Is Duct to Duct biliary Anastomosis the Rule in Orthotopic Liver Transplantation?

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Abstract Biliary complications after Liver Transplantation continue to be the major cause of morbidity in 11–25 % of patients. Biliary complications in patients who underwent orthotopic liver transplantation (OLT) at our institute between March 2007 and June 2010 were analyzed retrospectively. 32 patients underwent Deceased Donor Liver Transplantation (DDLT) and in 12 patients Living Donor Liver Transplantation (LDLT) was done. No patients were lost to follow up. Follow up ranged between 4 and 44 months. During the study period, 44 patients underwent orthotopic liver transplantation. Patients were divided into two groups: Biliary Complications group (BC) $n=5$ and Non Biliary Complications group (NBC) $n=39$. Biliary complications occurred in 15.9 % of patients. Bile leaks accounted for majority of biliary complications. Fifteen variables were analyzed as possible risk factors for biliary complications. Of these, split grafts, duct to duct biliary anastomosis and total blood loss were statistically significant ($P<0.05$) for biliary complications. Endoscopic treatment was successful in managing biliary complications in 75 % of patients. Biliary complications are the most common major complications in orthotopic liver transplantation. Significant risk factors are split liver grafts and duct to duct biliary anastomosis. Increased blood loss is a predictor for post operative biliary complications. These complications should be managed by endoscopic interventions. Surgery is indicated following failure of endoscopic interventions.

Keywords Liver transplantation · Biliary complications · Split grafts · Blood loss · Duct to duct anastomosis

Introduction

Biliary complications in liver transplantation have remained a major cause of morbidity and occur in approximately 10–15 % of patients. The most common biliary complications following liver transplantations are leaks and strictures. Nearly 70 % of all biliary complications occur within the first 3 months after orthotopic liver transplantation (OLT). Many factors may be responsible for the biliary complications which include the type of liver graft, duct-to-duct anastomosis, multiple bile ducts, etc. The management of biliary complications after OLT requires a multidisciplinary approach. Endoscopic as well as percutaneous management of these complications is attractive options in majority of cases. Surgery is usually contemplated after failure of endoscopic interventions.

Materials and Methods

Between March 2007 and June 2010, 44 consecutive liver transplantations done at our institute by the same transplant team were studied retrospectively. A total of 32 patients underwent deceased donor liver transplantation (DDLT) of which 2 patients received “in situ” split liver graft and 14 patients underwent living donor liver transplantation (LDLT). Standardized protocols for patient selection, surgical technique, preoperative, and postoperative care were followed. Bile duct edges were freshened till brisk bleeding was noted before the anastomosis. Biliary anastomosis was performed using 6 “0” PDS continuous suture using 3.5×

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Table 1 Stratification of data

1	Total cases	44
2	Total mortality	12
3	Patients under follow up	32
4	Patients with biliary complications	05
5	Number of leaks	04
6	Number of strictures	02
7	Number of stones	01

loupes. Tension as well as redundancy of the bile duct was avoided in duct-to-duct anastomosis. No biliary stents were used. Roux-en-Y hepaticojejunostomy (RYHJ) was performed in patients where recipient bile duct was not available. Abdominal drains were placed routinely.

Patients were classified into two groups—biliary complication (BC) group composed of patients who developed biliary complications in the immediate as well as late post-operative period and the rest as nonbiliary complication (NBC) group. The patients of both groups were followed up as per the protocol. The study population included patients from both sexes with end-stage liver disease due to varying etiology. Age varied between 14 months to 62 years. During follow-up, apart from routine biochemical parameters, all patients underwent ultrasound scan (USS) and Doppler examination daily for the first 7 days, weekly for the first 3 months after discharge from hospital, monthly for the next 3 months, and 3 monthly thereafter to assess the biliary and vascular anastomosis as well as to detect any intra-abdominal collections.

Fourteen variables were analyzed as possible risk factors for biliary complications. Significance of difference in means for quantitative variables was analyzed with Student's *t*-test (Table 1). The significance of difference for descriptive variables was calculated using Fisher's exact test. $P < 0.05$ was considered significant (Fig. 1).

