline characteristics	D2D group (*N*=20)	HJ group (*N*=20)	Test value	*P* value
Age (years)				
Mean±SD	54.55±13.43	48.90±18.15	*t*=1.119	0.270
Range	26–72	19–68		
Sex [*n* (%)]				
Female	3 (15.0)	8 (40.0)	χ^2=3.135	0.077
Male	17 (85.0)	12 (60.0)		
Weight (kg)				
Mean±SD	78.53±16.88	70.90±26.31	*U*=1.091	0.282
Range	50.5–132	45–119		
BMI [wt/(ht)^2]				
Mean±SD	26.58±3.64	26.25±6.22	*t*=0.210	0.834
Range	21–37.7	18.3–42.1		
Blood group [*n* (%)]				
A+ve	7 (35.0)	8 (40.0)		
AB+ve	0	1 (5.0)		
B+ve	6 (30.0)	3 (15.0)	χ^2=3.067	0.547
O-ve	0	1 (5.0)		
O+ve	7 (35.0)	7 (35.0)		
MELD				
Mean±SD	15.50±5.68	17.40±5.10	*U*=1.113	0.273
Range	9–26	8–29		
Child class [*n* (%)]				
A	5 (25.0)	2 (10.0)		
B	10 (50.0)	9 (45.0)	χ^2=2.481	0.289
C	5 (25.0)	9 (45.0)		
Child score				
Mean±SD	8.30±2.32	9.00±1.65	*t*=1.099	0.279
Range	5–13	6–12		
Donor's age (years)				
Mean±SD	31.85±5.47	29.05±5.16	*t*=1.666	0.104
Range	21–40	20–37		

t, independent sample *t* test; *U*, Mann–Whitney test; χ^2, χ^2 test. D2D, duct-to-duct; HJ, hepaticojejunostomy; MELD, model for end-stage liver disease. *P* value more than 0.05 NS; **P* value less than 0.05 S; ***P* value less than 0.001.

BMI [wt/(ht)^2], blood group, model for end-stage liver-disease, and Child class and Child score (*P*>0.05).

The main etiology of liver disease in Egypt is HCV, representing 45% of cases in our study, making it the most common cause of ESLD, and by logic, the second common cause in the HJ group is PSC in which removal of the CBD is mandatory. The third common cause in HJ group and the second in D2D group was HCC responsible for 40 and 35%, respectively.

The majority of HCV was 50% in group A compared with (40%) in group B. Table 2 clarifies that PSC was not an indication in group A compared with 45% in group B (*P*<0.001 significant), then AIH was 15% in each group, followed by cryptogenic (15%) in group A and 10% in group B, there is no statistically significant difference between groups (*P*>0.05 NS).

Table 2 shows that 35% of patients in group A had an underlying HCC compared with 40% in group B, there is no statistically significant difference between groups (*P*>0.05 NS). About 42% of patients in group A underwent a bridging/downstaging intervention where TACE was used in two (28.6%) patients and one (14.3%) patient had a more complex downstaging protocol for three hepatic local lesions with overall size and the largest was 4 cm and 2.5 cm and mildly elevated alpha-fetoprotein. He had microwave followed by TACE 2 months later and he received two cycles of Opivido interrupted by the decision of LDLT and the explant pathology revealed completely ablated lesions. While in group B, only a single (12.5%) patient had TACE as a bridging, even with this disparity, it did not achieve statistical significance.

According to operative data (Table 3), in group A, the mean GRWR was 1.13±0.25, cold ischemia time was 55.75±32.01 min, operative time was 9.97±1.86 h and HA R index was 0.62±0.09. While in group B, mean GRWR was 1.13±0.30, cold ischemia time was 48.75±32.38 min, operative time was 9.18±2.19 h, and HA R index was 0.62±0.09, there is no statistically significant difference between groups (*P*>0.05 NS).

