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Vito Distante
Marwan Farouk
Tomasz R. Kurzawinski
Sayed W. Ahmed
Andrew K. Burroughs
Brian R. Davidson
Keith Rolles

Duct-to-duct biliary reconstruction following liver transplantation for primary sclerosing cholangitis

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V. Distante · M. Farouk (✉) ·
T. R. Kurzawinski
S.W. Ahmed · A. K. Burroughs ·
B. R. Davidson
K. Rolles
University Department of Surgery,
Hepatobiliary and Liver Transplant Unit
and School of Medicine,
Royal Free Hospital,
Pond Street, Hampstead,
London NW3 2QG, UK
Fax: + 44 171 830 2198

Abstract The biliary complications in patients undergoing biliary reconstruction by duct-to-duct (D-D) anastomosis or with a Roux-en-Y loop (RL) at the time of liver transplantation for primary sclerosing cholangitis (PSC, 16 D-D, 10 RL) or primary biliary cirrhosis (PBC, 31 D-D, 1 RL) were reviewed and compared. Patients were followed up for a mean period of 32 months. Extrahepatic biliary strictures occurred in 18.7 %, 10 % and 9.7 % of DD-PSC, RL-PSC and DD-PBC patients, respectively, leaks in 6.2 %, 20 % and 6.4 % DD-PSC, RL-PSC and DD-PBC patients, respectively (P = NS). Four intrahepatic biliary abnormalities developed in the PSC group. Duct-to-duct anastomosis did not significantly increase the risk of stricture formation or bile leaks in PSC patients compared to PBC patients. We conclude that duct-to-duct biliary reconstruction following liver transplantation for PSC is satisfactory unless the distal common bile duct is strictured.

Key words Liver transplantation, biliary reconstruction, sclerosing cholangitis · Biliary reconstruction, sclerosing cholangitis · Primary sclerosing cholangitis, biliary reconstruction

Introduction

Biliary complications following orthotopic liver transplantation (OLT) are a major cause of morbidity [1, 2, 3, 5, 7, 8, 16, 18, 24, 26]. Possible aetiological factors include technical errors, ischaemia, infection and chronic rejection. Biliary duct ischaemia and other aetiologic factors such as ABO incompatibility, ductopenic rejection and prolongation of cold ischaemia time may play a role in postoperative stricture formation and anastomotic leaks. Finally, speculation and some evidence suggest that the primary hepatic disease may play a role in the development of biliary complications after OLT [9, 12, 15]. Liver transplantation patients with primary sclerosing cholangitis (PSC) usually undergo biliary-enteric rather than duct-to-duct (D-D) anastomosis because of anxiety of possible disease progression in the recipient common bile duct (CBD), resulting in stricture formation or even cholangiocarcinoma. Most of these patients only have evidence of intrahepatic disease on radiological assessment [27].

Cholangiocarcinoma in the CBD remnant after transplantation has not been described. We report the results of direct D-D anastomosis in PSC patients undergoing OLT and compare complications to those with primary biliary cirrhosis (PBC).

Patients and methods

From November 1988 to January 1994, 207 liver transplants were performed, 28 of which were for PSC and 36 for PBC. The median age of the PSC and PBC patients was 36 (range 17–63) years and 55 (range 30–69) years, respectively. The ratios male/female were 19/9 and 4/32 in the two groups, respectively. The median cold ischaemic times were 10.8 (range 4.5–16.8) hours and 12.5 (range 7.2–20.6) hours, respectively.

Four patients from the PBC group and two patients from the PSC group were excluded from this study because they died in the

immediate postoperative period (within 2 weeks) or peroperatively (one patient).

Orthotopic transplantation was performed in the standard fashion and the preferred form of biliary reconstruction was duct-to-duct (D-D) anastomosis. Ten PSC patients underwent biliary-enteric anastomosis because of insufficient bile duct length ($n = 4$), or on the grounds of stricturing seen on pretransplant radiological assessment ($n = 6$). The remaining 16 patients in the PSC group underwent D-D reconstruction. In the PBC group, only one patient had a biliary-enteric anastomosis. Anastomosis was performed using interrupted 5/0 PDS suture in both D-D anastomosis and biliary-enteric reconstruction. Biliary-enteric reconstruction was by a long unsplinted Roux-en-Y loop.

At the beginning of the programme T-tube splintage was used in five PBC patients and one PSC patient. This was later abandoned as it did not confer benefit in terms of postoperative biliary complications [19]. ABO-identical or -compatible donors were always used.

Protocol endoscopic retrograde cholangio-pancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) as well as technicium-labelled iminoacetic acid (HIDA) scan were performed between 2 and 3 weeks post-OLT to visualise the intra- and extrahepatic biliary tracts and to identify stricturing or anastomotic leaks. Rejection episodes were treated with 1 g methylprednisolone on 3 successive days. If rejection persisted after two cycles of steroid therapy, OKT3 monoclonal antibodies were used for 5 days.