Table 2 Tests of significance of qualitative variables

No	Variables	BC	NBC	P (fisher exact test 2 ailed)
1	Arterial abnormalities	1	18	0.374
2	Partial grafts	4	10	0.029
3	Roux-en-Y Biliary Anastomosis	1	9	0.021
4	Acute Rejections	0	6	0.596
5	Females: Males	1:4	6:33	1.000
6	Mortality	1	11	0.659
7	Multiple bile ducts	0	3	1.000

Results

A total of 44 patients underwent liver transplantation which included 32 DDLT and 12 LDLT, 36 males and 8 females with the mean age of 30.1 years. Of these 10 patients underwent Roux-en-Y hepaticojejunostomy (RYHJ) and 34 patients had duct-to-duct (DD) biliary anastomosis. The follow-up ranged from 4 months to 44 months. Median follow-up was 19 months. We had 100 % follow-up of the patients. Overall mortality was 18.1 % ($n=8$). Only one death was attributable to biliary complication. Incidence of biliary complications was 15.9 % (Table 2). Seven biliary complications occurred in 5 patients (Table 3)

Bile Leaks ($n=4$)

Leaks were the commonest complications. In the BC group, there were four leaks (57.1 %) and three of them occurred in split grafts; 2 occurred in LDLT and 1 occurred in a patient with “in situ” split right lobe graft (one RYHJ and two DD anastomoses). Only one bile leak occurred in DDLT with whole liver graft (DD anastomosis).

Fig. 1 Indications for transplantations

Table 3 Tests of significance of quantitative variables

No	Parameters	BC group	NBC Group	P value (student t test)
1	Mean Age	28.5 yrs	31.7 yrs	0.659
2	Mean CTP	10.80	9.64	0.819
3	Mean MELD	20.42	16.46	0.113
4	Mean CIT	291 min	317 min	0.153
5	Mean WIT	80 min	72 min	0.405
6	Mean Operation Time	558 min	545 min	0.819
7	Mean Blood loss	4780 ml	2604 ml	0.031
8	Mean Graft wt	830 gms	1074 gm	0.199

Anastomotic Strictures ($n=2$)

Two patients developed biliary strictures (28.5 %). Both these patients received partial grafts from the “in situ” split of the deceased donor liver (right lobe and left lateral lobe split grafts).

Sludge and Stone ($n=1$)

Sludge and stone occurred in one patient accounting for 14.2 % of biliary complications. Ultrasonogram (USG) and magnetic resonance cholangiopancreatogram (MRCP) revealed distal bile duct stone with sludge. It was successfully managed by endoscopic retrograde cholangiopancreatogram (ERCP) and bile duct clearance.

Results of Risk Factors Analysis

There were 19 arterial abnormalities in our series. Arterial abnormalities studied included multiple arterial anastomoses, arterial anastomoses done more than twice, early hepatic artery thrombosis (HAT) and late HAT. There was one biliary complication in the arterial abnormality group which occurred due to late HAT. This variable was not statistically significant.

Table 4 Description of patients

Patient	Biliary Anastomosis	Graft type	Complications
1	REY	Partial	Bile Leak
2	D-D	Partial	Bile Leak
3	D-D	Full	Bile Leak + HAT
4	D-D followed by REY	Partial	Bile Leak followed by stricture followed by secondary biliary cirrhosis
5	D-D	Partial	Biliary stricture

There were 14 split grafts in this study including 12 LDLT and 2 “in situ” split grafts. In this group, 4 patients had total of five (57 %) biliary complications. Of 30 patients who underwent DDLT with whole liver grafts, only 1 patient had two biliary complications in the form of biliary leak and later biliary calculi and sludge. Transplantation with split grafts emerged as a statistically significant variable for biliary complications in our series. On analysis of the type of biliary anastomosis as a risk factor, four biliary complications occurred in the DD group ($n=34$) versus one in RYHJ ($n=10$). Duct-to-duct biliary anastomosis was a significant risk factor (Table 1).

Three patients in the NBC group had multiple biliary anastomoses and none in the BC group. Multiple bile ducts for anastomosis were however not statistically significant. Of the seven quantitative variables analyzed, only blood loss was a significant factor in predicting biliary complications. Mean blood loss in the BC group was 4,800 ml, and in the NBC group it was 2,600 ml. This difference was statistically significant between the two groups. Of other variables analyzed, cold ischemia time, warm ischemia time, graft weight and recipient age were not found to be significant between two groups (Fig. 1).

Discussion

Biliary complications (BC) are the “Achilles heel” of liver transplantation. The worldwide incidence is 11–25 % [1]. In our series it was 15.9 %. BC increases morbidities such as delayed postoperative recovery, prolonged hospitalization, delayed graft failure, retransplantation, and rarely death of the patient [2]. LDLT resulting in split grafts formed 30 % of patients in our series. LDLT is technically challenging because of variable biliary anatomy. In addition a complication that is distinctive to split grafts is bile leakage from the cut surface [3]. Various authors have used different strategies with the underlying principle of obtaining a single healthy vascularized right duct in right lobe grafts. The importance of an adequately vascularized duct cannot be overemphasized [4] (Tables 4 and 5).

