

ORIGINAL ARTICLE

Duct-to-duct biliary reconstruction in orthotopic liver transplantation for primary sclerosing cholangitis: a viable and safe alternative

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Summary

Roux-en-Y loop is considered the reconstruction method of choice in Orthotopic Liver Transplantation (OLT) for Primary Sclerosing Cholangitis (PSC). We have adopted an approach of duct-to-duct (D-D) reconstruction when recipient common bile duct is free of gross disease. Patients were divided into two groups: patients who underwent a Roux-en-Y choledochojejunostomy and patients who had a D-D anastomosis. Morbidity, mortality, disease recurrence and graft and patient survival were compared between the two groups and analyzed. Ninety-one patients had OLT for PSC. Sixty-three patients underwent a D-D biliary reconstruction, whereas 28 patients had a Roux-en-Y loop. Biliary leak complicated 8% from the D-D group, and 14% from the Roux-en-Y group ($P = 0.08$), whereas biliary strictures were identified in 10% vs. 7% patients from the D-D and Roux-en-Y group, respectively ($P = 0.9$). Actuarial 1, 3 and 10 year survival for D-D and Roux-en-Y group was (87%, 80% and 62%) and (82%, 73% and 73%), respectively ($P = 0.7$). The corresponding 1, 3 and 10 year graft survival was (72%, 58% and 42%) and (67%, 58% and 53%), respectively ($P = 0.6$). No difference was seen in disease recurrence rates. D-D biliary reconstruction in OLT for selected PSC patients remains our first option of reconstruction.

Introduction

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and fibrosis of the bile ducts, resulting in end-stage liver disease and reduced life expectancy [1]. PSC is commonly associated with inflammatory bowel disease that often precedes the development of PSC [2]. The natural history of PSC is variable, but virtually always follows a progressive course; patients have a median survival of approximately 10–12 years after diagnosis [3]. No effective medical treatment is available. Thus, orthotopic liver transplantation (OLT) is the only definitive treatment for these patients. OLT has been shown to provide excellent

long-term patient and graft survival for patients with end-stage liver disease caused by PSC, with 5-year survival rates reaching around 85% [4,5].

Different types of biliary reconstruction in OLT for PSC have been used; however, the standard method of reconstruction remains a matter of debate. It has been previously reported that Roux-en-Y loop reconstruction reduces the incidence of postoperative stricture formation, and provides a better patient and graft survival when compared with duct-to-duct (D-D) reconstruction [6]. D-D anastomosis has been supported because it allows easier postoperative access to the biliary tree, and it also restores the normal anatomy of the biliary tree and restores the sphincter function potentially preventing

infection and sepsis. D-D reconstruction has also been found to be associated with a less operative time and a smoother postoperative recovery when compared with Roux-en-Y reconstruction [7–9]. A choledochoduodenostomy rather than a choledochojejunostomy has also been suggested for certain cases when bile ducts appear grossly diseased, and when choledochojejunostomy is difficult to accomplish because of a previous surgery or for retransplantation [10].

In this report, we analyzed our experience with D-D and Roux-en-Y biliary reconstruction for PSC patients undergoing OLT, with respect to surgical complications and long-term outcome.