Table 2 Comparison between duct-to-duct group and hepaticojejunostomy group according to hepatopathy

Hepatopathy	D2D group (*N*=20) [*n* (%)]	HJ group (*N*=20) [*n* (%)]	χ^2	*P* value
HCV	10 (50.0)	8 (40.0)	0.404	0.525
PSC	0	9 (45.0)	11.323	<0.001**
AIH	3 (15.0)	3 (15.0)	0.000	1.000
Cryptogenic	3 (15.0)	2 (10.0)	0.229	0.633
HBV	2 (10.0)	0	2.105	0.147
NASH	1 (5.0)	0	1.026	0.311
Budd–Chiari syndrome	1 (5.0)	0	1.026	0.311
Hepatopulmonary	0	1 (5.0)	1.026	0.311
PVT	4 (20.0)	5 (25.0)	0.143	0.705
HCC	7 (35.0)	8 (40.0)	0.107	0.744
Method bridging/downstaging				
Microwave, TACE, and Opivido/n*	1/7 (14.3)	0/8	1.444	0.486
TACE/n	2/7 (28.6)	1/8 (12.5)		

*One patient had received the three lines of management. *P* value more than 0.05 NS; **P* value less than 0.05 S; ***P* value less than 0.001. AH, autoimmune hepatitis; D2D, duct-to-duct; HBV, hepatic B virus; HCC, hepatocelluar carcinoma; HCV, hepatitis-C virus; HJ, hepaticojejunostomy; NA, not applicable; PSA, primary sclerosing cholangitis; PVT, portal vein thrombosis; TACE, transarterial chemoembolization.

Table 3 Comparison between duct-to-duct group and hepaticojejunostomy group according to operation

Operative data	D2D group (*N*=20)	HJ group (*N*=20)	Test value	*P* value
GRWR				
Mean±SD	1.13±0.25	1.13±0.30	*U*=0.038	0.970
Range	0.76–1.7	0.7–2.1		
Cold ischemia time (min)				
Mean±SD	55.75±32.01	48.75±32.38	*U*=0.688	0.496
Range	15–130	1–150		
Operative time (h)				
Mean±SD	9.97±1.86	9.18±2.19	*t*=1.229	0.227
Range	7–13	6.5–16		
Hepatic artery R index				
Mean±SD	0.62±0.09	0.62±0.09	0.018	0.986
Range	0.51–0.85	0.5–0.8		

D2D, duct-to-duct; GRWR, graft-to-recipient weight ratio; HJ, hepaticojejunostomy; *t*, independent sample *t* test; *U*, Mann–Whitney test; χ^2, χ^2 test. *P* value more than 0.05 NS; **P* value less than 0.05 S; ***P* value less than 0.001.

As regards the number of graft ducts (Table 4), it is far more pronounced that single-duct graft was more in group B (65% of grafts) with *P* value of 0.001, while in group A, a two-duct graft was more common (60% of grafts) in this group (*P*=0.001). This was reflected on the method of biliary reconstruction, 95% of recipients in group B had a single HJ (*P*=0.004) and the only recipient who received a two-duct graft had two HJ in the same limb using two separate orifices. While in group A (D2D anastomosis), 1×1 technique was used in seven recipients, 2×2 technique in eight recipients from which a recipient received a graft with three ducts (right right ducts and an accessory duct) where two right hepatic ducts anastomosed to the recipients' left hepatic duct and an accessory right hepatic duct to the recipients' right hepatic duct. Ductoplasty was used only in one recipient in group A in the whole study as it is not a preferred option in our practice (*P*>0.05 nonsignificant).

The incidence of biliary-related complications (Table 5) was higher in group A reaching 30%, double that recorded in group B (15%, *P*=0.262). Upon stratification of those complications, the incidence of biliary leakage was reversed being doubled in group B 10 versus 5% in group A (*P*=0.553). After exclusion of seven mortalities (one in group A and six in group B) who did not complete the 6-month follow-up period necessary for complete observation of BAS, there was an insignificant difference between the two groups.

As regards group A (Table 6), we had two recipients with biliary leakage, one was managed conservatively and the other needed ERCP and stenting, the later one developed BAS later on and underwent ERCP and stenting. Only one patient had biloma (biliary collection) in which an ultrasound-guided pigtail was inserted, later on, he developed BAS that required ERCP and stenting. Another three recipients developed BAS only, two of them had ERCP and stenting, and the last one, the wire failed to pass the stricture and rendezvous was done in the same session.