The median follow-up period was 32 months (range 12–78 months) for both groups. All complications in liver transplant patients were recorded prospectively in our transplant database and these records were analysed retrospectively to identify biliary complications. All biliary contrast studies and HIDA scans were also re-examined in each of these patients. A biliary complication was defined as radiological evidence of stricture or leak that required surgical or endoscopic intervention. All patients with biliary complications were assessed by selective visceral angiography.

Fischer's exact test was used for comparing categorical variables.

Table 1 Biliary complications according to type of biliary anastomosis in patients following liver transplantation for primary sclerosing cholangitis *(PSC)* and primary biliary cirrhosis *(PBC)*. (*DD* duct-to-duct, *RL* Roux-en-Y loop)

Patients	Biliary anastomosis	Stricture	Leaks	Total
26 PSC	16 DD	3 (18.7 %)	1 (6.2 %)	4 (25.0 %)
	10 RL	1 (10.0 %)	2 (20.0 %)	3 (30.0 %)
32 PBC	31 DD	3 (9.7 %)	2 (6.4 %)	5 (16.1 %)
	1 RL	–	–	–

Table 2 Site and treatment of biliary complications in primary biliary cirrhosis in patients following liver transplantation (*DD* duct-to-duct, *RL* Roux-en-Y loop)

Age (years)/ Sex	Complication	Anastomosis	Site	Treatment	Day diagnosed
55/F	Stricture	D-D	Anastomosis	Balloon dilatation + RL reconstruction	23
53/M	Stricture	D-D	Anastomosis	Balloon dilatation	20
49/F	Stricture	D-D	Donor	Balloon dilatation + RL reconstruction	299
64/F	Leak	D-D	Anastomosis	Stent + surgical repair	62
56/F	Leak	D-D	Anastomosis	RL reconstruction	33

Results

Twelve patients with biliary complications were identified. Seven of these patients were in the PSC group and five in the PBC group, yielding an incidence of 26.9 % and 15.6 %, respectively ($P = 0.8$ on comparison of the two groups). The median time interval during which biliary complications developed was 76 days (range 14–298 days) for PSC patients and 87 days (range 20–299 days) for PBC patients. The types of biliary complication for each group of patients are recorded in Table 1.

Extrahepatic strictures associated with radiological (ERCP or PTC) and biochemical evidence of cholestasis were the most common biliary complications and occurred in a total of five patients (Tables 2, 3). In patients with D-D anastomosis biliary strictures were situated in four cases at the level of the anastomosis (two PSC and two PBC) and in two cases in the donor common duct (one PSC and one PBC). The single PBC patient with a primary biliary-enteric anastomosis also had an anastomotic stricture.

ERCP and PTC detected a total of five anastomotic bile leaks: three occurred in PSC patients and two in PBC patients. Three of these had a D-D anastomosis and two had a biliary-enteric anastomosis (Tables 1–3).

HIDA scans identified the presence of five biliary strictures and three biliary leaks. Hence HIDA scanning failed to detect two of the five biliary leaks seen on cholangiography. In addition, HIDA suggested the presence of two additional strictures by detecting delayed excretion of the isotope from the transplanted organ. This investigation did not identify the site of the stricture in either of these cases, and neither of these patients required surgical intervention or stent placement.

In the PSC group, four patients (15.4 %) developed intrahepatic biliary abnormalities. Two of these had synchronous anastomotic strictures. Two of the more severe intrahepatic biliary abnormalities had features similar to the original disease in the form of segmental intrahepatic strictures but this could not be distinguished from chronic rejection on histology.

Table 3 Site and treatment of biliary complications in primary sclerosing cholangitis patients following liver transplantation (*DD* duct-to-duct, *RL* Roux-en-Y loop)

Age (years)/ Sex	Compli- cation	Anasto- mosis	Site	Treatment	Day diagnosed
22/F	Stricture	D-D	Anasto- mosis	Balloon dilatation + retrans- plantation	21
17/M	Stricture	D-D	Donor	Balloon dilatation + retrans- plantation	103
20/F	Stricture	RL	Anasto- mosis	Surgical revision	238
37/M	Stricture	D-D	Anasto- mosis	RL recon- struction	53
20/M	Leak	RL	Anasto- mosis	RL recon- struction	24
56/F	Leak	RL	Anasto- mosis	Stent	15
22/M	Leak	D-D	Anasto- mosis	Stent and RL reconstruc- tion	14

Nine of the twelve biliary complications required surgical repair. Five of the six strictures that occurred following D-D anastomosis were initially treated by balloon dilatation (8- to 10-mm balloon at 10–12 atmospheres) and nasobiliary drainage. This mode of treatment was only successful in one patient. The treatment of the five bile leaks consisted of three conversions to a biliary-enteric anastomosis, one T-tube insertion, and one patient required percutaneous stenting (Tables 2, 3).