The bile duct and its branches are supplied by a rich network of small vessels that form a plexus over the bile duct [5]. The feeding arteries to the plexus are from the right and left hepatic arteries from the top and the gastroduodenal artery from the bottom. Hence, it is important to freshen the donor stump as short as possible to maintain adequate blood supply

Table 5 Management modalities in our series

Management	Number	Success rate
ERCP	Leaks-4	75 %
	Stones-1	100 %
Surgery	Leak-1	0 %

[6]. The high hilar dissection technique in the recipient hepatectomy ensures preservation of the blood supply [2, 7, 8].

Multiple ducts especially in right lobe grafts can be technically demanding. The single right duct is identified in only 50 % of donors [8]. Some studies have indicated that multiple bile ducts in the graft are strongly correlated with a high risk of biliary complications [9]. However, multiple bile ducts did not show any increase of BCs in our study. This is possibly because of low sample size in our study [10]. Among 3 patients with multiple bile ducts, none had BCs, whereas in 41 patients with a single bile duct, BCs occurred in 5 patients. Dissection between the bile duct and the hepatic artery is kept minimal to prevent the disruption of the ductal vascularity.

In our series, incidence of biliary complications was significantly more in DD anastomosis (80 %) when compared to RYHJ (20 %). It is well documented that DD anastomosis is more prone to ischemia when compared to RYHJ as both donor as well as recipient bile ducts are at risk of ischemia. In RYHJ the jejunum is well vascularized and offers collateral supply to the anastomosis. However, DD has several advantages over RYHJ. DD allows easier access for endoscopic interventions of the biliary tract. Also, the incidence of bacteremia associated with biliary complications was significantly lower in the DD than in the RYHJ, possibly due to increased reflux in the RYHJ group. Therefore, DD is our technique of choice for biliary reconstruction. Technical errors contribute to complications in the DD group as reported in literature [11]. This includes handling of the bile duct ends, ensuring brisk bleeding from the ends before anastomosis, and avoiding tension as well as redundancy at the anastomosis.

There is no literature review available for intra-operative blood loss as the significant factor for biliary complications after liver transplantation. Our study has revealed that blood loss of more than 2.5 liters is significant for biliary complications after liver transplantation. Prolonged cold ischemia time (CIT) and warm ischemia time (WIT) have also been found to be responsible for biliary complications [12]. It was not found to be significant in our study. This is probably because the CIT was uniformly kept short in most of our patients (mean of 300 min) which was possible because the retrieval of donor organs and transplantation were carried out in the same center. Graft weight (GW) was also not found to be of any significance in the split graft (SG) group as we ensured a graft weight of 1 % and more in all our patients [13].

Management of Biliary Complications

(1) Management of Leaks

The appropriate therapy for bile leak depends on the clinical presentation, the location of the leak, and the presence of hepatic artery thrombosis. Bile leak is usually

obvious when abdominal drains are in situ. Unfortunately three of the four bile leaks in our series were diagnosed in the third postoperative week after the drain removal. Routine USS detects most of these biliomas. The preferred treatment is USS or CT-guided percutaneous drainage as these leaks usually close spontaneously. In cases of persistent leak, treatment of choice is ERCP with placement of a plastic stent [13]. Of the four bile leaks in our study, all except one underwent ERCP and stenting. Surgery is reserved for endoscopic failure or when bile leak causes generalized peritonitis [14]. None of our patients needed urgent laparotomy. One patient with anastomotic leak in our series underwent revision of DD to RYHJ. In case of a leak from an RYHJ, the anastomosis should be taken down and the hepatic duct shortened to the level of brisk capillary bleeding before performing the new RYHJ. Attempts to place additional stitches in the primary anastomosis will increase the size of the fistula, with a consequent persistent bile leak.

(2) Management of Strictures

Endoscopic or percutaneous balloon dilatation should be the first choice in the treatment of anastomotic biliary stricture after OLT [15]. Of the two biliary strictures in our series, one is awaiting endoscopic dilation while the other had a failed attempt of endoscopic dilatation of RYHJ through the access loop. Success of the percutaneous techniques with low morbidity and mortality has been demonstrated even in small size recipients with nondilated intrahepatic bile ducts in literature [16]. Surgical treatment of strictures after OLT is technically difficult and has the risk of damaging the hepatic artery. In our series one patient is waiting for retransplantation for failed surgical as well as endoscopic attempts to address the RYHJ stricture.

Conclusion

Liver transplantation is at present the only modality of treatment for end-stage liver disease. Despite advances in surgical techniques and better understanding, biliary complications continue to cause prolonged morbidity and graft loss in the recipients. BC is significantly more in recipients with split grafts and in patients with DD biliary anastomosis. Increased blood loss during surgery is a significant factor for BCs. Most of the biliary complications can be managed endoscopically with surgical intervention reserved for failed endoscopy.

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