In the HJ group (Table 6), we had two recipients with biliary leakage and both were managed conservatively,

Table 4 Comparison between duct-to-duct group and hepaticojejunostomy group according to number of donor ducts and biliary reconstruction

	D2D group (*N*=20) [*n* (%)]	HJ group (*N*=20) [*n* (%)]	χ^2	*P* value
Number of donor duct				
1	7 (35.0)	19 (95.0)	15.429	<0.001**
2	12 (60.0)	1 (5.0)	13.444	<0.001**
3	1# (5.0)	0	1.000	0.317
Biliary reconstruction				
1×1	7 (35.0)	19 (95.0)	8.485	0.004*
2×1				
With ductoplasty	1 (5.0)	0	1.026	0.311
Without	4 (20.0)	0	4.444	0.035*
2×2	8 (40.0)	1## (5.0)	6.849	0.009*

#Two right hepatic ducts anastomosed to the recipients' left hepatic duct and an accessory right hepatic duct to the recipients' right hepatic duct. ##The two ducts were anastomosed to two separate orifices. χ^2, χ^2 test. D2D, duct-to-duct; HJ, hepaticojejunostomy. *P* value more than 0.05 NS; **P* value less than 0.05 S; ***P* value less than 0.001.

Table 5 Comparison between duct-to-duct group and hepaticojejunostomy group according to biliary complications

Biliary complications	D2D group [*n* (%)]	HJ group [*n* (%)]	χ^2	*P* value
No. of patients	6/20 (30)	3/20 (15)	1.258	0.262
Biliary leak	1/20 (5)	2/20 (10)	0.351	0.553
Biloma	0/20	0/20	–	NA
BAS	3/19 (15.8)	0/14	2.360	0.125
Biliary leak followed by BAS	1/19 (5.3)	1/14 (7.1)	0.044	0.833
Biloma followed by BAS	1/19 (5.3)	0/14	0.742	0.389

χ^2, χ^2 test. *P* value more than 0.05 NS. BAS, biliary anastomotic stricture; D2D, duct-to-duct; HJ, hepaticojejunostomy; NA, not applicable.

Table 6 Comparison between duct-to-duct group and hepaticojejunostomy group according to intervention for complications

Intervention for complication	D2D group [*n* (%)]	HJ group [*n* (%)]	χ^2	*P* value
Intervention for biliary leakage				
Drainage/operatively placed drain	1/3 (33.3)	2/3 (66.7)	0.558	0.455
Drainage/pigtail	1/3 (33.3)	1/3 (33.3)	0.000	1.000
PTC and balloon dilatation	0/3	0/3	–	NA
ERCP	1/3 (33.3)	1/3 (33.3)	0.000	1.000
Rendezvous	0/3	0/1	–	NA
Intervention for BAS				
PTC and balloon dilatation	0/5	0/1	–	NA
ERCP	4/5 (80.0)	1/1 (100)	0.200	0.655
Rendezvous	1/5 (20.0)	0/1	0.200	0.655
Operative treatment	0/5	0/1	–	NA

χ^2, χ^2 test; *P* value more than 0.05 NS. BAS, biliary anastomotic stricture; D2D, duct-to-duct; ERCP, endoscopic retrograde cholangiopancreatography; HJ, hepaticojejunostomy; NA, not applicable; PTC, percutaneous transhepatic cholangioplasty.

one of them developed BAS later on and underwent ERCP and stenting. The third recipient, an ultrasound-guided pigtail was inserted to drain biloma followed by ERCP and stenting to control the leakage.

The overall mortality, defined as patients that die within less than 3 months of liver transplant that were excluded from this study, was 17.5% (seven out of eight recipients), and all died from non-BC-related causes (Table 7). The only recipient who died from biliary sepsis following ERCP and stenting for BAS, was included in the results as he died after 5 months from the operation.

In a trial to understand the relation between the biliary reconstruction and the complication rate (Table 8), we found that there was a higher frequency of complications in both 1×1 and 2×2 technique in group A (33% each). In contrast, all complications that happened in group B were in 1×1 technique. In addition, we could not apply the statement that the higher the number of ducts, the higher the rate of complications in the study as two-duct grafts represent 66.7% of complications in group A compared with 100% in single-duct graft in group B.

Discussion

LDLT is the standard of care for patients with ESLDs and HJ being the initial standard technique for biliary reconstruction [8]. Wachs *et al.* [9] were the first to use

Table 7 Comparison between duct-to-duct group and hepaticojejunostomy group according to mortality

	D2D group (*N*=20) [*n* (%)]	HJ group (*N*=20) [*n* (%)]	χ^2	*P* value
Mortality	2/20 (10.0)	6/20 (30.0)	2.438	0.119
Cause				
Biliary-related sepsis	1/2 (50)	0/6	3.000	0.083
Non-biliary-related sepsis	1/2 (50)	3/6 (50)	–	NA
Cardiogenic causes	0	1/6 (16.7)	0.334	0.563
Pulmonary embolism	0	1/6 (16.7)	0.334	0.563
Bleeding	0	1/6 (16.7)	0.334	0.563

χ^2, χ^2 test; *P* value more than 0.05 NS. D2D, duct-to-duct; HJ, hepaticojejunostomy; NA, not applicable.