The aetiology of the complications was not always detected. Hepatic artery thrombosis was responsible for one of the early leaks, but ischaemic arterial occlusion was not seen in any of the other patients who developed biliary strictures who were investigated by Doppler ultrasound scanning and/or coeliac angiography. Three patients, one with an extrahepatic stricture and two with intra- and extrahepatic strictures, had biopsy-proven chronic rejection associated with ductopenia. The latter two patients with multiple strictures were known to suffer from biliary sepsis.

Biliary strictures occurred in four (14.8%) of the grafts with a cold ischaemic time of 12 h or less and in three (9.7%) of the organs with a cold ischaemic time of more than 12 h ($P > 0.05$).

There were two deaths related to biliary tract complications, one from each group. The first developed a biliary leak that was repaired by biliary reconstruction and drainage. This patient died 16 days later because of severe haemorrhage secondary to erosion of a transhepatic biliary drain into the portal system. The second patient died from recurrent biliary sepsis following reconstruction for a biliary leak.

Discussion

The aetiology of biliary complications after liver transplantation can usually be traced to vascular, technical or immunological problems [13, 14, 17, 25]. Some evidence suggests that the type of liver disease before transplantation may predispose the patient to the development of biliary strictures [9, 12, 15]. Recurrent non-malignant biliary tract disease in the allograft is exceptional. In a single case report intrahepatic recurrence of sclerosing cholangitis in a patient 1 year after transplantation in the absence of graft rejection was suggested on the basis of serial biopsy changes consistent with recurrent sclerosing cholangitis. This report was, however, subsequently retracted when the whole organ was re-examined at the time of retransplantation [4]. No definite evidence of recurrent extrahepatic disease exists to our knowledge. Notwithstanding this fact, PSC patients usually undergo a choledocho-enteric reconstruction to avoid anastomosis to a potentially diseased or strictured recipient duct remnant. The incidence of anastomotic biliary strictures has been reported to be similar in patients undergoing transplantation for PSC and other disease groups [7, 21, 23]. Sheng et al. compared the prevalence and types of biliary strictures in patients transplanted for PSC where biliary-enteric anastomosis had been performed with other types of end-stage liver disease [23]. They found no significant difference in biliary strictures at the level of the anastomosis. Similar results have been reported by other groups. The only exception is a report by Letourneau et al., who reported a sixfold increase in the incidence of anastomotic strictures in PSC patients with biliary-enteric drainage [10]. All of these strictures occurred in the early postoperative period and did not require surgical reconstruction but were treated by radiological intervention in the form of balloon dilatation. This mode of treatment was only of temporary benefit in our experience, and suggests that these strictures were of a lesser degree than those observed in our study where bile duct stricturing occurred at a later stage.

The overall biliary complication rate reported in this study after D-D anastomosis (19%) is similar to most published data [11, 20, 22]. The only exception is a more recent publication by Neuhaus et al., who report a very significant reduction in the incidence of these complications, particularly early anastomotic leakage, after using a side-to-side bile duct anastomosis [16]. We have subsequently addressed this problem by instituting

a randomised controlled trial in this institution comparing end to end and side-to-side anastomosis.

Intrahepatic biliary abnormalities only developed in the PSC group but recurrent primary disease could not be proven on biopsy as the histological features of chronic rejection and sclerosing cholangitis overlap to a considerable extent. In addition, other factors such as biliary sepsis and concurrent extrahepatic strictures were observed in these patients and may have played a contributing role. Sheng et al. have also demonstrated a similar higher incidence of intrahepatic biliary strictures in patients with PSC than in patients with other liver disease [23].

Cholangiography by ERCP or PTC remains the best investigation for identifying strictures and leaks. HIDA scanning was found to be accurate at diagnosing significant leaks but was less accurate at confirming the presence of stricture formation. HIDA scanning was found to be particularly useful in patients in whom a less invasive diagnostic procedure was required, in whom ERCP/PTC was unsuccessful, or in whom the degree of stricturing on ERCP was in some doubt and needed to be quantified.

Other authors have demonstrated that the development of biliary strictures is associated with the duration of cold ischaemic storage of allografts in both Euro-Collins solution and University of Wisconsin solution [6, 21, 22]. In our series cold preservation times were similar in both groups (PSC and PBC), suggesting that preservation damage was not a factor in stricture formation.

Although extrahepatic biliary strictures were more frequent in PSC patients in this study, these were not caused by recurrent disease in the duct remnant and were primarily of anastomotic origin. In our small series, biliary leaks were more common after biliary-enteric anastomosis than after D-D drainage and the cause of considerable morbidity. In addition, biliary leaks were the only cause of mortality attributable to biliary complications.

Although the prevalence of biliary complications was higher in the PSC group than in the PBC group in this study, this did not reach statistical significance, primarily because of the relatively small number of patients. The location of strictures at the anastomosis would suggest that they are unrelated to the primary disease, although this was not confirmed histologically.

In our opinion, provided pretransplant work-up has excluded distal common bile duct strictures, PSC patients can undergo a standard D-D anastomosis, thus allowing easier postoperative access to the biliary tree with no additional risk of morbidity or mortality compared to other types of biliary reconstruction.

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