Methods

Patients who had OLT for PSC were identified from the Royal Free Liver Transplantation database that represents prospectively collected data, and then each patient record were reviewed and analyzed retrospectively. Diagnosis of PSC was made by cholangiographic features with biochemical and histologic data. Patients were divided into two groups: the first group consisted of patients who underwent a Roux-en-Y choledochojejunostomy for biliary reconstruction, and the second group was patients who had a D-D anastomosis. A decision was made to go for a Roux-en-Y reconstruction if on the last (within 6 months) endoscopic retrograde cholangio-pancreatography (ERCP)/magnetic resonance cholangio-pancreatography (MRCP), there was dominant mid or distal bile duct stricture requiring balloon dilatation, and/or intraoperatively the common bile duct appeared thickened and narrowed with failure to pass a 6 mm General Maingot Bile Duct Dilator through it, or if the patient has had a previous biliary procedure (bile duct exploration and/or drainage). Pathologic examination of the bile duct using frozen section studies was not used as part of the assessment. In the D-D group, anastomosis was either performed side-to-side or end-to-end, according to surgeons' preferences. Anastomosis was performed using interrupted 5/0 PDS suture in both D-D anastomosis and Roux-en-Y reconstruction. At the beginning of the program, T-tube splintage was used, this was later abandoned, as it did not confer benefit in terms of postoperative biliary complications. ABO-identical or -compatible donors were always used. Mortality was defined as death within 30 days from the operation. Intraoperative and postoperative complications were defined as any adverse event occurring between the induction of anesthesia and the 30th day after the operation that required intervention. ERCP or percutaneous transhepatic cholangiography (PTC) were performed when clinically indicated to identify strictures or anastomotic leaks. A bile leak was defined as radiologically evi-

dent persistent drainage of bile with an intra-abdominal collection or symptoms of biliary peritonitis requiring intervention. A biliary stricture was defined as a narrowing within the biliary tree, radiologically evident, sufficient to cause clinical symptoms or biochemical abnormalities requiring intervention. The diagnosis of recurrent PSC was based on a liver biopsy and radiologic assessment (with magnetic resonance cholangiography and/or ERCP) showing changes consistent with PSC (defined as nonanastomotic focal strictures in the intra- and/or extrahepatic biliary tree more than 3 months after OLT) in the absence of dominant anastomotic stricture or hepatic artery thrombosis identified using Doppler ultrasonography and/or hepatic angiography [11]. Graft and patient survival in the two groups were analyzed and compared. Patient and graft survival was estimated using the Kaplan–Meier method. Statistical comparisons between groups of patients were performed using the log-rank test. Chi-square test was used to compare between variables. A value of $P < 0.05$ was considered statistically significant. Significance was accepted with 95% confidence. Results are reported as mean \pm standard deviation unless otherwise specified.

Results

Between November 1988 and September 2008, a total of 1095 patients underwent liver transplantation, and of them, 91 patients had liver transplantation for PSC. Overall, patient group consisted of 56 (62%) men and 35 (38%) women aged 43.5 ± 14 years. Sixty-three patients (69%) underwent a D-D biliary reconstruction, whereas 28 patients (31%) had a Roux-en-Y loop. Patient demography and operative parameters did not differ among the two groups (Table 1).

The overall mean follow-up period was 7 years \pm 6. Mean patient survival for D-D and Roux-en-Y group was 11 and 13 years, respectively ($P = 0.6$) (Fig. 1). The corresponding graft survival rates were 11 years for the D-D group and 10 years for the Roux-en-Y group ($P = 0.2$) (Fig. 2). Actuarial 1, 3, 5 and 10 year survival for D-D and Roux-en-Y group was (87%, 80%, 67% and 62%) and (82%, 73%, 73% and 73%), respectively ($P = 0.7$). The corresponding 1, 3, 5 and 10 year graft survival was (72%, 58%, 48% and 42%) and (67%, 58%, 53% and 53%), respectively ($P = 0.6$).

Graft failure occurred in 32% and 32% in D-D and Roux-en-Y group, respectively. Of those, 55% and 56% lost their graft within 3 months of transplantation. Causes of graft failure are listed in Table 2. The percentage of those who died with a functioning graft did not significantly differ between the two groups; 20% and 10% from the D-D and Roux-en-Y group, respectively. In addition,