Table 8 Comparison between duct-to-duct group and hepaticojejunostomy group as regards number of donor ducts and technique of anastomosis in relation to biliary complications

	D2D complications (*N*=6) [*n* (%)]	HJ complications (*N*=3) [*n* (%)]	χ^2 test	
			χ^2	*P* value
Number of donor ducts				
1	2 (33.3)	3 (100.0)	3.203	0.074
2	4 (66.7)	0	3.203	0.074
3	0	0	–	NA
Biliary reconstruction				
1×1	2 (33.3)	3 (100.0)	3.203	0.074
2×1				
With ductoplasty	1 (16.7)	0	0.501	0.479
Without	1 (16.7)	0	0.501	0.479
2×2	2 (33.3)	0	1.141	0.285

χ^2, χ^2 test. D2D, duct-to-duct; HJ, hepaticojejunostomy. *P* value more than 0.05 NS; **P* value less than 0.05 S; ***P* value less than 0.001.

the technique of D2D for LDLT using RLG, but BAS developed 4 weeks after the operation and the biliary anastomosis was revised to a Roux-e-Y HJ.

Clear selection criteria for bile-duct reconstruction method were not stated in most of the publications, and there is a considerable variation in the techniques of bile-duct reconstruction. At many transplant centers, the potential advantages of D2D seem so beneficial that it has become the preferable biliary-reconstruction technique [10,11].

As posttransplantation BCs are a multifactorial issue, in this study, we tried to reduce contributing factors in data analysis to study the outcomes properly. We chose to exclude recipients with vascular complications, for example, hepatic artery thrombosis, CMV infection activity, and acute and chronic rejection.

We also believe that right lobe and left lobe should be discussed separately when the issue of LDLT is to be discussed due to the essential differences in the graft nature and operative procedures. Beside, left-liver graft regeneration causes narrowing of the lumen due to stretching of the pedicle and even its twist around its axis damaging the duct, and resulting in stricture formation [12]. Zhang *et al.* [13] had contraindicated D2D reconstruction when using left lobes due to the increased rate of biliary leakage that has been reported in adult left-lobe LDLT. It was reported by Quian *et al.* [14] who reported that the use of left lobes was less suitable for D2D reconstruction because of concerns that blood supply of the left duct may arise from segment IV or even the RHA, making it more vulnerable for ischemia.

In our study, the overall rates of biliary leakage and BAS were 15% for both. On comparing D2D to HJ using collected data, D2D was found to be associated with a bigger chance of BAS rather than HJ, 26.3 and 7.1%, respectively. Inspite of having a similar incidence regarding biliary leakage, three patients out of 20 in each group. Similar results were reported in a retrospective study from South Korea done by Yi *et al.* [15] on 74 adult patients who underwent LDLT that indicated lower incidence of BCs (11.1%) with HJ than D2D anastomosis (33.3%) and they recommended that HJ was associated with improved long-term survival outcomes.

Another study from Hwang *et al.* [10] from Asan medical center agreed with the same results that D2D anastomosis was associated with more frequent BCs following LDLT, but they oppositely reported that the overall outcomes were significantly better with D2D. And he also observed that BC rate gradually increased from 8.9% at 3 months to 12.9, 18.2, and 20.2% at 1, 3, and 5 years, respectively. A North American study

from the adult-to-adult LDLT cohort-study group reported that the rate of BCs was 40% with some cases of complications presenting up to 10 years after transplantation [16].

In the same context, a meta-analysis of 16 trials analyzed by Jeong *et al.* [17] demonstrated no definite evidence of a preponderance of either of the two major types of biliary reconstruction. Chok and Lo [18] had concluded the same in a single-center retrospective study on adult LDLT using the right-liver lobe, he stated that D2D or HJ was used and did not significantly influence the incidence of BAS.

It is worth noting that the complexity of biliary reconstruction and the multiplicity of graft ducts, that is more 2 × 2 biliary reconstruction in group A in comparison with group B, played a significant role in the increased incidence of BCs and also explaining it. Another explanation was given by Jeon *et al.* [19] highlighting two risk factors, namely a long caudal segment of the right posterior bile duct of the graft or a short right bile duct. In a study done by Baker *et al.* [20], he observed BC in 42% of transplant recipients with D2D reconstructions during the first posttransplant year and he emphasized that reconstruction with higher-order biliary radicals was associated with the highest incidence of early biliary leaks and late biliary strictures. This is likely secondary to ischemia associated with devascularization of the ducts, but he did not identify a strong association between biliary-reconstructive techniques and ultimate graft and patient outcome [21].