	D-D	Roux-en-Y	P value
No. of patients	63 (69%)	28 (31%)	
Age (years)	44 ± 15	41 ± 12	0.3
Sex (M:F)	40:23 (64:36%)	16:12 (57:43%)	0.4
MELD score	19 ± 9.7	17 ± 4.7	0.2
Inflammatory bowel disease (IBD), No. (%)	38 (60%)	18 (65%)	0.5
Cold ischemia time (min)	644 ± 195	689 ± 189	0.3
Warm ischemia time (min)	44 ± 10	40 ± 8	0.06
Organ appearance (healthy/suboptimal)	55/8	25/3	0.9
PRBCs (U) (given within 3 days after the operation)	8.3 ± 10	5.6 ± 3	0.07
Graft condition			
Inotropes, No. (%)	31 (49%)	17 (61%)	0.2
ITU stay (days)	5.8 ± 11	8 ± 15	0.7
Total hospital stay (days)	29 ± 13	26 ± 15	0.4

Table 1. Patients' characteristics and operative parameters.

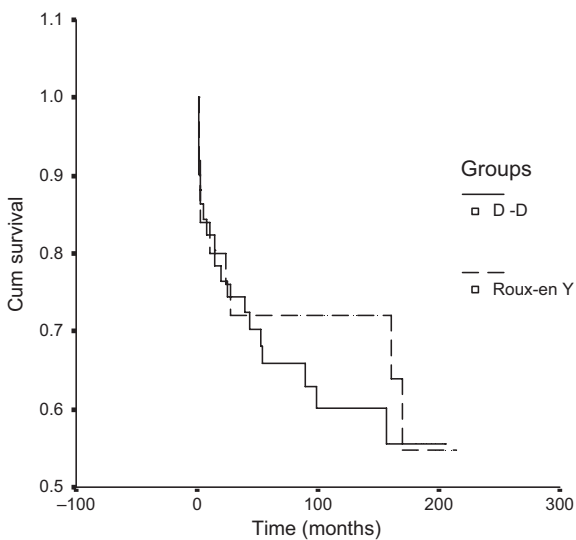


Figure 1 Survival for patients who had D-D biliary reconstruction (11 years) versus patients who had a Roux-en-Y anastomosis (13 years) ($P = 0.6$).

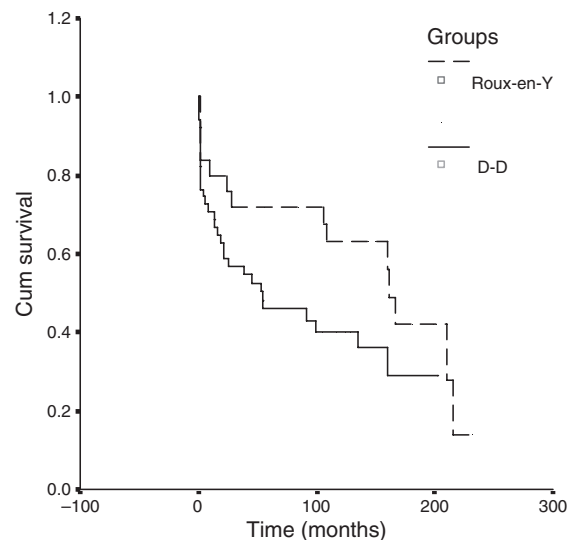


Figure 2 Graft survival for patients who had D-D biliary reconstruction (11 years) versus patients who had a Roux-en-Y anastomosis (10 years) ($P = 0.2$).

the percentage of those who had septicemia and multi-organ failure as the cause of their death was similar in both groups (Table 3).

Eleven (18%) and six (21%) patients with biliary complications were identified in the D-D and Roux-en-Y group, respectively. Biliary leak complicated a total of nine patients; five patients (8%) from the D-D group and four (14%) from the Roux-en-Y group ($P = 0.08$), whereas eight patients had biliary strictures; 6 (10%) vs. 2 (7%) patients from the D-D and Roux-en-Y group, respectively ($P = 0.9$). All biliary strictures were anastomotic (Table 4).

T-tube insertion in the D-D patients ($n = 22$) resulted in a 9% biliary complication rate (2 leaks, no

strictures), whereas patients who did not have a T-tube ($n = 41$) had a 22% complication rate (3 leaks, 6 strictures). Although stricture rate was higher in the nonstented patients, there was no statistical significance detected ($P = 0.3$).

Management of bile leak in the D-D group was through operative T-tube insertion, conversion to Roux-en-Y, and radiologic stent insertion in one, two, and one patient, respectively. However, two patients from the Roux-en-Y group had a stent inserted operatively, and two had a stent inserted radiologically. All cases of biliary strictures that occurred in Roux-en-Y patients ($n = 2$) were managed by refashioning of anastomosis. In the

Table 2. Causes of graft failure.

	D-D No. (%)	Roux-en-Y No. (%)
Graft failure	20 (32)	9 (32)
Time to graft failure (days)	857 ± 1242	978 ± 1714
Causes of graft failure		
Chronic rejection	5 (26)	2 (20)
Primary non-function	2 (11)	1 (10)
Acute vascular occlusion	4 (21)	2 (20)
Non-thrombotic infarction	1 (5)	0
Ductopenic rejection	3 (16)	0
Recurrent disease	0	2 (20)
Biliary complications	3 (16)	2 (20)
Other	2 (11)	0
Unknown	1 (5)	0
Re-transplantation	12 (19)	4 (14)

Table 3. Causes of death over the entire study follow-up period.

	D-D No. (%)	Roux-en-Y No. (%)
Causes of mortality		
Multi-organ failure	6 (29)	1 (11)
CVA	0	2 (22)
Liver failure	1 (5)	0
Hemorrhage	4 (19)	1 (11)
Sudden unexplained cardiac death	2 (10)	0
Septicemia	2 (10)	1 (11)
Recurrent cholangiocarcinoma	1 (5)	2 (22)
Recurrent PSC	0	2 (22)
Lymphoid malignancy induced by immunosup	2 (10)	0
Non-lymphoid malignancy induced by immunosup	1 (5)	0
Non-lymphoid malignancy not induced by immunosup	2 (10)	0

Table 4. Postoperative complications.

	D-D No. (%)	Roux-en-Y No. (%)	P value
Biliary leak	5 (8)	4 (14)	0.08
Biliary stricture	6 (10)	2 (7)	0.9
Hepatic artery thrombosis	2 (3)	3 (11)	
Portal vein thrombosis	3 (5)	0	
Hemorrhage	9 (14.5)	7 (25)	
Chest infection	15 (24)	8 (29)	
Bacteraemia	8 (13)	5 (18)	
UTI	3 (5)	1 (4)	
Abdominal infection	9 (15)	4 (14)	
Wound infection	9 (15)	2 (7)	
CMV infection	10 (16)	6 (21)	

D-D group, three patients had balloon dilatation, two had their anastomosis converted into a Roux-en-Y loop, and one patient had a stent inserted radiologically.

Other complications included the following: hepatic artery thrombosis that complicated two transplantations from the D-D group and ended in graft failure and re-transplantation. While three patients from the Roux-en-Y group had hepatic artery thrombosis, one of them died because of massive hemorrhage, and the other two had graft failure and re-transplantation. Portal vein thrombosis occurred in three patients from the D-D group, of whom two had graft failure, one was managed by retransplantation, whereas the other one died as a result of multi-organ failure. The rest of complications are listed in Table 4.

The rate of biliary-related graft failure and biliary-related deaths did not significantly differ between the two groups. In the D-D group, three graft failed because of biliary complications (two leaks and one stricture) and one patient died after a bile leak that led to disseminated septicemia and multisystem failure. In the Roux-en-Y group, two grafts failed following bile leak. One patient died after a bile leak-induced septicemia.

There was no significant difference in the length of ITU and hospital stay between the two groups: 5.8 ± 11 and 29 ± 13 days for the D-D group and 8 ± 15 and 26 ± 15 days for the Roux-en-Y group, respectively. Post-operative mortality was also comparable between the two groups, where three patients (4.7%) from the D-D group and one patient (3.5%) from the Roux-en-Y group died within 30 days following the operation.