To avoid this, Kim *et al.* [16] recommended the preservation of the vascular plexus around the duct by avoiding extensive dissection of the right hepatic-duct complex accomplished by dividing the liver parenchyma at the base of segment 4b beneath the plane of the middle hepatic vein to preserve a good liver-tissue volume around the right hepatic-duct complex and avoid skeletonizing it. The Roux-en-Y HJ does not harbor this consideration as it has a more reliable blood supply to the anastomosis and the ability to consistently obtain a tension-free anastomosis. Whatever the technique of biliary reconstruction, almost all the studies specially stress that the blood supply for biliary anastomosis is a major concern in LDLT [13]. As we are also concerned with the vascularity of the D2D anastomosis during the study, we added to the above-mentioned precaution discussed by Kim, the preferential use of the left hepatic artery for arterial anastomosis preserves the blood supply of the recipient bile duct untouched.

On the other side, we have no clear explanation why single-duct anastomosis in group A had a similar incidence of BCs (33.3%). This may be explained by the retrospective study of Hwang *et al.* [10] on adult LDLTs, including 225 RLG, who reported that a single biliary anastomosis for a graft bile-duct size smaller than 4 mm in diameter was a risk factor for BAS with D2D but not HJ. Unfortunately, we did not document in our study the diameter of the graft bile duct, so we could not comment on this issue.

As opposed, Greif *et al.* [22] reported more strictures in cases of Roux-en-Y HJ and that strictures that occurred early were due to technical issues, while late strictures were due to fibrosis that resulted from the healing process.

There are some publications that could not reach a recommended biliary-reconstruction method over the other as in the meta-analysis study done by Azzam and Tanaka [1], there was no significant difference between two groups in the BCs. As well, the systemic review and meta-analysis by Zhang *et al.* [13] of 16 trials found no concrete evidence of superiority of either of the two biliary-reconstruction methods.

Regarding BAS, one-third of the patients in our study who had BAS, had experienced biliary leakage earlier in the posttransplant course, making it a blamed risk factor. This was the assumption adopted by Kasahara *et al.* [23] that the predisposing factors for anastomotic strictures were ischemia or secondary to biliary leakage, then came the other causes, including hepatic artery complications and CMV infection, while blood-type incompatibility was not a significant factor in biliary stricture. In addition, there is no definite evidence that the method of biliary reconstruction is related to the formation of BAS. A retrospective study by Chok *et al.* [24], University of Hong Kong, compared D2D anastomosis and HJ in terms of the incidence of BAS after adult RLDLT, but no significant difference was observed.

Finally, most of biliary leaks occurred early and were successfully managed and there was a gradual decrease in the amount of leak till complete resolution, except in one case. Biliary strictures mostly occurred after discharge and during the follow-up period, and were successfully treated by ERCP in 83.3%, except for one case in which ERCP in combination with PTC.

PTC with balloon dilatation and drainage with or without stenting had proved its effectiveness at the site of anastomosis. In patients with D2D anastomosis, ERCP and stenting appeared to be of benefit in

treating multibranched strictures or single strictures by inserting single or multiple stents with success rate that reached 74.5–75% [1]. Due to the unavailability of the internal stent used by the PTC in our center, we used a retrograde double-balloon enteroscope and ERCP for the patient with leaking HJ by which we were able to place internal stents.

Limitation

Our study had several limitations. This is a single-center study, therefore, the results may not be generalizable to other transplant centers. Second, the small sample size resulting in a smaller number of some less-common anatomic biliary variants beside limiting the power of the study and hinders the statistical capacity to do multivariate analysis. Third, most of the patients in our study in group B were associated with single-duct graft, while duct multiplicity was far more pronounced in group A.

Conclusion

In conclusion, BC is a bottleneck along the path of a successful LDLT as it is multifactorial, making it impossible to specify a single predictable risk factor to avoid. The advantages of D2D over HJ, especially the beneficial use of ERCP in management of complications, are buffered by the higher incidence of BC that is involved with D2D. Therefore, we think that surgeons should master both reconstruction techniques and weight the risk-and-benefit case-by-case.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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