Disease recurrence rates were similar between both groups. Three patients (4.8%) from the D-D group and three patients (10.7%) from the Roux-en-Y group had disease recurrence after a mean time of 6 and 7 years, respectively ($P = 0.37$). Similarly, the rate of re-transplantation did not significantly differ between the two groups, where 12 (19%) and 4 (14%) from the D-D and the Roux-en-Y group had re-transplantation, respectively (0.07). Post-OLT cholangiocarcinoma occurred in two patients from the Roux-en-Y group (one patient was diagnosed with it preoperatively and the other one was found on the explant histopathology after the transplantation) after a mean time of 24 months, and in one patient from the D-D group (who was found to have a small focus on the explants histopathology) after a mean time of 8 months. All three patients who developed cholangiocarcinoma eventually died within a mean time of 9 months from the development of cholangiocarcinoma. None of the patients in both groups developed cholangiocarcinoma in the remnant duct following OLT in our series.

Discussion

We present what we believe is the largest series of a single institution, and this follows on our previous report

published in 1996 [7], where D-D reconstruction was pioneered for selected patients as a safe alternative method of biliary reconstruction in OLT for PSC patients.

A D-D reconstruction for PSC patients following OLT has been previously criticized for claims that it increases the risk of stricture formation and lowers the rates of patient and graft survival, when compared with a Roux-en-Y approach [6]. Our report clearly demonstrates comparable results between D-D and Roux-en-Y reconstruction in terms of biliary complications rates, disease recurrence, and long-term patient and graft survival.

There was no significant difference in the rate of biliary complications, strictures, and leaks, between the two groups, and of note, the management of stricture following D-D anastomosis was accomplished conservatively in most of the cases, whereas reoperation was necessary for managing strictures in the Roux-en-Y group. The rate of cholangitis because of reflux of bowel content into the biliary system was difficult to assess in the Roux-en-Y group, as the signs and symptoms were non-specific and could be attributed to disease recurrence or anastomotic strictures, and thus it was difficult to assess this using patients records.

As for survival, there was no statistical difference in graft and patient survival rates between the two groups. In addition, initial patient and graft survival rates were higher in the D-D group; this has changed on the long-term where 5 and 10 years survival became slightly, but not significantly, higher in the Roux-en-Y group. Having comparable long-term graft survival indicates that the difference noted in patient survival is attributed to factors other than graft failure in the D-D group. This difference cannot be attributed to cholangitis caused by disease recurrence, as the percentage of sepsis-related deaths and the percentage of patients dying with functioning grafts are similar between the two groups. In this study, we report an overall 1- and 5 years patient survival of 85% and 70%, respectively, and a corresponding graft survival of 71% and 51%, respectively, which is slightly lower than survival rates reported in other studies [4,5]. Possibly more patients with incidental cholangiocarcinoma were identified post transplantation in this series compared with others, lowering patient and graft survival. Another factor can be put down to a long study period, where initially, overall and graft survival rates were relatively lower than in recent years that is characterized by better surgeons' experience and improved patients care.

The rate of graft failure and death attributed to biliary complications was similar in both groups. Of note, biliary leak had a detrimental impact on patient and graft survival and was observed more in the Roux-en-Y group.

Recurrence rates were comparable between the two groups and similar to other reported series [3,4]. In cases with recurrent PSC, all strictures were non-anastomotic

strictures. Furthermore, no cholangiocarcinoma developed de novo in the D-D group following OLT.

In conclusion, D-D biliary reconstruction in OLT for selected PSC patients is safe and remains our first option of reconstruction when compared with Roux-en-Y biliary reconstruction; however, this warrants a randomized controlled trial to compare these two reconstruction methods.

Authorship

OD: designed and performed the study, collected and analyzed the data and wrote the paper. DS, AB, NR, BF, BD, KR: responsible for critical review.

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